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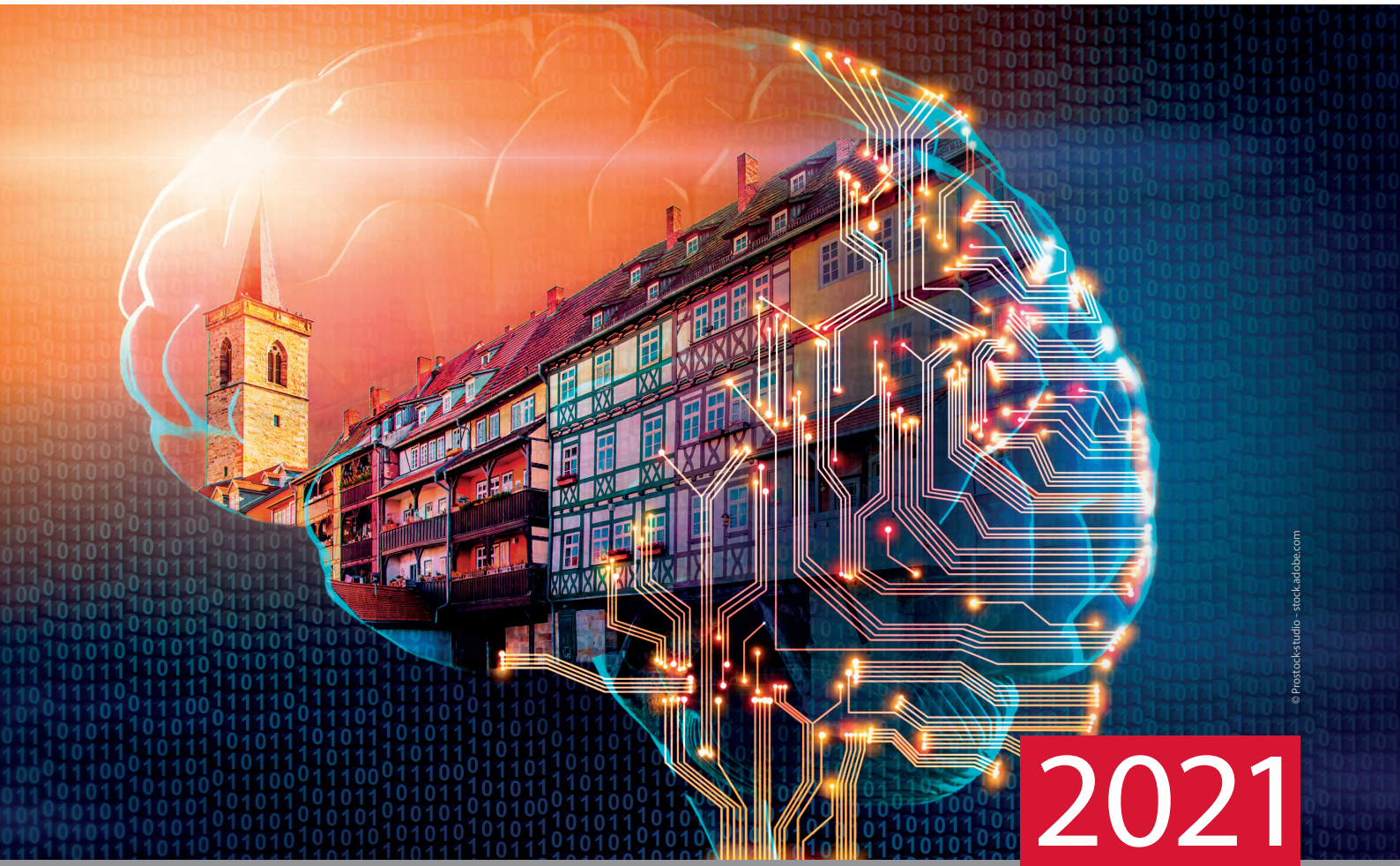
72. Jahrestagung

Deutsche Gesellschaft für Neurochirurgie



ABSTRACTS

2021
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Joint Meeting mit der Polnischen Gesellschaft für Neurochirurgie

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Inhalt

Neuroonkologie I/*Neurooncology I*

V001

18F-FET PET Bildgebung im Verlauf einer Immuntherapie mit DC Vakzinierung bei Glioblastom-Patienten
18F-FET PET imaging following immunotherapy with DC vaccination in glioblastoma patients

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Objective

In the ongoing phase-II GlioVax trial, patients with newly diagnosed glioblastoma are treated with DC vaccination as add-on to standard temozolomide chemoradiation after fluorescence-guided surgery. Due to the multimodal therapy including vaccination immunotherapy, the specificity of contrast-enhanced MRI to differentiate between tumor recurrence and treatment-related changes is low. We examined the diagnostic value of amino acid PET using O-(2-[18F]-Fluoroethyl)-L-Tyrosine (18F-FET) PET for this clinically important differentiation.

Methods

Patients enrolled in the GlioVax trial and with progressive MRI findings according to the RANO criteria underwent additional 18F-FET PET imaging. Treatment-related changes on 18F-FET PET were considered if the mean tumor-to-brain ratio was ≤ 2.0. Subsequently, MRI and 18F-FET PET findings were correlated with the clinicoradiological follow-up or neuropathological findings.

Results

Seventeen patients (n=10 vaccinated patients; n=7 control group, with temozolomide chemoradiation alone) received 23 additional 18F-FET PET scans (n=14 scans in vaccinated patients; n=9 scans in patients with standard therapy). In vaccinated patients, the median time between radiotherapy completion and progressive MRI was 6 months (range, 1-18 months). In contrast, in the control group, the median time to MRI progression was 2 months (range, 1-7 months).

In 8 18F-FET PET scans (performed in 4 vaccinated patients, and 4 patients with standard therapy) PET and MRI were congruent and indicated tumor progression. Further treatment of these patients: Vaccinated patients: 2 were referred to best supportive care, in two patients a re-resection was performed (NP diagnosis: 1: therapy induced changes; 1: recurrent tumor). Control group: one patient was referred to best supportive care, in 3 patients a re-resection was performed and tumor recurrence was confirmed.

In contrast to the corresponding MRI, findings of 15 18F-FET PET scans (performed in 10 vaccinated patients, and in 5 patients with standard therapy) were consistent with treatment-related changes and the patients remained stable for at least 3 months.

Conclusion

Following multimodal therapy including DC vaccination, treatment-related changes occurred more often and later than in patients undergoing standard therapy. Additional 18F-FET PET imaging is helpful to distinguish tumor progression from treatment-induced changes related to the applied multimodal therapy including DC vaccination.

Neuroonkologie I/*Neurooncology I*

V002

Chirurgische Behandlungsstrategie für spinale Metastasen
Comprehensive surgical treatment strategy for spinal metastases

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Objective

Based on a large consecutive single-center series of patients with spinal metastases (SM), we devised a comprehensive treatment algorithm for surgical strategies and adjunct therapies.

Methods

Between January 2007 and December 2018, patients with a SM were screened for study inclusion after an interdisciplinary neurooncological board meeting decided on the treatment plan. We report baseline characteristics, surgical procedures, complication rates, functional status and outcome of a consecutive cohort managed in accordance to a stratified treatment algorithm and adjunct therapy.

Results

667 consecutive patients underwent 989 operations for SMs at our institution. Mean age was 65 years (range 20 – 94), median preoperative KPS was 80. Most common primary entities were prostate (21.7%), breast (15.9%) and non-small cell lung cancer (10.0%). The thoracic spine was affected in 48.3% of cases, followed by the lumbar spine in 26.7%. We conducted posterior instrumentation with or without vertebral body replacement in a staged approach in 69.5%, sole decompression in 12.4% and vertebral body augmentation in 18.0% of cases. Follow up was available for 58.9% of patients. Median OS amounted to 18.4 months (95% CI 9.8 – 26.9), OS after 12 months was 56.0% and median KPS improved from 70 to 80 by discharge.

Conclusion

Surgical management of SMs should generally represent the first step of a conclusive treatment algorithm. The need to preserve long-term symptom control and biomechanical stability stems from the growing life expectancy of patients with SMs, and requires a staged invasive surgical strategy currently not supported by level I evidence.

Neuroonkologie I/*Neurooncology I*

V003

Assoziation der prä-operativ erfassten Gebrechlichkeit mit einer erhöhten post-operativen Morbidität und kürzeren Überlebenszeit bei geriatrischen Glioblastom Patienten

Frailty detected with the Geriatric 8 health status screening tool (G8) and Groningen Frailty Index (GFI) are associated with increased post-operative morbidity and shortened overall survival in geriatric patients with glioblastoma

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Objective

Glioblastoma is the most common primary malignant brain tumor in adults with dismal prognosis. Treatment of glioblastoma in elderly patients is particular challenging due to their general condition and comorbidities. In this study we aim to evaluate the impact of age and frailty on the surgical outcome and long-term survival in geriatric patients with glioblastoma.

Methods

Data acquisition was conducted as a single-center retrospective analysis. From 2015 to 2017 patients over 70 years of age presenting to our department with glioblastoma were included in our study. Demographic data, tumor size, Karnofsky Performance Index (KPI) and Eastern Cooperative Oncology Group Performance status (ECOG), as well as treatment modalities were documented. The Geriatric 8 health status screening tool (G8) and Groningen Frailty Index (GFI) were compiled pre- and postoperatively.

Results

50 consecutive patients were included in our study. The mean patient age was 76.86±4.11 years and 28 (56%) patients were female. 35 patients underwent microsurgical tumor resection,15 patients tumor biopsy, only. Frailty on admission was 5.0+-2.5 (GFI) and 12.4+-2.0 (G8), respectively. In our cohort, frailty was independent of patient age, tumor size or localization. Surgical decision making between biopsy or tumor resection was not based on preoperative frailty and did not correlate with it. Both, GFI and G8 were significant predictors of post-operative morbidity (GFI: r2=0.31, p

Conclusion

In this study, frailty proved to be a more accurate predictor for a poorer surgical outcome, the occurrence of postoperative complications and an impaired overall survival compared to age. Frailty screening tests offer an additional assessment tool to stratify geriatric patients with glioblastoma and identify those at risk for a detrimental outcome and should be considered for surgical decision making.

Neuroonkologie I/*Neurooncology I*

V004

Langzeit Überlebensdaten von 343 WHO Grad II/III Gliom Patienten eines neuroonkologischen Zentrums – Implikationen für Grading und Temozolomid Therapie

A 25-year retrospective, single-centre analysis of 343 WHO grade II/III glioma patients – implications for grading and temozolomide therapy

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Objective

Classification and treatment of WHO grade II/III gliomas have dramatically changed. Implementing molecular markers into the WHO classification raised discussions about the significance of grading and clinical trials showed overall survival (OS) benefits for combined radiochemotherapy. As molecularly stratified treatment data outside clinical trials are scarce, we conducted this retrospective study.

Methods

We identified 343 patients who had been treated in our neurooncologic center (1995-2015) with newly diagnosed WHO grade II/III gliomas and analyzed molecular markers, patient characteristics, symptoms, histology, treatment, time to treatment failure (TTF) and OS.

Results

IDH-status was available for all patients (259 mutant, 84 IDH1-R132H-non-mutant). Molecular subclassification was possible in 173 tumors, resulting in diagnosis of 80 astrocytomas and 93 oligodendrogliomas. WHO grading remained significant for OS in astrocytomas/IDH1-R132H-non-mutant gliomas ($p<0.01$) but not for oligodendroglioma ($p=0.27$, figure 1). Chemotherapy (and temozolomide (TMZ) in particular) showed inferior OS compared to radiotherapy (RT) in astrocytomas (median 6.1/12.1 years; $p=0.03$) and oligodendrogliomas (median 13.2/not reached (n.r.) years; $p=0.03$). While radiochemotherapy improved TTF in oligodendroglioma (median radiochemotherapy n.r./chemotherapy 3.8/radiotherapy 7.3 years; $p<0.001/=0.06$; OS data immature) the effect, mainly in combination with temozolomide, was weaker in astrocytomas (median radiochemotherapy 6.7/chemotherapy 2.3/radiotherapy 2.0 years; $p<0.001/=0.11$) and did not translate to improved OS (median 8.4 years, figure 2).

Conclusion

This is one of the largest retrospective, real-life datasets reporting treatment and outcome in low-grade gliomas incorporating molecular markers. Current histologic grading features remain prognostic in astrocytomas while being insignificant in oligodendroglioma with interfering treatment effects. Chemotherapy (temozolomide) was less effective than radiotherapy in both astrocytomas and oligodendrogliomas while radiochemotherapy showed the highest TTF in oligodendrogliomas.

Fig. 1

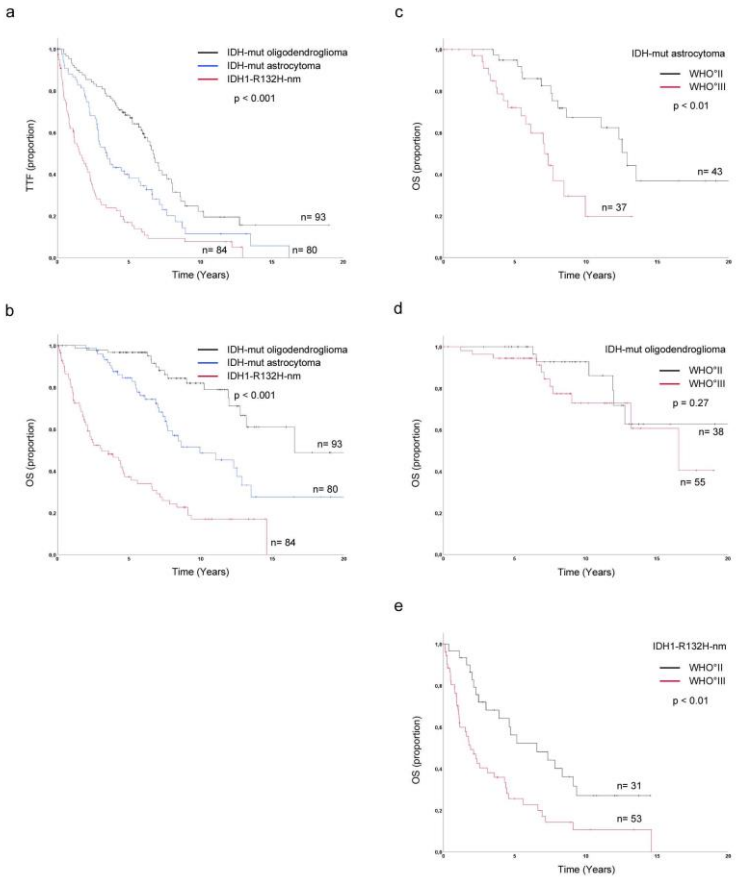
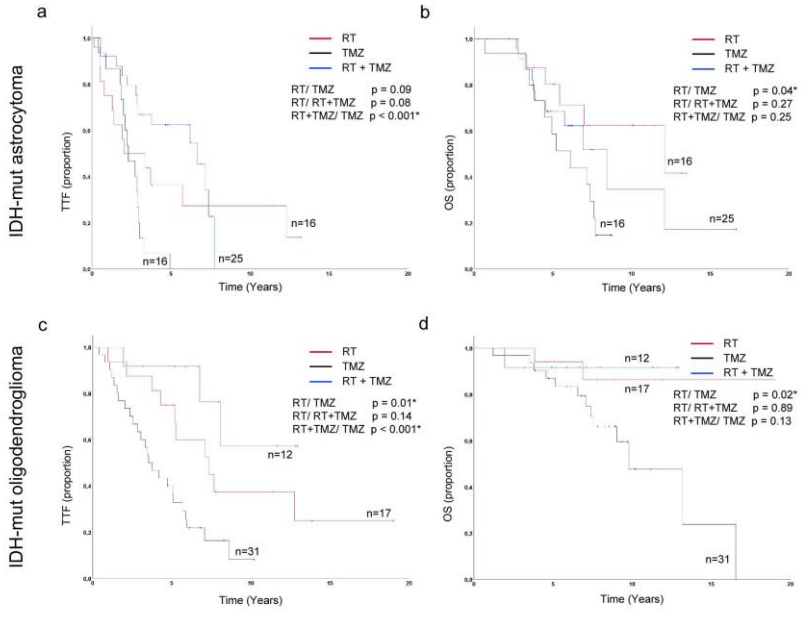

a
IDH-mut oligodendroglioma
IDH-mut astrocytoma
IDH1-R132H-nm
p < 0.001
TTF (proportion)
n= 93
n= 84
n= 80
Time (Years)
c
IDH-mut astrocytoma
WHO°II
WHO°III
p < 0.01
OS (proportion)
n= 43
n= 37
Time (Years)
b
IDH-mut oligodendroglioma
IDH-mut astrocytoma
IDH1-R132H-nm
p < 0.001
OS (proportion)
n= 93
n= 80
n= 84
Time (Years)
d
IDH-mut oligodendroglioma
WHO°II
WHO°III
p = 0.27
OS (proportion)
n= 38
n= 55
Time (Years)
e
IDH1-R132H-nm
WHO°II
WHO°III
p < 0.01
OS (proportion)
n= 31
n= 53
Time (Years)

Fig. 2


a
IDH-mut astrocytoma
RT
TMZ
RT + TMZ
RT/ TMZ p = 0.09
RT/ RT+TMZ p = 0.08
RT+TMZ/ TMZ p < 0.001*
TTF (proportion)
n=16
n=16
n=25
Time (Years)
b
RT
TMZ
RT + TMZ
RT/ TMZ p = 0.04*
RT/ RT+TMZ p = 0.27
RT+TMZ/ TMZ p = 0.25
OS (proportion)
n=16
n=16
n=25
Time (Years)
c
IDH-mut oligodendroglioma
RT
TMZ
RT + TMZ
RT/ TMZ p = 0.01*
RT/ RT+TMZ p = 0.14
RT+TMZ/ TMZ p < 0.001*
TTF (proportion)
n=12
n=17
n=31
Time (Years)
d
RT
TMZ
RT + TMZ
n=12
n=17
RT/ TMZ p = 0.02*
RT/ RT+TMZ p = 0.89
RT+TMZ/ TMZ p = 0.13
OS (proportion)
n=31
Time (Years)

Neuroonkologie I/*Neurooncology I*

V005

Der Einfluss von navigiertem intraoperativen 3D-Ultraschall auf die Gliomchirurgie
Impact of navigated intraoperative 3D ultrasound in glioma surgery

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Objective

Neuronavigation is widely used in neurosurgical procedures, providing a low target registration error depending on the type of registration. However, surgical progress is associated with a decrease in accuracy caused by brain shift. This issue can be addressed by intraoperative live imaging. Here, we demonstrate the impact of navigated intraoperative 3D ultrasound (i3D US) in glioma surgery, comprising its ability of brain shift compensation and resection control.

Methods

19 patients underwent glioma surgery utilizing intraoperative computed tomography (iCT)-based registration. The target registration error (TRE) was calculated. At least two navigated i3D US datasets were acquired with a co-registered high-resolution probe (frequency: 5 – 13 MHz; contact surface: 10 x 29 mm) before dural opening and after tumor resection, and additionally if necessary. Initial brain shift was demonstrated in live imaging.

Results

The mean ± standard deviation (SD) TRE was 0.90 ± 0.15 mm, demonstrating an excellent registration accuracy. Brain deformation could be visualized in live imaging. Patient age was 51.2 ± 18.8 years (mean ± SD). Mean tumor volume was 29.2 ± 35.3 cm3 in preoperative MRI vs. 28.6 ± 36.2 cm3 in pre-resectional US, which did not significantly differ ($p = 0.4431$, paired t-test). In 9 cases of intentional subtotal resection a tumor volume of 6.7 ± 11.2 cm3 was detected in post-resectional navigated i3D US. In 4 (21.1 %) cases of intended gross total resection post-resectional ultrasound demonstrated tumor remnants of a mean volume of 0.20 ± 0.05 cm3, resulting in an expansion of the resection extent.

Conclusion

Being widely available, cost and time efficient, navigated i3D US supplements multimodal neuronavigational setups with live imaging, providing information on brain deformation and tumor resection extent in glioma surgery.

Neuroonkologie I/*Neurooncology I*

V006

Beurteilung der psychischen Belastung in Patienten mit Meningeom unter Beobachtung und nach einer kompletten Resektion

Assessment of psychological distress in meningioma patients under watchful waiting and after complete resection

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Objective

Asymptomatic meningiomas can be found in 1-2% of cranial MRIs. Due to increasing availability of cranial MRI, the number of patients being managed with follow-up imaging and at the same time facing a diagnosis of a brain tumor is rising. The aim of this study was comparing the psychosocial burden of meningioma patients under wait-and-watch strategy and in patients with an uneventful complete resection.

Methods

In our prospective study in a single tertiary neurosurgical center we included patients with either 1) an incidental meningioma under a watchful waiting (WW) strategy or 2) no neurologic deficits after complete resection (postoperative - PO). Sociodemographic, clinical, and health-related quality of life and clinical data were assessed, inter alia by the ECOG and Neurologic Assessment in Neuro-Oncology (NANO) scale. Psychosocial factors were measured by the Distress Thermometer (DT), Hospital Anxiety and Depression Scale (HADS), Brief Fatigue Inventory (BFI), and the Short Form (SF-36). Student"s t, Mann–Whitney, Chi-squared tests, Spearman"s rho, logistic regression were used as appropriate. $P<0.05$ was considered as statistically significant.

Results

In total, 62 patients were included into the study (31 patients each group, n = 51 female, mean age 61, SD=13 years). We found a high prevalence of depression (61% (n=19) in PO and 87% (n=27) in WW group) and anxiety (45% and 42%, respectively). 43% of patients under WW and 37% of PO patients reported significant distress (≥6) on DT scale, 45% patients under WW and 58% PO patients reported significant fatigue. Mean SF-36 values were lower in WW group; however, it was statistically significant only for General Health subscale and Physical Health Component. There was no significant difference between the groups according to objective ECOG and NANO assessments (mean NANO score 0.4 (SD 0.8) vs. 0.5 (SD 1.0). There was no correlation between HADS and DT scores and time since surgery or tumor diagnosis. WW was associated with higher prevalence of depression (odds ratio 4.26 (95% CI: 1.19—15.25).

Conclusion

Meningioma patients suffer from high prevalence of psychological distress, independent from the management strategy and the time since the diagnosis. In our patient sample, WW strategy was associated with a higher burden than uneventful tumor resection, indicating that frequent assessment is necessary also in patients under WW to identify the patients in need of psychooncological support.

Neurovaskuläre Zentren I/*Neurovascular centres I*

V007

7- Jahreserfahrung mit einer interdisziplinären AVM Konferenz – aus neurochirurgischer Sicht
7-year experience with an interdisciplinary AVM conference – from a neurosurgical perspective

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Objective

Indication and treatment of intracerebral arterio-venous malformations (AVMs) are complex and referring to the current literature in some aspects controversial. Besides conservative observation, widely-accepted treatment options encompass microsurgical resection, embolization, a combination of both, or radiotherapy.

Methods

In order to address this issue, we implemented an interdisciplinary AVM conference in our University hospital in 2012, where Neurosurgeons, Neurologists, interventional Neuroradiologists, and Radiotherapists discuss each patient. On a monthly basis, clinical data, MRI images and angiographies (DSA) are evaluated and a common treatment recommendation is assigned.

Results

The number of yearly evaluated patients has continuously increased from 38 (2012) to 75 (2019). In addition, the indication for surgery has also significantly increased in this time period. During an overall observation time from 2004 until 2019, 122 patients were surgically treated or in combination (embolization + surgery). 31% of all cases showed an intracerebral hemorrhage, whereas 69% were elective cases. In accordance with the Spetzler-Martin score, we considered 22% as grade I, 35% as grade II, 37% as grade III, 6% as grade IV, and 0% as grade V. In 96% of patients, the AVM was totally resected without any hints of remaining pathological vessels on the postoperative angiography. Overall, we achieved a favorable outcome (mRS 0-1) in 72% of all cases, however, considering the elective cases without a hemorrhage only, 94% of all patients had a favorable outcome.

Conclusion

Due to the implementation of an interdisciplinary AVM conference, decision making for treatment indication was pulled-up, the number of surgical interventions increased and the overall treatment quality for AVM patients could be improved.

Neurovaskuläre Zentren I/*Neurovascular centres I*

V008

Aneurysma-Behandlung Vasospasmusphase – Ein Grund zur Besorgnis?
Aneurysm treatment during cerebral vasospasm phase – A reason for concern?

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Objective

Aneurysm surgery during the cerebral vasospasm (CVS) phase (days 4 to 14 after subarachnoid haemorrhage [aSAH]) is frequently considered as particularly dangerous, mainly because of the risk of cerebral infarct. We aimed to evaluate the risk of aSAH-specific complications and functional outcome in patients treated during CVS phase.

Methods

We retrospectively analysed a large, comprehensive retro- and prospectively collected database of all patients acutely admitted to our department due to an aSAH between March 2006 and March 2020. We conducted an univariable and multivariable logistic regression analysis in order to evaluate influencing factors on rebleeding, cerebral infarct, GOS at discharge and mortality. Vasospasm phase was defined as between 4-14 days after aSAH. Additionally, we assessed the rate of angiographic vasospasms on admission defined as the narrowing of the arterial diameter of more than 30%.

Results

We included a total of 853 patients. The majority of patients was female (66.6%), mean age was 57.3 years. Out of 853 included patients, 92 (10.8%) were treated during CVS phase. Overall, 312 (36.6%) underwent clipping and 541 (63.4%) endovascular treatment. Treatment during CVS phase was indeed significantly associated with cerebral infarct in the multivariable logistic regression analysis, unrelated to the nature of intervention (OR 2.42, 1.29-4.54 95% CI, p-value=0.006). However, patients treated during CVS phase did not have increased risk of unfavourable outcome measured by GOS on discharge. Additionally, they did not have a higher rate of rebleeding or mortality.

Conclusion

Treatment during CVS phase was significantly associated with a higher rate of cerebral infarcts as confirmed by imaging during the hospital stay. Despite this finding we could not confirm any significant effect on dichotomized GOS on discharge, rebleeding, or mortality. According to our experience, aneurysm treatment during CVS phase appears to be relatively safe and should therefore not be postponed due to the risk of rebleeding and subsequently devastating deterioration.

Neurovaskuläre Zentren I/*Neurovascular centres I*

V009

Vergleich von Clipping und endovaskulärer Behandlung mit dem Woven EndoBridge (WEB) bei der Behandlung von unrupturierten Aneurysmen im vorderen Hirnkreislauf

Comparative analysis of microsurgical clipping and endovascular embolisation with the Woven EndoBridge (WEB) device for the treatment of unruptured anterior circulation aneurysms

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Objective

The Woven EndoBridge (WEB) is an intrasaccular device for endovascular treatment of intracranial aneurysms. It consists of a self-expanding, balloon-like mesh of nitinol wires, which is placed within the aneurysm sac and causes immediate flow-disruption through the aneurysm ostium. The WEB allows endovascular treatment of wide-necked bifurcation aneurysms. Hence, there exists an overlap of indications with microsurgical clipping. In the current study, the WEB was retrospectively compared with microsurgical clipping for the treatment of unruptured anterior circulation aneurysms using propensity score adjustment.

Methods

Patients treated with the WEB at three institutions and by microsurgical clipping at one institution between 2011 and 2019 were retrospectively reviewed and included based on the intention-to-treat principle. Aneurysms larger than 11 mm were excluded, since the WEB is not recommended for such aneurysms. Immediate technical treatment success, complications, ischemic stroke, functional outcome and 6-month aneurysm occlusion status were compared. To mitigate a potential selection bias, the inverse probability treatment weighting method was performed based on individual propensity scores.

Results

The final study population consisted of 103 aneurysms (mean size: 6.6±2.2 mm) treated by microsurgical clipping and 63 (mean size: 6.7±2.2) treated with the WEB. The technical success rate was higher in the clipping group (100%) than in the WEB group (83%, adjusted p=0.01). Procedure-related complications occurred more frequently during clipping (13%) than during WEB embolization (6%, adjusted p<0.01). However, the rates of major adverse events were comparable between the clipping group (4%) and the WEB group (3%, adjusted p=0.53). At the 6-month follow-up, a favorable functional outcome (modified Rankin scale ≤ 2) was achieved in 98% of the WEB group and in 99% of the clipping group (adjusted p=0.19). Complete aneurysm occlusion rates were significantly higher in the clipping group (94%) than in the WEB group (75%, adjusted p<0.01).

Conclusion

Microsurgical clipping was associated with higher technical success and complete occlusion rates, while WEB had a lower complication rate. A similar portion of patients achieved favorable functional outcome in both groups. The decision to use a specific treatment modality should be made on an individual basis and in accordance with the patient"s preferences.

Neurovaskuläre Zentren I/*Neurovascular centres I*

V010

Inkrementelle oder direkte Induktion von Hypertension in der Behandlung von delayed cerebral ischemia nach Subarachnoidalblutung

Incremental versus immediate induction of hypertension in the treatment of delayed cerebral ischemia after subarachnoid haemorrhage

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Objective

Delayed cerebral ischemia (DCI) is a common complication after aneurysmal subarachnoid hemorrhage (SAH) and significantly worsens outcome. In patients with neurological deterioration despite prophylactic nimodipine treatment, induced hypertension (iHTN) can be considered, though the safety and efficacy of induction is a matter of debate. It was the purpose of this study to compare an incremental and an aggressive approach to induction of HTN in patients with DCI.

Methods

In a prospective cohort of 325 consecutive SAH patients, 123 developed DCI and were treated by induced hypertension as a first tier rescue strategy. In 35 patients, blood pressure was incrementally raised in 20 mmHg steps (iHTNincr), whereas 88 patients were treated by immediate induction to systolic values above 180mmHg (iHTNimm). Both groups were compared concerning the need for additional endovascular rescue treatment, the occurrence of DCI caused infarction and clinical outcome assessed by the extended Glasgow outcome scale after 12 months.

Results

The rate of refractory DCI requiring additional rescue therapy was comparable in both groups (48.9% in iHTNincr, 40% in iHTNimm; p=0.332). However, immediate induction was associated with a significantly lower risk of DCI induced infarction (29.5% vs. 51.1%; p=0.015). This is also reflected in a higher rate of favorable outcome after 12 months in the iHTNimm group (60.5% vs. 45.2%; p=0.110), though this was not statistically significant, but also with a higher proportion of lower good recovery (22.4% vs. 11.6%; p=0.045).

Conclusion

In this observational trial, initial aggressive elevation of blood pressure was associated with a lower rate of DCI induced infarction and better outcome when compared to an incremental adjustment of blood pressure, possibly due to a more timely compensation of misery perfusion. Future studies will have to determine the additional value of more tailored approaches such as optimal cerebral perfusion pressure (CPPopt) in the treatment of delayed cerebral ischemia.

Neurovaskuläre Zentren I/*Neurovascular centres I*

V011

Langzeitverlauf von Patienten mit einer arteriovenösen Malformation unter Berücksichtigung der Lebensqualität und des sozioökonomischen Status

Long-term follow-up in patients with arteriovenous malformation based on the quality of life scale and socio-economic status

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Objective

The rupture of a congenital brain arteriovenous malformation (AVM) is a rare aetiology of hemorrhagic strokes especially in young patients which can cause high mortality and morbidity. Disability after stroke often leads to deterioration of the quality of life (QOL). The aim of our study is to assess the quality of life of ruptured AVM patients in long-term follow-up at least five years after hemorrhage and to compare their QOL with unruptured AVM patients.

Methods

We performed a prospective assessment using the Quality of Life Scale (QOLS), the Patient Health Questionnaire for depressive symptoms (PHQ-9) and evaluated the socio-economic status (SES) and general health features (pack years, alcohol consumption, BMI). World Federation of Neurological Surgeons (WFNS) and modified Rankin Scale (mRS) were assessed for outcome in log-term follow-up.

Results

We included 73 ruptured and non-ruptured AVM patients. 57.53% had an AVM hemorrhage whereas 42.47% had non-ruptured AVM. At least the mRS was favourable in 93.06% (n=67) and unfavourable in 6.94%. Mean QOLS was 85.63 (ruptured 86,12 and unruptured 84.97). AVM patients with hemorrhage did not show statistical significance in quality of life compared to patients without AVM rupture ($p=0.23$). Additional analysis in the non-ruptured group showed strong correlation between QOLS and PHQ-9 score ($rho=-0.73$; $p<0.001$). The untreated AVM group also showed strong correlation between QOLS and PHQ-9 ($rho= -0.81$; $p<0.002$).

Conclusion

Long-term follow up showed no difference in quality of life between ruptured and non-ruptured AVM patients. Outcome and quality of life were high in both groups. Further studies are necessary to evaluate depression and anxiety symptoms in patients with treated vs. untreated AVM patients.

Neurovaskuläre Zentren I/*Neurovascular centres I*

V012

Multimodale Kombination aus Standard STA-MCA Bypass und therapeutischem Gefäßverschluss als effektive Revaskularisationsstrategie von komplexen und riesigen ACI Aneurysmen – die Wiener Serie

STA-MCA bypass followed by parent artery occlusion is an effective flow replacement strategy for giant and complex ICA aneurysms – the multimodal Vienna experience

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Objective

Treatment of giant and complex ICA aneurysms remains a major neurosurgical challenge. The aim of this study was to investigate the safety and efficacy of our low-flow replacement strategy in patients not amenable to conventional therapeutic options.

Methods

Between 1998 and 2017, 382 patients harboring unruptured ICA aneurysms were treated at our department. Only patients with an a priori planned combined strategy, including standard bypass and parent artery occlusion, were included. Thus, our cohort comprised 47 giant/complex ICA aneurysms in 41 patients. Clinical and radiological outcome was assessed according to the modified Rankin scale, the bypass patency rate and the Raymond classification. Our median follow-up time was 3.9 years.

Results

Intraoperative patency was confirmed in 100% of completed, predominantly double-barrel, procedures. Endovascular (n=37) or microsurgical (n=1) parent artery occlusion was executed as planned in 38 patients, in most cases immediately after positive balloon occlusion test (BOT). Long-term patency rate in patients with completed bypass surgery and successful PAO was 99% (66/67 bypass grafts in 36/37 patients) at last follow-up, which underscores the importance of flow demand of a maturing bypass. A satisfactory aneurysm occlusion rate of 94% became evident at last follow-up. We observed a procedure-related mortality of 0% while 97% of patients presented with excellent or good outcome (mRS 0-2) at last follow-up. Thus, a statistically significant improvement compared to the preoperative clinical status was evident ($p< 0.001$). An improvement of cranial nerve compression syndromes was also observed in 83% of patients.

Conclusion

Our results suggest that combined STA-MCA bypass surgery followed by PAO presents a safe and effective alternative to high-flow arterial or venous graft interponates and to flow diversion in selected symptomatic giant/complex ICA aneurysms.

Neuroonkologie I/*Neurooncology I*

V013

Patientnahe Tumororganoide als neuartige Medikamentenscreeningplattform identifiziert Panobinostat und OTSSP167 als hoch effektive Medikamente in Meningeomen

Cancer-derived organoids as novel drug screening platform identifies panobinostat and OTSSP167 as highly potent drugs in meningioma

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Objective

Cancer-derived organoids (CDOs) are novel, complex three-dimensional *ex vivo* tissue cultures that accurately reflect genotype and phenotype of the original tumor with preserved cellular heterogeneity and structural architecture. They offer a new and exciting platform for studying cancer biology and developing personalized therapies. The aim of our study was to establish CDOs from meningioma (MGM) and using them as a novel platform for large-scale drug screening in a patient-individual manner.

Methods

CDOs were established by controlled reaggregation of freshly prepared single cell suspensions of MGM tissue samples in non-adhesive 96-well plates. Size and shape were continuously monitored by light microscopy. Morphology was assessed by H&E stainings. Live/dead (Invitrogen) staining was used to control integrity of CDOs. CDOs were treated with drug concentrations ranging from 10 nM to 30 µM and viability was assessed with CellTiterGlo3D (Promega).

Results

This workflow allowed us to generate several hundred mini tumors from one sample equal in size. CDOs reaggregated within 3 days by a considerable contraction of cellular mass. Thereafter, CDO diameter remained stable throughout a 14 days observation period. CDOs consisted of largely viable cells, whereas dead cells were predominantly found outside of the organoid. On H&E stainings, CDOs recapitulated the tissue of origin. As a next step, we queried if CDOs may be suitable for large-scale drug testing. First, we excluded that drug responses depend on CDO size and then used a standardised number of 25.000 cells/CDO for further experiments allowing an appropriate representation of low abundance cell types such as T-cells. As a next step, nine highly potent compounds, derived from a drug screening on MGM cell lines, were tested on CDOs. When treating CDOs generated from 35 MGM patients including three grade II and two grade III MGMs, especially the experimental MELK inhibitor OTSSP167 and the FDA-approved HDAC inhibitor Panobinostat were highly effective in most of the CDOs at the lowest tested concentration of 10 nM.

Conclusion

Taken together, we developed cancer-derived organoids from MGM reflecting accurately the original phenotype and applied them in the frame of a novel drug testing platform. Thereby, we identified Panobinostat and OTSSP167 as highly potent drugs for the treatment of aggressive meningioma.

Neuroonkologie I/*Neurooncology I*

V014

Vergleich von endoskopischer und endoskopisch-assistierter transsphenoidaler Operationstechnik bei Resektion von Hypophysenadenomen

Comparison of endoscopic and endoscope-assisted microscopic transsphenoidal surgery for pituitary adenoma resection

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Objective

The value of endoscopic transsphenoidal surgery of pituitary adenomas compared to the traditional microscopic technique is still discussed in the literature. Here we analyse our long-term results of both approaches in 38 consecutive cases, using patient- as well as clinician-related outcome measurements.

Methods

This double-blind randomised prospective study involves 20 patients who underwent endoscopic (E) and 18 patients treated with endoscope-assisted microscopic (M) transsphenoidal surgery of pituitary adenoma between 2009-2012. 2 cases were lost to follow-up. We analysed history, perioperative course as well as quality of life, resection rate, ophthalmological, rhinological and endocrinological outcomes with focus on patients´ satisfaction. The average follow-up was 5.7 years (E) and 4.7 years (M), range: 1.5 – 10.1 years.

Results

Most pathologies were non-secreting adenomas (E: 50.0%, M: 61.1%). Tumor sizes were comparable (p=0.1), mainly °II according to Hardy classification (E: 40.0%, M: 66.6%). The duration of surgery was shorter in microscopic cases ($p<0.05$). Angled endoscopes revealed residual tumor in 65.0% (E) and 33.3% (M) during surgery. There were no major complications. Surgical revision of CSF-leak was necessary in 1-1 cases. At a patient (M), early postoperative MRI revealed residual tumor with consecutive surgery. Gross total tumor removal was achieved in 91.1% (E), 84.6% (M) at the earliest and in 75.0% and 84.6% at the latest examination. Subjective well-being was timely achieved comparable in both groups (p=0.27), however, 13.2% of patients still had complaints at the latest evaluation. Ophthalmological results improved in 100.0% (E) and 85.7% (M). Pathologic hormone excess normalised in 85.7% (E) and 100.0% (M). Subjective and objective olfactory tests showed highly varying results.

Conclusion

Long-term results were similar. Endoscopic inspection offers better tumor removal, serving as an aid for microscopic surgeons. Patient-related outcomes mostly did not align clinical results, thus a comparison of subjective and objective evaluation is necessary.

Neuroonkologie I/*Neurooncology I*

V015

Die Kultivierung humaner Meningeomzellen bei 20-25 mmHg induziert dedifferenzierende Prozesse
Cultivation at 20-25 mmHg induces dedifferentiating processes in human meningioma cells

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Objective

Meningiomas are characterized by their slowly displacing growth from the meninges and their usually benign clinical behavior. However, under conditions that have not yet been fully elucidated, even these can exhibit malignant progression with deletions effects. It is known that their suppressive growth leads to an increase in intracranial pressure (ICP), which in turn is blamed for many of the unspecific symptoms of meningeal disease. This study is the first to investigate the role of ICP in the possible malignancy.

Methods

In this study a special culture system was developed which allowed the cultivation of different primary meningioma cell cultures (PMCs, n=3) under different pressures (5, 15, 20, 25 and 35 mmHg). The analysis of the cells was performed after 4, 7 and 14 days by immunocytochemical staining against meningioma specific (vimentin, EMA, nestin) and stem cell specific antigens (SOX2, OCT4, NANOG) as well as quantitative polymerase chain reaction (qPCR).

Results

It was shown that the gene expressions SOX2 ($R^{20\ mmHg}_{7d}$=8.11; $R^{25\ mmHg}_{7d}$ =224.88; $R^{20\ mmHg}_{14d}$=491.98; $R^{25\ mmHg}_{14d}$ =303.35), OCT4 ($R^{20\ mmHg}_{7d}$=611.29; $R^{25\ mmHg}_{7d}$ =2462.22; $R^{20\ mmHg}_{14d}$=12.34; $R^{25\ mmHg}_{14d}$ =0.13) after 7 and 14 days as well as NANOG ($R^{20\ mmHg}_{4d}$=4.42; $R^{25\ mmHg}_{4d}$ =37.42) after 4 days from a cultivation below 20 mmHg were strongly increased compared to the physiological brain pressure (15 mmHg). In immunocytochemical analysis we found elevated levels of positive cells for SOX2, NANOG and nestin in the study period. It was also noticeable that the meningioma-specific marker EMA was significantly less expressed when cultivated above 20 or 25 mmHg.

Conclusion

We were able to cultivate meningioma cells under different pressure conditions with the help of hydrostatic pressure. Moreover, we observed that cell cultivation between 20-25 mmHg for at least 7 days induced clearly dedifferentiating processes towards stem cell properties. This increase in the stem cell pool could be a possible factor that promotes the malignant transformation of a tumor.

Neuroonkologie I/*Neurooncology I*

V016

Hochgradig progressive Meningeome können in 3 Gruppen unterteilt werden
Distinct genomic subclasses of high-grade/progressive meningiomas – NF2-associated, NF2-exclusive, and NF2-agnostic

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Objective

Genomic studies of high-grade/progressive meningiomas have reported a heterogeneous mutation spectrum, identifying few recurrently mutated genes. Most studies have been underpowered to detect genomic subclasses of aggressive meningiomas due to relatively small number of available samples. Here, we present a genomic survey of one of the largest multi-institutional cohorts of high-grade/progressive meningiomas to date.

Methods

850 high-grade/progressive meningiomas, including 441 WHO grade 2 and 176 WHO grade 3 meningiomas and 220 progressive WHO grade 1 meningiomas, were tested as part of a clinical testing program by hybridization capture of 406 cancer-related genes to detect base substitutions, indels, amplifications, deletions, and rearrangements. Information from pathology reports, histopathology review, and patient clinical data was assessed.

Results

Genomic analyses converged to identify at least three distinct patterns of biologically-aggressive meningiomas. The first and most common contained NF2-mutant tumors (n = 426, 50%), was associated with male sex (64.4% %, p = 0.0001) and often harbored additional mutations in CDKN2A/B (24%), and the chromatin regulators ARID1A (9%), and KDM6A (6%). A second group (NF2-agnostic) featured TERT promoter (TERTp; n = 56) or TP53 mutations (n = 25) and were either NF2-mutant or wild-type, and displayed no association with either sex (p = 0.39). The remaining group generally lacked NF2 mutations, and accounted for 40% of the cases-with three subgroups. One consistent primarily of grade 3 lesions harboring alterations in chromatin regulators BAP1 (n = 22) or PBRM1 (n = 16). A second subgroup contained AKT1 (n = 26), PIK3CA (n = 14) and SMO (n = 7) mutant skull-based meningiomas, and a third mixed subgroup included 237 meningiomas with a heterogeneous spectrum of low frequency and non-recurrent alterations.

Conclusion

Our findings indicate that the patterns of genomic alterations in high-grade/progressive meningiomas commonly group into three different categories. The most common NF2-associated canonical group frequently harbored CDKN2A/B alterations, which is potentially amenable to targeted therapies. An NF2-agnostic group harbored frequent TERTp and TP53 mutations. The final subclass, distinct from the canonical NF2 mutant associated

pathway, was partly characterized by BAP1/PBRM1 alterations (rhabdoid/papillary histology) or skull-base disease.

Neuroonkologie I/*Neurooncology I*

V017

Progredienzangst bei Patienten mit neu diagnostizierten Hirntumoren und ihren Angehörigen
Fear of progression in patients with new diagnosed brain tumours and their caregivers

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Objective

Despite therapeutic progress resulting in increased survival data, tumor recurrence is unavoidable. Fear of progression (FoP) refers to specific anxiety or concern about the recurrence or progression. Moderate to severe FoP are reported in 49% of patients and affects their QoL. Caregivers are also at risk for psychological distress. But less in known about FoP in brain tumor patients and the impact on their caregivers.

Methods

Since July 2019 consecutively all patients (n = 158) with a new diagnosed brain tumor and their caregivers were asked to participate in a survey. FoP (Progression Anxiety-Questionnaire), anxiety and depression (Hospital Anxiety and Depression Scale, HADS), psychological distress (Distress Thermometer, (DT) was assessed direct (T0), 3 months (T1) and 6 months (T2) postoperatively. Quality of life was assessed using the EORTC-QLQ-C30 and -B20. Psychological burden of patients and caregivers as well as group differences were calculated.

Results

Seventy-one patients and caregivers could be included. Regarding DT, caregivers indicate a significant higher distress level postoperatively ($p = .002$). This was reflected in the HADS ($p < .001$). This observation was also reflected in the FoP with significant increased levels of anxiety ($p = .028$). A significant positive correlation between the patients´ and caregivers´ expression of FoP could be demonstrated ($p < .001$). Three months later, patients distress level did not change significantly ($p = .529$), but caregivers show a significant decreased DT level ($p = .037$). HADS as well as FoP assessment remained stable at T1 for patients and caregivers. Nevertheless, caregivers were significantly more stressed that patients ($p = .003$).

Conclusion

Our analyses clearly demonstrate higher psychological burden for caregivers and a positive correlation of patients - caregivers levels of FoP, regardless of the survey point. These data underline the importance to offer further psychooncological support not only to the patients but also to the caregivers in the early phase of tumor therapy

Neuroonkologie I/*Neurooncology I*

V018

Machbarkeit und Evaluation eines neuen Sprachparadigmas zur intraoperativen Sprachtestung
Feasibility and evaluation of a novel language paradigm for intraoperative language testing

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Objective

Mapping language capacity with its subfunctions during direct cortical stimulation (DCS) in the stetting of awake craniotomy might be challenging without using more than one language paradigm. Applying several language tasks leads to increasing surgery times and to patient"s exhaustion. Additionally, language tasks must satisfy the demands of DCS by not exceeding the assessment time of 4 seconds in a single language trial to avoid DCS-induced seizures. We aimed to (1) design a single language paradigm which pictures the complete language system and (2) simultaneously to restrain the assessment time of single trials up to 4 seconds.

Methods

The intraoperative language task was designed as a single stimulus trial comprising a combination of the classical picture naming task using the DO 80 figures and a semantically associated verb. During DCS periods patients are supposed to generate grammatically and semantically correct sentences according to the language stimulus in a time interval not exceeding 4 seconds. To assess the intraoperative feasibility of the language task we also included 30 healthy subjects in a pilot study to measure subjects" speed of performing a single language task trial and to evaluate the language paradigm according to its language sensitivity by using the paradigm as a task for functional magnetic imaging (fMRI). Intraoperatively, 21 patients without presurgical language deficits with brain tumors in language associated brain areas were included in the study. All patients received neuropsychological testing including language tests before and after surgery.

Results

The pilot study showed in healthy subjects that by applying the novel paradigm during fMRI there is activation in a strongly language associated left accentuated network of inferior frontal regions, the supramarginal and angular gyrus as well as the superior and middle temporal gyrus ($p<.05$, FEW) and, that it was feasible to conduct a single language trial of the novel paradigm in a time frame of 4s (performance speed 2.53 s; SD=.32s). Intraoperatively, all tumor patients showed DCS-associated language errors while conducting the novel language task. Postoperatively, mild or no neuropsychological impairments appeared compared to presurgical assessment ($p<.05$).

Conclusion

We present a novel language paradigm which intraoperatively safely pictures and monitors the whole language system and consequently can minimize postoperative language deficits.

Highlights DGNC – beste Vorträge und Poster 2020

Sektion Wirbelsäule

BO-01

Correlation analysis of CT- and DXA- measured BMD in patients with lumbar spine instrumentation

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Introduction

Reduced bone mineral density (BMD) is a well-known risk factor for postoperative mechanical complications in spinal instrumentation of the elderly. In addition to dual x-ray absorptiometry (DXA) scans considered to be the gold standard for BMD screening, the use of computed tomography (CT) increases. The aim of this study was to investigate a correlation of BMD measured preoperatively using CT- and DXA-scans in patients planned for lumbar spinal fusion surgery.

Material & Methods

All patients scheduled for lumbar spinal instrumentation who were screened by both preoperative lumbar CT- as well as DXA scans between 2009 and 2019 were retrospectively included. CT-BMD was measured using the "Schreiber-technique", with a recommended time span between CT and DXA below 12 months. Patients with cervical or thoracic surgery as well as tumor-associated spine disease were excluded from the study.

Results

64 patients (51 women, 13 men) with a mean age of 65 years were analyzed. The mean BMD was 95.2 ± 32.5 Hounsfield units (HU) on CT, while the BMD measured by DXA revealed to be 1.0 ± 0.3 and 0.6 ± 0.2 g/cm2 for the lumbar spine and the femoral neck, respectively. The Pearson correlation analysis demonstrated a significant correlation between CT-HU units and DXA scans of the femoral neck ($R2 = 0.41$, $p<0.001$), while no significant correlation between DXA scans of the lumbar spine and CT scans was shown ($p>0.05$). The correlation between DXA scans of the femoral neck and lumbar spine was also poor ($p>0.05$).

Discussion

DXA scans particularly of the lumbar spine may not assess bone mineral density effectively. Due to various influential factors and local variations BMD measurement of the lumbar spine by the means of CT may be a more reliable tool. Further studies are necessary to evaluate the assessment of osteoporosis by preoperatively routinely available CT.

Highlights DGNC – beste Vorträge und Poster 2020

Sektion Wirbelsäule

BO-02

Ergebnisse nach der direkten posterioren Atlasringosteosynthese von instabilen Jefferson Berstungsfrakturen auf Entscheidungsgrundlage der intraoperativen Stabilitätsprüfung

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Fragestellung

Die posteriore direkte Atlas- oder C1-Ringosteosynthese (C1-RO) ist eine operative Behandlungsoption bei instabilen Jefferson Berstungsfrakturen (JBF) mit möglicher C1-C2 Funktionswiederherstellung. Seit der Erstbeschreibung anteriorer C1-RO 2004 durch Ruf et al., wurden auch posteriore und kombinierte C1-RO beschrieben. In 2 biomechanischen Studien wurde belegt, dass trotz rupturiertem Ligamentum transversum atlantis durch Reposition und C1-RO sekundäre Stabilisatoren in ausreichendem Maße wirksam werden können. Diese Arbeit zeigt die Ergebnisse der posterioren C1-RO und C1-C2 Osteosynthesen, die auf der Entscheidungsgrundlage der von uns beschriebenen intraoperativen Stabilitätsprüfung (Abb.1) nach Reposition und C1-RO erfolgt sind.

Methoden

Die klinischen und radiologischen Ergebnisse (CT HWS, Funktionsaufnahmen, klinische Kopfrotation, Schmerzangabe) von 5 Fällen (47-75 J., Mean 61 J.) mit instabilen JBF von 2017-2019 mit posteriorer C1-RO oder C1-C2 Osteosynthese mit Therapientscheidung nach intraoperativer Reposition und C1-RO und Stabilitätsprüfung C1-C2 wurden analysiert.

Ergebnisse

Insgesamt wurden 5 Patienten mit JBF von 2017-2019 einer intraoperativen Stabilitätsprüfung nach angestrebter Reposition und C1-RO unterzogen. Bei 4 Patienten wurde die OP als C1-RO beendet, in einem Fall wurde zu einem C1/C2 Harms/Goel Konstrukt mit Querverbinder erweitert. Alle Patienten mit C1-RO waren schmerzfrei, zeigten knöcherne Konsolidierungen des Atlasringes, und die atlantodentale Distanz in den Funktionsaufnahmen nahm im Verlauf nicht zu. In 2 von 4 Fällen mit C1-RO verblieb eine unvollständige Reposition des Atlasringes. Eine Beziehung des Repositionsergebnisses zur möglichen Kopfrotation bestand nicht.

Schlussfolgerungen

Die intraoperative Stabilitätsprüfung C1-C2 bei der Versorgung instabiler JBF bei reponiertem und fixiertem C1-Ring mittels posteriorer direkter C1-RO ermöglicht die Abgrenzung zu einer erforderlichen Erweiterung der Osteosynthese (oder einer Fusion) auf C2 (z.B. durch ein C1/C2 Harms/Goel Konstrukt mit Querverbinder s. Abb.2). Im Verlauf kommt es nach der C1-RO zu stabilisierenden knöchernen Konsolidierungen des Atlasringes, und die atlantodentale Distanz in Funktionsaufnahmen nimmt nicht zu. Eine unvollständige Reposition des Atlasringes intraoperativ zeigt keinen Bezug zur klinischen Funktionswiederherstellung. Es bedarf dennoch besserer Repositionshilfen für eine vollständige Reposition von dorsal.

Abb. 1

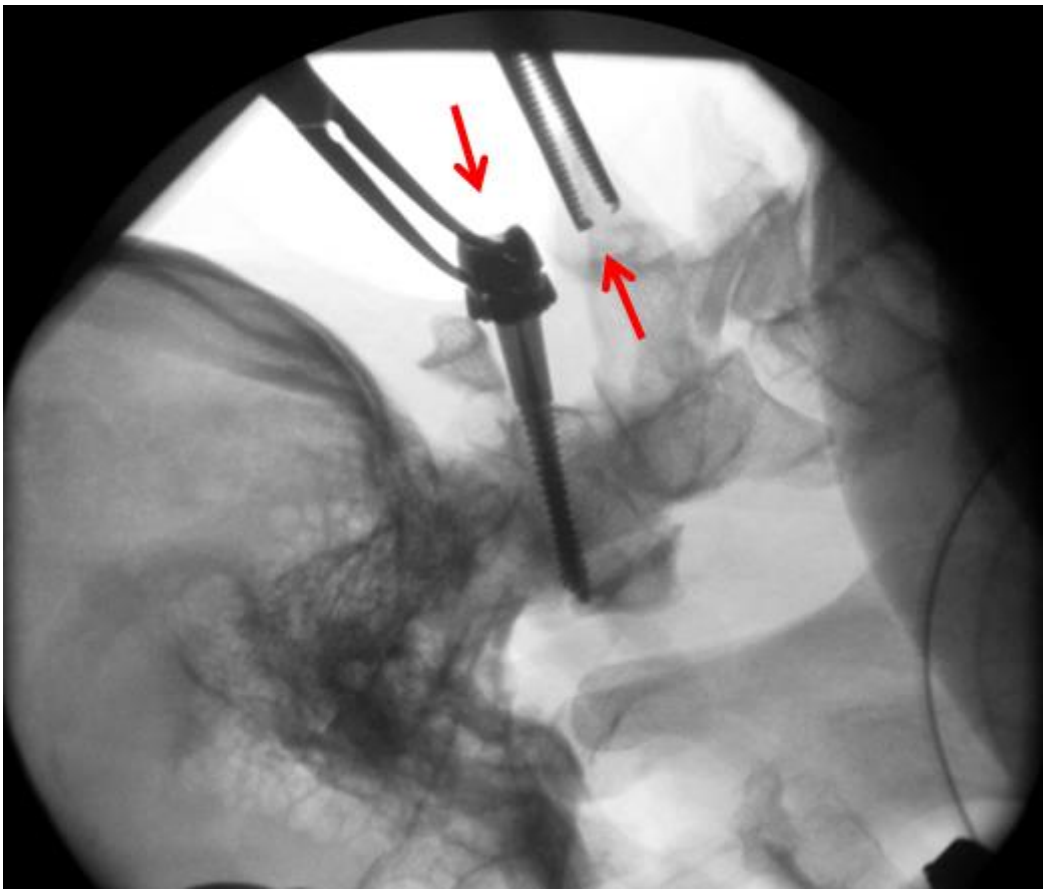
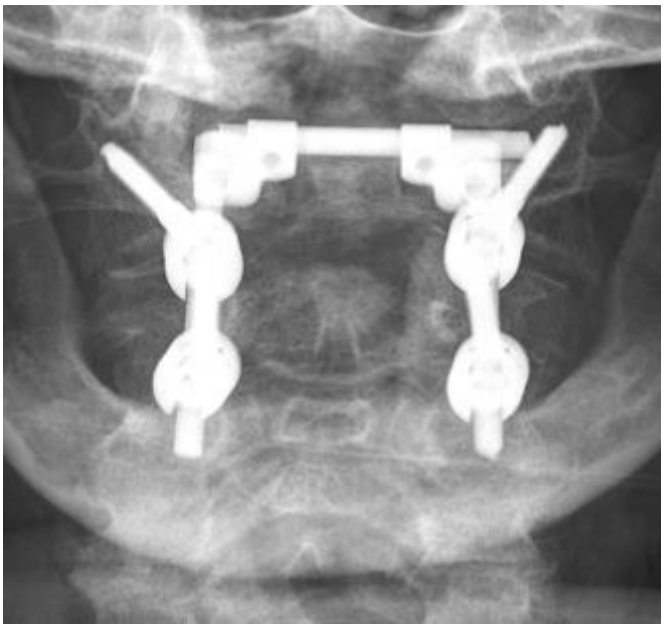


Abb. 2



Highlights DGNC – beste Vorträge und Poster 2020

Sektion Wirbelsäule

BO-03

Development of a novel *in vitro* model of osteoporotic bone to examine new biodegradable and osteoinductive bone cement for the management of osteoporotic vertebral fractures

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Objective

Osteoporosis is the most common age-related progressive skeletal disease characterized by bone loss and concomitant tendency for osteoporotic vertebral fractures (OVF). The management of OVF often necessitates fusion surgery, with high rates of implant failure due to the brittle bone substance. *In vitro* models of osteoporosis to test implant pull out strength are scarce. Here we present a novel ovine model of osteoporotic bone to test an new composite osteoinductive and biodegradable bone cement to boost the anti-osteoporotic therapy and improve long term implant integrity.

Methods

12 sheep vertebrae were perfused with 25% TBD-1 decalcifier solution using a double syringe pump set-up for 24h. Bone density was measured prior and after decalcification using dual-energy X-ray absorptiometry (DEXA). Osteoinductive synthetic collagen I mimetic peptide (P15) was mixed with biodegradable calcium phosphate cement (CaP). Pedicle screws were introduced into one pedicle of each vertebrae and augmented with CaP/P15. Standard polymethylmethacrylate (PMMA) cement and non-augmented screws served as control. Linear pullout testing was performed.
Osteoblastic transformation of human mesenchymal stem cells (MES) was verified via osteoblast-related gene expressions of bone-specific alkaline phosphatase2 (ALPII) and osteocalcein using Immunofluorescence and RT-PCR.

Results

Bone marrow density (BMD) prior to decalcification was 0.72±0.02 g/cm2 prior and 0.53±0.04 g/cm2 after decalcification. BMD was decreased by 28.75±2.6 %.
mRNA expression of ALPII increased 32.76±0.212 %, while osteocalcein was increased by 16.15±0.72 % after co-culture of MES with Cap/P15. Immunofluorescent staining was increased in a similar manner.
Biomechanical testing in untreated vertebrae showed pullout loads of 2010±83 NM after augmentation with CaP/P15 compared to 2112±49 NM after augmentation with PMMA and 1405±25 without augmentation. ($p < 0.001$). In decalcified vertebrae, pullout strength untreated was 827±33 NM and1250±65 NM after augmentation with Cap/P15.

Conclusion

The CaP/P15 composite cement is capable of inducing osteoblastic differentiation in human MES *in vitro*. The ovine decalcification model provides a similar loss of bone marrow density as expected from osteoporotic vertebrae *in vivo* and is capable of mimicking the decreased pull out loads of pedicle screws in vitro. Pull out loads of CaP/P15 augmented pedicle screws are superior to controls in our model.

Highlights DGNC – beste Vorträge und Poster 2020

Sektion Neuroonkologie

BO-04

Infiltration der subventrikulären Zone ist mit schlechterem Outcome in Gliomen WHO Grades II assoziiert
Subventricular zone involvement is associated with unfavourable outcome in glioma of WHO grade II

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Introduction

The subventricular zone represents the largest niche of adult neural stem cells. Involvement of the subventricular zone is associated with less favourable outcome in malignant glioma. It is unclear whether a similar association applies to low-grade gliomas.

Methods

We retrospectively searched our institutional database for patients with glioma WHO grade II according to the 2016 classification. Demographics, histological and molecular information, imaging, and therapeutic approaches were reviewed and outcome was analysed for gliomas with and without infiltration of the subventricular zone.

Results

We identified 182 patients with glioma WHO grade II, including 97 oligodendrogliomas and 85 astrocytomas. Subventricular zone involvement was present in 78 of 182 patients (43%). Neither demographics, histopathology, nor molecular signature including MGMT promotor status and IDH mutation status differed between patients with and without subventricular zone involvement. First-line management included early therapeutic approaches (surgery, chemotherapy, radiotherapy, or brachytherapy) or wait-and-scan approaches. Median follow-up was 43 months. Median time to malignant progression as determined per tissue-based analysis was 122 months; median overall survival was not reached. Subventricular zone involvement was a negative prognostic marker for both time to malignant progression (p= 0.002) and overall survival (p= 0.023) in the entire cohort, but also in the subgroup of patients who were managed with wait-and-scan approaches. This also held true when patients were stratified according to tumor size. Among patients in which early therapy was provided, subventricular zone involvement was not prognostic for overall survival. In multivariate analysis, subventricular zone involvement was associated with worse prognosis independent of molecular markers or treatment approaches including use of resection.

Conclusions

Subventricular zone involvement represents a key risk factor for worse outcome in glioma WHO grade II which might be independent from molecular markers or tumor size. Early first-line therapy may form the basis for favourable outcome in such patients.

Seltene Erkrankungen I/*Rare diseases I*

V019

Klinische Bedeutung der frühen postoperativen CT-Angiographie nach EC-IC-Bypass-Anlage bei Moyamoya-Patienten

Clinical value of early postoperative CT-angiography imaging after EC-IC bypass in patients with Moyamoya

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Objective

To evaluate the clinical value of early postoperative computed tomographic angiography (CTA) after direct extracranial-intracranial (EC-IC) bypass surgery in moyamoya patients.

Methods

A retrospective analysis of all adult moyamoya patients treated at our center from 2013 to 2019 with a direct EC-IC bypass was performed. Early postoperative CTA (within 24 hours after surgery) was compared with conventional digital subtraction angiography (DSA) 6-12 months after surgery. If available, magnetic resonance time-of-flight angiography (MR-TOF) was evaluated 3 months and 6-12 months postoperatively as well. Imaging results were analyzed and compared with CTA, MR-TOF and DSA, whereat DSA was used as the final and definite modality to decide on bypass patency.

Results

A total of 103 direct EC-IC bypasses in 63 moyamoya patients were analyzed. All inclusion criteria were met in 33 patients (57 direct bypasses). In 82.5% the bypass appeared definitively, in 8.8% uncertainly and in 8.8% not patent according to early postoperative CTA. MR-TOF suggested definitive bypass patency in 87.5% 3 months after surgery and in 95.9% 6-12 months after surgery. Six-to-twelve months postoperative DSA showed a patency of 98.2% (56 of 57) of all bypasses. The positive predictive value (to correctly detect an occluded bypass) on postoperative CTA was 10%, the negative predictive value (to correctly detect a patent bypass) was 100% with a sensitivity of 100% and a specificity of 83.9%.

Conclusion

Early postoperative CTA has a high predictive value to confirm the patency of a bypass. On the other hand, a high false positive rate of (according to CTA) occluded bypasses after direct EC-IC bypass surgery can be seen. This must be considered critically when initiating possible clinical consequences if the bypass appears occluded in postoperative CTA.

Seltene Erkrankungen I/*Rare diseases I*

V020

Longitudinale Reproduzierbarkeit der CO2 getriggerten BOLD MRT Bildgebung zur hämodynamischen Evaluation bei Moyamoya Patienten

Longitudinal reproducibility of CO2-triggered BOLD MRI for the haemodynamic evaluation of patients with Moyamoya angiopathy

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Objective

Hemodynamic evaluation of moyamoya patients is crucial to decide the treatment strategy. Recently, CO2-triggered BOLD MRI has been shown to be a promising tool for the hemodynamic evaluation of moyamoya patients. However, the longitudinal reliability of this technique in follow-up examinations is unknown. This study aims to analyze longitudinal follow-up data of CO2-triggered BOLD MRI to prove the reliability of this technique for long-term control examinations in moyamoya patients.

Methods

Longitudinal CO2 BOLD MRI follow-up examinations of moyamoya patients with and without surgical revascularization have been analyzed for all six vascular territories retrospectively. If revascularization was performed, any directly (by the disease or the bypass) or indirectly (due to change of collateral flow after revascularization) affected territory was excluded based on angiography findings (group 1). In patients without surgical revascularization between the MRI examinations all territories were analyzed (group 2).

Results

18 moyamoya patients with 39 CO2 BOLD MRI examinations fulfilled the inclusion criteria. The median follow-up between the two examinations was 12 months (range 4-29 months). For 106 vascular territories analyzed in group 1 the intraclass correlation coefficient (ICC) was ICC=0.784, $p<0.001$ and for group 2 (84 territories) it was ICC=0.899, $p<0.001$. Within the total follow-up duration of 140 patient months, none of the patients experienced a new stroke.

Conclusion

CO2 BOLD MRI is a promising tool for mid- and long-term follow-up examinations of cerebral hemodynamics in moyamoya patients. Systematic prospective evaluation is required prior to making it a routine examination.

Seltene Erkrankungen I/*Rare diseases I*

V021

Mini-Kraniektomie bei EC-IC Bypass – Single-Center-Erfahrungen aus 100 Eingriffen bei Moya-Moya Patienten
Mini-craniectomy for EC-IC bypass – single-centre experience of 100 procedures on Moya-Moya patients

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Objective

Bei Moyamoya-Angiopathie hat sich als Therapie die Anlage eines extra-intrakraniellen Bypasses (EC-IC-Bypass) von einem Ast der Arteria temporalis superficialis (STA) auf einen M4-Ast der Arteria cerebri media (MCA) als Gold-Standard etabliert. Operativ erfolgt dafür standardmäßig eine osteoplastische frontotemporale Trepanation mit basalem osteoklastischem Defekt für den Bypass-Durchtritt. In unserem Zentrum erfolgt über einen kurzen geraden Hautschnitt eine osteoklastische Mini-Kraniektomie direkt über der Sylvischen Fissur. Ziel dieser retrospektiven Single-Center-Analyse ist die Erfassung der Größe und Fläche des Trepanationsdefektes, der Lokalisation in Bezug zum Meatus acusticus externus, der Durchführbarkeit der EC-IC Bypässe und deren Durchgängigkeitsrate sowie der Komplikationen.

Methods

Retrospektiv wurden Daten von 100 EC-IC-Bypass-Operationen bei Moyamoya-Patienten von Juni 2017 bis August 2020 in unserer neurochirurgischen Klinik ausgewertet. Im ersten postoperativen CT erfolgte die Flächenmessung der Mini-Kraniektomie und Bestimmung des Abstands zum Meatus acusticus externus. Mittels Duplexsonographie am dritten postoperativen Tag und einer MRT-Angiographie am sechsten postoperativen Tag sowie drei Monate nach OP wurde die Durchgängigkeit des EC-IC-Bypasses kontrolliert. Im Anschluss erfolgte einmal jährlich eine ambulante Wiedervorstellung mit erneuter MRT-Bildgebung.

Results

Das Durchschnittsalter der Patienten lag bei 44 Jahren (17-72 Jahre). 68 waren Frauen, 32 Männer. Die durchschnittliche Größe der Mini-Kraniektomie betrug in der Höhe 26,69 mm und in der Breite 19,73 mm (Fläche 529 mm^2). Der durchschnittliche Abstand zum Meatus acusticus externus maß 47mm.In den postoperativen Untersuchungen lag die Offenheitsrate der EC-IC-Bypässe bei 100%. Eine Wundheilungsstörung trat bei einem Patienten auf. Weitere Komplikationen wurden nicht beobachtet.

Conclusion

Die Mini-Kraniektomie scheint aufgrund der guten technischen Machbarkeit mit 100%iger Offenheitsrate der Bypässe keinen Nachteil gegenüber der herkömmlichen Trepanation darzustellen. Hinsichtlich Wundheilungsstörungen scheint sich aufgrund des kurzen Hautschnittes ein klarer Vorteil gegenüber der größeren Standard-Trepanation zu zeigen. Durch die kleine Trepanationsfläche konnten zufriedenstellende kosmetische Ergebnisse erzielt werden. Ferner werden durch die osteoklastische Trepanation Metallimplantate zur Knochendeckelrefixation vermieden, sodass postoperativ auch eine 7-Tesla MR-Bildgebung erfolgen kann.

Seltene Erkrankungen I/*Rare diseases I*

V022

Beeinträchtigung der Lebensqualität bei erwachsenen Patienten mit Moyamoya – präoperative Beurteilung und Korrelation mit MRT und H215O-PET

Quality of life in adult Moyamoya patients – preoperative assessment and correlation to MRI and H215O-PET findings

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Objective

The diagnosis of Moyamoya Angiopathy (MMA) is a life-changing condition for patients. Disease-related cerebral perfusion deficits or infarctions might influence the quality of life (QoL). This study examines preoperative QoL in adult patients with MMA and correlates these results with imaging findings.

Methods

Preoperative QoL data (SF-36, SCL-90, BDI, BVI) of 67 adult moyamoya patients was analyzed for a possible correlation with territorial hypoperfusion seen on H215O PET with acetazolamide (ACZ) challenge (cerebrovascular reserve) and infarction patterns observed in MRI (FLAIR). Each vascular territory was analyzed separately and correlated to QoL.

Results

Physical role function was restricted in 41.0% of cases and emotional role function in 34.4% of cases. Compulsivity (39.3%), psychoticism (34.4%) and depression (29.5%) were also very common. Psychoticism was significantly more frequent in cases of perfusion deficits as seen in PET CT in both MCA territories (left p=0.0124, right p=0.0145) and infarctions as seen in MRI in the right MCA territory (p=0.0232). Depression was significantly associated with infarctions in the right MCA territory (p=0.0174), physical role function impairment with perfusion deficits in both MCA territories (left p=0.0178, right p=0.0428). Women were significantly more frequently affected by depression (p=0.0234).

Conclusion

This analysis shows significant impairment of QoL in preoperative testing of Moyamoya patients. The results show a correlation between individual QoL parameters and affected brain areas. Especially the right MCA territory might play a key-role for neuropsychological disorders in Moyamoya patients as also shown in previous analysis. Additional postoperative testing of Moyamoya patients is needed in the future to control the development of QoL parameters after revascularization and to possibly support patients with neuropsychological treatment.

Seltene Erkrankungen I/*Rare diseases I*

V023

Veränderungen der Kontrast-Aufnahme in der arteriellen Gefäßwand als Marker einer Krankheitsprogression bei Moyamoya Patienten

Vessel wall contrast enhancement as sign of disease progression in Moyamoya disease

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Objective

Vessel wall contrast enhancement has been shown to possibly predict disease progression in Moyamoya patients. Aim of this study is to investigate the natural course of vessel wall contrast enhancement in MMD and its association with local disease progression as seen in conventional angiography.

Methods

This retrospective blinded cohort study included all consecutive MMD patients at our department with availability of CE-HR-MRI (contrast-enhanced high-resolution magnetic resonance imaging). The imaging was analyzed and graded for vessel wall contrast-enhancement according to the following scale: 1.) none, 2.) mild, 3.) moderate, 4.) strong and characterized by concentric or eccentric enhancement. Patients were only included if serial CE-HR-MRI (≥2) and at least one conventional cerebral angiography were available.

Results

79 patients received CE-HR-MRI in the course of their treatment. 35 of these have received more than one CE-HR-MRI to allow serial vessel wall contrast enhancement analysis. In total, 97 MRI (194 hemispheres) of 35 MMD patients were included in our analysis. 10 patients did not have any contrast enhancement in their vessel wall. 25 patients had 49 locations with vessel wall contrast-enhancement throughout their treatment and follow-up period. The most common location for contrast-enhancement was the terminal carotid artery (41%) and proximal MCA (M1) (39%). Vessel wall contrast enhancement was found in 8% in the ACA (A1), 6% in the periopthalmic ICA and 2% in each in the cavernous ICA, PCOM and petrous ICA. There was a dynamic change of increase and decrease in intensity of the contrast enhancement (increase/decrease of >2 grades) of 15.24 months (± SD 8.19). Contrast enhancement of the vessel wall was significantly associated with local stenosis as seen in conventional cerebral angiography (p-value < 0.05) and disease progression (p value <0.05) seen in follow-up imaging.

Conclusion

Vessel wall contrast enhancement in MMD is a sign for disease activity. This dynamic increase and decrease of contrast enhancement can be seen in a time-frame of approximately one and a half year and is significantly correlated with angiographically proven local stenosis and disease progression. High-resolution vessel wall imaging might be an important predictor of disease progression in MMD patients and should be used for follow-up examinations. The pathophysiological process causing the contrast enhancement have to be investigated in the future.

Seltene Erkrankungen I/*Rare diseases I*

V024

Das zervikale intramedulläre Ödem ist eine der Hauptkomplikationen in Patienten mit arterio-venöser Fistel am kraniozervikalen Übergang

Cervicale intramedullary oedema plays a key role in patients with arteriovenous fistulas of the craniocervical junction

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Objective

Arteriovenous fistulas of the craniocervical junction (ccdAVF) are rare sorts of cranial vascular malformations. Symptoms leading to hospital admission can grow slowly or present acute. Possible symptoms are progressive myelopathy or sudden bleeding. By their low prevalence and versatile presentation diagnosis is crucial and often prolonged. Therapeutic options are endovascular embolization, microsurgical dissection or a combination of both. In this study we focused on the myelopathy and its role as symptom as well as permanent problem for affected patients.

Methods

We performed a retrospective analysis of the clinical dataset for a 12 year time period. Predefined inclusion criteria were a angiographically confirmed ccdAVF and analyzable health- and radiological records. General patient information, symptoms and neurological status on admission as well as at discharge were extracted from the health record. CcdAVF was reviewed according the Cognard classification. MRI scans were reviewed for presence and extent of myelopathy.

Results

In total 12 patients met the defined study inclusion criteria. 5 patients presented with progressive myelopathy and increasing neurological deterioration as initial symptom. In 4 cases diagnosis was made due to minor symptoms. Acute neurological detoriation due to bleeding was seen in 3 cases. For all patients long term follow-up was available. Myelopathy persisted in all patients who became symptomatic due to CcdAVF and was documented as being progressive in 3 cases during follow-up.

Conclusion

Arteriovenous fistulas of the craniocervical junction are complex malformations in diagnosis, treatment and outcome. Congestive myelopathy due to venous overload is the leading component in this disease. Prognosis of neurological deficits after obliteration of a CcDAVF seems as unpredictable as in spinal dAVF. Wether treatment modalities i.e. surgery vs. embolisation influence the disease course remains unresolved and consortional studies of collateral measures focussing on the sequelae of sudden changes of hemodynamics after treatment are recommended.

Neurotraumatologie/*Neurotraumatology*

V026

Wirkt sich ein zusätzliches spinales Trauma bei Patienten mit Schädel-Hirn-Trauma auf das Behandlungsergebnis aus? Daten von 164 Patienten aus der CENTER-TBI Studie

Does concomitant spine injury in patients with traumatic brain injury affect the outcome? Data on 164 patients from the CENTER-TBI study

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Objective

Spine injury is highly prevalent in poly-trauma patients, but data on the co-occurrence of spine trauma in TBI patients is scarce. This study used the CENTER-TBI database to assess patients' prevalence, characteristics, and outcomes with TBI and concurrent spine trauma.

Methods

Data from the European multi-center CENTER-TBI study were analyzed. Only adult TBI patients (≥18 years) presenting with a concomitant, isolated (no injuries in other body regions) serious (AIS ≥3) spine injury were included. For outcome analysis, a comparison group of TBI patients without spine trauma was created by propensity score matching. Hospital length-of-stay and 6-month GOSE and mortality were compared between both groups ($p<0.05$ was considered significant).

Results

From the 4255 adult patients within the CENTER-TBI core study, a total of 164 (4%) suffered from a concomitant isolated spine trauma of at least serious severity. The median age was 53 (IQR: 37-66) years, 70% of patients were males, and alcohol intoxication was present in 24%. Incidental falls were the most common injury type (47%), and on admission, mild TBI was documented in 62% of cases, followed by severe TBI in 26%. Spine injuries were mostly located in the cervical spine (65%), followed by the thoracic spine (32%). In total, 57% of patients were admitted to the ICU. Surgical spine stabilization was performed in 23% of cases, and cranial surgery was necessary for 20%. The median hospital length-of-stay was 8 (5-105) days and thus significantly longer compared to the matched cohort without spine trauma (3 (1-90) days). Moreover, only 48% of patients with a combined injury compared to 57% with TBI only could be discharged home (p=0.0356). After six months, with 11%, the mortality rate in patients with TBI and spine trauma was not significantly different from the TBI only group (14%; p=0.6127). However, significantly fewer patients with TBI and spine trauma regained full recovery (GOSE 8) than the matched patients with TBI only (23% vs. 35%; p=0.0379).

Conclusion

Concurrent, isolated, serious spine trauma was identified in 4% of TBI patients in the CENTER-TBI study. While mortality was not increased, patients with both injuries had longer hospital length-of-stays and regained full recovery less frequently.

Neurotraumatologie/*Neurotraumatology*

V028

Einfluss eines Neurokinin-1 Rezeptor Antagonisten auf die Integrität der Blut-Rückenmarksschranke, die Ödembildung und die funktionelle Erholung nach thorakaler Rückenmarksverletzung im Tiermodell

Effects of a neurokinin-1 receptor antagonist on the integrity of the blood-spinal cord barrier, oedema formation and functional recovery in an animal model of thoracic SCI

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Objective

Traumatic spinal cord injury (SCI) remains a devastating event with no neuroprotective treatment currently available. Disruption of the blood-spinal cord barrier (BSCB) with subsequent edema formation and neuroinflammation contributes to the disease's seriousness. It has been linked to the release of the neuropeptide Substance-P (SP). In our current study, we, therefore, aimed to antagonize the binding of SP to its neurokinin-1 (NK1) receptor with N-acetyl-L-tryptophan (NAT) in a rodent SCI model.

Methods

66 female Wistar rats were subjected to either a thoracic clip-contusion/compression SCI at the T10 level or sham surgery (laminectomy). After trauma application, an osmotic micropump was additionally implanted, and infusion of NAT or Vehicle into the intrathecal space over the spinal cord lesion was initiated. The Basso, Beattie, Bresnahan (BBB) score, the Gridwalk test, and the CatWalk gait analysis were performed to assess functional recovery. After infusion of NAT/Vehicle for 1, 3, or 7 days, animals were sacrificed, immunohistological analyses were conducted, and results were statistically compared between groups ($p < 0.05$ was considered significant).

Results

In immunohistological analyses, the inhibition of SP via NAT in the injured spinal cord showed no significant effects on macrophages' infiltration and their polarization towards the M1- or the M2-subtype 7 days after SCI. However, the invasion of T-lymphocytes was significantly reduced with the NAT treatment. Furthermore, a reduced leakage of Fibrinogen and an attenuated expression of ß-Catenin was found, indicating a significant effect of NAT on the integrity of the BSCB. Correspondingly, a trend towards reduced spinal cord edema could be observed 7 days after the injury. Fine motor recovery measured by the Gridwalk test was not significantly affected after intrathecal NAT infusion for 7 days. However, animals in the NAT group showed a significantly increased BBB score and significantly improved recovery in the CatWalk gait analysis.

Conclusion

In our study, the intrathecal administration of the NK1 receptor antagonist NAT led to increased integrity of the BSCB in the acute phase after thoracic SCI, potentially attenuating aspects of neuroinflammation, reducing edema formation, and improving functional recovery. Our findings suggest that NAT might have neuroprotective properties, which should be further assessed in the context of SCI.

Neurotraumatologie/*Neurotraumatology*

V029

Einfluss des Inzisionstyps auf die Wundheilung bei dekompressiver Hemikraniektomie
Impact of incision type on wound healing in decompressive hemicraniectomy

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Objective

The goal of this study was to determine the differences in wound healing aspects between the classic reversed question mark incision and the retroauricular frontoparietooccipital incision in decompressive hemicraniectomy. The preliminary results of our observations were analyzed.

Methods

A total of 60 patients were recruited between 2018 and 2020 (Group A: 30 patients with reverse question mark incision & Group B: 30 patients with retroauricular frontoparietooccipital incision). The medical documentation of the included patients was analyzed for the occurrence of wound healing disturbances (dehiscence, infection). A two-sample t-test between proportions was performed to determine whether there was a significant difference between the two groups

Results

12 patients from Group A (40%) and 8 patients from Group B (27%) developed wound healing disturbances. There were no statistical significant differences referring wound healing disturbance in both groups and the demographic parameters did not statistically differ from each other.

Conclusion

In our preliminary results there was no statistical significance referring the rate of wound healing disturbances between the analyzed groups. Nevertheless we observed a noticeable trend to better wound healing rates with the retroauricular frontoparietooccipital incision compared to the classic question mark incision. A larger patient sample size is needed for a representative statistical analysis of wound healing aspects in decompressive hemicraniectomy.

Neurotraumatologie/*Neurotraumatology*

V030

Evaluierung der AMM Embolisierung bei cSDH
MMA embolisation for chronic subdural haematoma

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Objective

The aim of this study was to assess the value of ipsilateral meningeal artery (MMA) embolisation after burr hole evacuation of chronic subdural hematoma (cSDH)

Methods

Retrospective study to compare post-interventional results (i.e. recurrence rate and complications) of cSDH after burr hole evacuation and consecutive embolisation of MMA versus a historic control group of only burr hole evacuated patients.

91 embolized patients (2018-2020) versus 142 non-embolized patients (2015-2017) were compared.

Results

Embolized versus non-embolized patients showed the following distributon of parameters and outcomes:

med. age: 79 vs. 76.6 years; m/w ratio: 67 / 33% vs. 35.2 / 64.8%; pre-op symptoms : cephalgia: 57 vs. 47.2%; hemisympt. : 53 vs. 51%; aphasia: 26,4 vs. 28.2%; seizures : 5.5 vs. 7.7%; anamnestic trauma : 56 vs.57%.

Post-op/post-interventional: complications and morbitity post-op 13.2 vs. 41.5%; mortality 1,1 vs.4,2%; median hospital stay: 10 vs. 13.1 days.

Twelve weeks after treatment, an ambulatory assessment was completed and revealed: recurrence rate of 9.8 vs. 31.7% ($p<0.01$), refractory cSDH requiring re-operation 0% vs. 9.3%, peri-operative seizures 1.1 vs. 13%; post-op pneumonia: 1,1 vs. 9%, pulmonary embolism 1.1% vs. 0%. The average modified Rankin scale assessment changed from 2.0 pre-op to 0.3 post-op.

Conclusion

Selective AMM-embolisation was an effective adjunct treatment in addition to burr hole evacuation leading to a dramatic decrease of recurrent cSDH and lowered the overall complication rate

Neurotraumatologie/*Neurotraumatology*

V031

Die Applikation von Interleukin-4 reduziert den sekundären Hirnschaden nach experimentellem Schädel-Hirn-Trauma im Mausmodell

The administration of Interleukin-4 ameliorates secondary brain damage after experimental traumatic brain injury in mice

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Objective

Recent focus of experimental research in traumatic brain injury (TBI) has been directed towards the role of inflammatory processes. It has been shown that activation of the Interleukin-4 (IL-4) pathway ameliorates secondary brain injury; therefore, we assessed the effect of therapeutic application of IL-4 on secondary brain damage after experimental TBI in mice.

Methods

C57/Bl6 wildtype mice were subjected to controlled cortical impact (CCI) injury (tip diameter 2mm, impact depth 1mm, velocity 8m/s, contact time 150ms). IL-4 was administered subcutaneously at a dose of 5mg/kg 15 minutes after trauma induction. Neurological function was assessed using hole board, video open field and CatWalk XT gait analysis tests 24 hours as well as three, seven, 14 and 28 days after CCI. In addition, contusion volume was determined by Nissl staining. Finally, inflammatory response (quantification of macrophages and microglia as well as astrogliosis, M1/M2 microglia differentiation) and proliferation (quantification of oligodendroglial differentiation and myelinization) was assessed in the pericontusional area as well as in the hippocampus by immunofluorescent staining.

Results

IL-4 treatment resulted in reduced contusion volumes throughout days one to 28 (e.g. 7.82 vs. 10.03 mm^3 on day seven), improved gait and motor function as well as reduced inflammatory response. Macrophages tended to differentiate into the anti-inflammatory M2-type more often and proliferation processes were observed more frequently after IL-4 application.

Conclusion

As application of Interleukin-4 plays leads to reduced structural damage and improves neurological function after experimental TBI, it poses an interesting treatment option. The current results provide the basis for a potential translation into clinical research that might be possible in the near future.

Neurotraumatologie/*Neurotraumatology*

V032

Nutzen der CatWalk XT® Ganganalyse zur Beurteilung der funktionellen Erholung nach schwerer zervikaler Rückenmarksverletzung im Rattenmodell

Use of the CatWalk XT® gait analysis to assess functional recovery after severe cervical spinal cord injury in rats

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Objective

Objective and consistent assessment of gait and motor function remains challenging in rodent spinal cord injury (SCI) models. Therefore, we studied the validity and relevance of the CatWalk XT® gait analysis as an automated method for outcome assessment in a clinically relevant cervical SCI model in rats.

Methods

20 Wistar rats were randomly assigned to either a C6 clip compression/contusion SCI (SCI group) or a sham laminectomy (Sham group). Locomotion recovery was assessed weekly using the BBB open field score and the CatWalk XT® gait analysis. At the end of the experiment, six weeks after SCI, the percentage of preserved spinal cord tissue was measured by GFAP immunohistochemistry (IHC) staining. Linear regression analyses were performed to assess the BBB open field score's and the percentage of preserved tissue's correlation with 30 different CatWalk XT® parameters (R^2 values are presented).

Results

The compression/contusion injury caused a bilateral and significant functional impairment in all CatWalk XT® parameters in the SCI group. Over the course of the experiment, a significant level of spontaneous recovery compared to the first postinjury measurement was observed in most of the CatWalk XT® parameters and the BBB open field score. Histologically, the overall percentage of preserved tissue within +/- 1200 µm of the lesion epicenter was 60.42 ± 2.82%. Correlation analysis of the hindlimb CatWalk XT® parameters, including regularity index, stride length, print area, max contact area, and body speed with the BBB open field score yielded relatively high R^2 values (> 0.6) in 53%. Moreover, an even better correlation of the CatWalk XT® parameters of both the forelimbs and the hindlimbs with the percentage of preserved tissue could be observed (83% of R^2 values > 0.6).

Conclusion

The CatWalk XT® system is an objective and consistent tool for assessing the impairment and recovery of locomotor function after cervical contusion/compression SCI in rats, showing a good correlation with the classic behavioral scaling system of the BBB open field score, and more importantly also with the percentage of preserved spinal cord tissue.

Neurovaskuläre Zentren II/*Neurovascular centres II*

V033

Schlaganfalltherapie in Zeiten von COVID-19 unter Einschluss endovaskulärer und operativer Verfahren – eine deutschlandweite Studie innerhalb eines großen Krankenhausnetzwerkes

Management of acute ischemic stroke in times of COVID-19 in Germany with emphasis on endovascular and surgical interventions – a nationwide study in a large hospital network

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Objective

During the COVID-19 pandemic, a decrease in hospital admissions of acute ischemic stroke (AIS) was observed globally. On a national scale, no data specific to Germany have emerged on this issue so far. This investigation was designed to detect possible changes in mortality and clinical management of AIS before and during the pandemic with special emphasis on neurosurgical and endovascular interventions.

Methods

Using administrative data from a nationwide network of 67 hospitals we identified patients with AIS associated with atrial fibrillation by respective codes according to the International Statistical Classification of Diseases (ICD). The time period with the highest load of hospitalized COVID-19 cases between March 26 and May 13, 2020 was defined as "peak phase" followed by a "recovery phase" up until Sept. 22, 2020. We compared therapeutic interventions in both phases to corresponding time periods in 2019 ("prepandemic phases"). The following categories of AIS management were examined: thrombolysis (TL), thrombectomy (TE), decompressive hemicraniectomy (DHC), mechanical ventilation (MV) and intensive care (ICU).

Results

A total of 3.752 AIS cases were included. During the peak phase in 2020, AIS hospitalizations decreased by 23% compared to 2019 (607 vs. 467; p<0.01). In contrast, during the COVID-19 recovery phase AIS hospitalizations did not differ from 2019 (1.388 vs. 1.290; p=0.06). The distribution of AIS management types during the peak period in 2020 did not differ significantly from 2019: TL: 12% vs. 13%; TE: 9% vs. 11%; DHC: 1% vs. 1%; MV 6% vs. 6%; ICU: 73% vs. 79%; respective p-values >0.05). In contrast, during the recovery phase in 2020, we observed slight increases in the proportions of cases receiving TE (14% vs. 10%; p=0.01) and ICU (81% vs. 73%; p<0.01) when compared to 2019 while the proportion of the other management types remained unchanged (TL: 13% vs. 14%; DHC: 1% vs. 1%; MV: 7% vs. 7%; respective p-values >0.05). In-hospital mortality of AIS was 13% during the peak phase (vs. 10% in 2019 [p=0.08]), and 10% during the recovery phase (vs. 10% in 2019 [p=0.93]).

Conclusion

Even though the amount of AIS cases hospitalized in Germany decreased substantially during the COVID-19 peak phase, in-hospital mortality and treatment strategies remained the same as before the pandemic. This suggests that even during times of high pressure on medical capacities, providing the full spectrum of AIS management options remains paramount.

Neurovaskuläre Zentren II/*Neurovascular centres II*

V034

Dekompressive Hemikraniektomie nach Subarachnoidalblutung – Angesichts der Langzeitergebnisse gerechtfertigt?
Decompressive hemicraniectomy after subarachnoid haemorrhage – Justifiable in light of long-term outcome?

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Objective

Decompressive hemicraniectomy (DHC) is a potentially lifesaving procedure able to alleviate refractory intracranial hypertension and thus prevent death from uncal herniation. The spectrum of indications for this procedure is expanding and we present long-term results in a series of patients suffering from aneurysmal subarachnoid hemorrhage (aSAH). DHC for this indication remains controversial as refractory intracranial pressure is indicative of severe and diffuse cerebral damage. The goal of this analysis was to identify predictors of favorable outcome after DHC in aSAH patients.

Methods

All aSAH cases treated between 2010 and 2019 in a single institution were included. Patients additionally treated with decompressive hemicraniectomy due to refractory intracranial hypertension, were identified and the occurrence of DCI and DCI-related infarctions was noted alongside clinical outcome, assessed by means of the Glasgow outcome scale after 12 months. In the DHC subgroup the effect of patient- and disease specific aspects on long-term outcome were examined.

Results

Of 337 aSAH cases presented between 2010 and 2019, 64 (19.0%) were treated with DHC. In ten cases, DHC was performed during initial clip ligation (primary DHC). In the remainder of cases DHC was performed on average 4.0 ± 3.9 days after the initial hemorrhage (secondary DHC). Of all DHC treated patients, 12 month mortality was 32.8%, and only 9 (14.0%) cases reached favorable outcome. DHC was more commonly performed in younger patients ($p = 0.002$) with more severe aSAH according to Hunt & Hess ($p < 0.001$) and modified Fisher grading ($p < 0.001$). In multivariate analysis, only younger age ($p = 0.017$) but not the absence of DCI or DCI-related infarction nor milder aSAH severity, were associated with favorable outcome after DHC.

Conclusion

Decompressive hemicraniectomy, though lifesaving has only a limited probability of offering survival in a clinical favorable state. The decision to perform DHC has to be critically evaluated on an individual basis. We identified young age to be the sole independent predictor of favorable outcome after DHC in SAH patients.

V035

Dauer zwischen Aneurysmaruptur und Versorgung – Assoziation mit Outcome nach aneurysmatischen Subarachnoidalblutung

Duration between aneurysm rupture and treatment – association with outcome in aneurysmal subarachnoid haemorrhage

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Objective

Timely treatment of an aneurysmal subarachnoid haemorrhage (aSAH) is key in order to prevent further rupture and increased poor functional outcome. We aimed to evaluate complications and outcome in patients treated for aSAH depending on the time from haemorrhage to treatment and analysed the influence of treatment delay.

Methods

We retrospectively analysed a prospectively collected database of patients with aSAH admitted to our institution due to the acute haemorrhage between March 2006 and March 2020. Demographic, clinical, and imaging data were collected using standardized case report forms. We compared risk factors using multivariable logistic regression.

Results

We included 853 patients. Mean age was 57.3 years, 568 (66.6%) of the patients were female. Out of 853 included patients, 698 (81.8%) were treated within 24 hours from acute haemorrhage and 155 (18.2%) after. Patients who were admitted within 24 hours were additionally stratified into following subgroups if exact time from the haemorrhage was available: <4h, <6 h, and <12 h, respectively. Patients with higher Hunt and Hess (HH) grades were admitted and treated significantly faster than those with lower aSAH grades (overall p-value <0.001). Overall, 15 patients (1.8%) rebled before or during intervention. In the multivariable logistic analysis adjusting for age, time from haemorrhage to intervention, Barrow Neurological Institute (BNI) score and intracerebral haemorrhage (ICH), BNI score and ICH were significantly associated with rebleeding before aneurysm occlusion (overall p-value 0.008; OR 3.11, 95%CI 1.09-8.91, p=0.04, respectively). Treatment within 24 hours was associated with a lower mortality and cerebral infarction in lower grades aSAH in our cohort (OR 0.32, 0.1-0.98 95%CI, p-value=0.05; OR 0.13, 0.04-0.41, p-value<0.001, respectively). There were no major differences to these results if treatment proceeded within 12 hours or earlier.

Conclusion

Treatment within 24 hours after aneurysm rupture is associated with a lower mortality and cerebral infarction rate. In our study, the delay in treatment with consequently higher complication rates primarily affected patients with initially lower grade aSAH. Regardless of the initial mild symptoms and the presumably stable clinical state, treatment delay in patients with lower grade aSAH appears to be obsolete; they ought be treated with the same urgency as higher-grade aSAH.

V036

Assoziation von Kontrastmittelanreicherung in der Wand von intrakraniellen Aneurysmen mit einer verminderten intraaneurysmatischen Konzentration von IL-10 und morphologischen Instabilitätsparametern

Aneurysm wall enhancement is associated with decreased intrasaccular IL-10 and morphological features of instability

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Objective

High resolution vessel wall imaging plays an increasingly important role in assessing the risk of aneurysm rupture. We aim to introduce an approach towards the validation of the wall enhancement as a direct surrogate parameter for aneurysm stability.

Methods

19 patients harboring 22 incidental, intracranial aneurysms were enrolled in this study. The aneurysms were dichotomized according to their aneurysm-to–pituitary stalk contrast ratio using a cut-off value of 0.5 (stable <0.5; unstable ≥0.5). We evaluated the association of aneurysm wall enhancement with morphological characteristics, hemodynamic features and inflammatory chemokines directly measured inside the aneurysm.

Results

Differences in plasma concentration of chemokines and inflammatory molecules, morphological and hemodynamic parameters were analyzed using the Welch test or Mann-Whitney-U test. The concentration Δinterleukin-10 in the lumen of intracranial aneurysms with low wall enhancement was significantly increased compared to aneurysms with strong aneurysm wall enhancement ($p = 0.014$). The analysis of morphological and hemodynamic parameters showed significantly increased values for Aneurysm Volume ($p = 0.03$), Aneurysm Area ($p = 0.044$), maximal diameter ($p = 0.049$) and non-sphericity index ($p = 0.021$) for intracranial aneurysms with strong aneurysm wall enhancement. None of the hemodynamic parameters reached statistical significance, however, the total viscous shear force computed over the region of low wall shear stress showed a strong tendency towards significance ($p = 0.053$).

Conclusion

Aneurysmal wall enhancement shows strong associations with decreased intrasaccular IL-10 and established morphological indicators of aneurysm instability.

Neurovaskuläre Zentren II/*Neurovascular centres II*

V037

Adenosin induzierter Kreislaufstillstand zur Erleichterung des Clippings intrakranieller Aneurysmen – gewonnene Erkenntnisse nach 72 Patienten

Adenosine-induced transient asystole to facilitate intracranial aneurysm clip ligation – lessons learnt in a series of 72 patients

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Objective

The morphology of cerebral aneurysms is highly variable which may result in difficult surgical exposure for clip ligation in particular cases. Secure clip application is often not feasible without temporary intraaneurysmal pressure reduction. Such softening can be accomplished with transient adenosine-induced asystole. We here describe our experience with this technique in 72 patients.

Methods

We analyzed demographic data, aneurysm characteristics, application characteristics, radiological and clinical outcome, and procedure specific complications.

Results

Adenosine was applied in 72 patients (55 women, 17 men; mean age 56 years) who underwent microsurgical clipping of intracranial aneurysms: paraclinoid internal carotid artery (33 patients), anterior communicating artery (23 patients), middle cerebral artery (12 patients), and posterior inferior cerebellar artery (4 patients). 34 (47%) patients had suffered a subarachnoid hemorrhage from aneurysm rupture, 38 patients had carried incidental aneurysms. Mean aneurysm size was 10 mm (range 3-30 mm). Reasons for adenosine application were impracticality of temporary proximal vessel clipping (33 patients with paraclinoid internal carotid artery aneurysm), better visualization with softening of aneurysm (39 patients), and a very thin aneurysm neck (mycotic, blister like aneurysm) in 4 patients. Mean applied adenosine dosage was 21 mg (range 9-50 mg) with a mean cardiac flow arrest of 21 sec (range 0-69 sec). In 39 patients a single dose of adenosine was given, in 23 patients a repeated dose, in 7 patients a third, in 2 patients a fourth and in 1 patient a fifth dose. In 62 (86%) patients adenosine-induced asystole facilitated clip application but in 8 patients transient parent vessel clipping was additionally necessary, while in 2 patients aneurysm clipping was not possible (1 patient with a calcified aneurysm and 1 patient with blister like aneurysm). In 2 patients adenosine triggered transient atrial fibrilliation, in 1 patient it was self-limited, in the other cardioversion was required. Postoperative femoral angiography showed complete aneurysm occlusion in 70 (97%) patients. Postoperative cranial computed tomography revealed no cerebral infarction due to adenosine use.

Conclusion

In selected patients adenosine-induced transient cardiac arrest is a usesul technique to facilitate clip ligation. The use of adenosine is limited in patients with calcified, partially thrombosed and very thin walled (blister like, mycotic) aneurysms.

Neurovaskuläre Zentren II/*Neurovascular centres II*

V038

Adrenomedullin als Biomarker für den Schweregrad einer aneurysmatischen Subarachnoidalblutung und delayed cerebral ischemia

Adrenomedullin as a biomarker for severity of aneurysmal subarachnoid haemorrhage and delayed cerebral ischemia

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Objective

Adrenomedullin (ADM) is a potent vasodilator which has been identified as a promising marker of mortality and outcome in sepsis, heart failure and after major surgery. A recently developed assay specific for biologically active (bio-ADM) has not yet been assessed in patients suffering aneurysmal subarachnoid hemorrhage (aSAH). The objective of this prospective trial was to assess the time course of bio-ADM after aSAH in relation to the development of delayed cerebral ischemia (DCI) and clinical outcome.

Methods

Plasma levels of adrenomedullin were measured daily in 31 aSAH patients. Clinical and radiological severity was assessed by the Hunt and Hess (H&H) and modified Fisher (mFisher) grading scales, respectively. DCI was diagnosed clinically or based on CT perfusion imaging, and the occurrence of DCI-related cerebral infarction, as a result of treatment failure, was noted. Overall mortality was registered alongside clinical outcome after 12 months defined by the extended Glasgow Outcome scale (GOSE).

Results

Delayed cerebral ischemia was diagnosed in 14 (45.2 %) cases of which 7 (22.6 %) developed DCI-related cerebral infarction. Initial ADM levels were representative of clinical (H&H, $p = 0.024$) and radiological (mFisher; $p = 0.012$) aSAH severity. No significant differences in ADM levels before and after diagnosing DCI were noted ($p = 0.889$). After day four, ADM levels were higher in patients who developed DCI-related infarction (0.002) or died during hospitalization ($p = 0.030$). Favorable outcome (GOSE5-8) was noted in 13 (41.9 %) cases after 12 months. In multivariate analysis, only poor H&H ($p < 0.001$) and modified Fisher grading ($p = 0.004$) were associated with a decreased likelihood of achieving favorable outcome, but not ADM levels ($p = 0.493$).

Conclusion

Initial early ADM levels reflect the severity of aSAH but did not have predictive value on long-term clinical outcome. However, ADM levels were higher in patients who later developed DCI-related cerebral infarction or died during their hospital stay.

Neurovaskuläre Zentren II/*Neurovascular centres II*

V039

Einfluss der mikrovaskulären Dekompression bei Trigeminusneuralgie auf Depression und Patient*innenzufriedenheit

Effects of microvascular decompression for trigeminal neuralgia on depression and patient satisfaction

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Objective

Trigeminal neuralgia (TN) is associated with severe pain and reduced quality of life. Patients often develop fear of triggering pain, aggravates potential depression. This study aimed to investigate patient satisfaction and the prevalence and risk factors for depression before and after microvascular depression (MVD).

Methods

Barrow Neurological Institute Pain Score (BNI), Beck Depression Inventory (BDI), Chronic Pain Acceptance Questionnaire (CPAQ), Perceived Stress Questionnaire (PSQ) and McGill questionnaire were used to evaluate depression and anxiety disorders before and 3 months after MVD. The clinical data were collected prospectively and statistically analyzed.

Results

A total of 34 patients (19 (55.9%) females) with a mean age of 55.4 (21-79) years were included in this study. The mean BNI pain score of 4.6 preoperatively was significantly reduced to 1.8 postoperatively ($p<0.00001$). The BDI improved from 2.5 (± 1.4) preoperatively, to 1.2 (± 0.6) ($p < 0.0001$) postoperatively. CPAQ changed from 63.8 (± 13.4) to 67.1 (± 9,9) ($p = 0.006$). PSQ decreased from 46.9 (± 21.9) to 19.6 (± 18.6) ($p < 0.0001$)postoperatively and McGill from 31.0 (± 11.7) to 9.4 (± 12.9, $p < 0.0001$).

Conclusion

Depression is prevalent in patients with idiopathic TN. MVD not only provides high rate of satisfaction through pain-relief, but also leads to significant improvements in depression and anxiety symptoms. In patients with TN, microvascular decompression should be considered early in the course of the disease to minimize depression.

Wirbelsäulenzentren/*Spine centres*

V040

Erfahrung in interdisziplinärem re-zertifizierten level one Zentrum
Experience in a multidisciplinary re-accredited level one spine centre

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Objective

According to the DAK health insurance report from 2018, hospital treatment for spinal diseases is constantly rising. As the result of a rising need for treatment quality and the socioeconomic burden, establishment of specialized spinal centers seems to be of great importance, not only to be able to offer the complete interdisciplinary range of spinal treatment in high quality, but also for a recruitment of professions needed in future for those patients. This article reviews the experience of the first level one accredited spinal center in the eastern part of Germany.

Methods

Description of structures and performances of a multidisciplinary spine center founded 4 years before. To give a frank insight of the benefits associated to the foundation of an interdisciplinary center health professional of all associated medical disciplines and occupational categories at the university center were interviewed using in house generated questionnaire for quality control and later analyzed.

Results

In 4 years of the interdisciplinary university comprehensive spinal center, based on the DWG database we have been able to constantly increase the number of in and out hospital treated patients from 2016 to 2020. Due to process optimization (spinal boards, common treatment standard procedures, telephone back pain triage, uniform pain-protocol, continuing staff education, joint research, short communication channels etc…), patients treatment could be standardized. Indication quality and surgical skills improved due to interdisciplinary conferences, discussions and interdisciplinary surgeries of spinal cases.

Conclusion

Especially at university hospitals, the establishment of interdisciplinary spinal centers is inevitable. The way to establish such centers deeply depends on local structures, the will to find compromises and a motivated team. Development of a new medical profession combining the neurosurgical, trauma, orthopedic and conservative skills might be a consequential necessity to ensure the best quality in spine surgery. Furthermore, collaboration with other conservative professions and broad spinal education of surgeons treating those patients is imminent and a future challenge.

Wirbelsäulenzentren/*Spine centres*

V041

Lässt sich bei cervicaler Rückenmarksverletzung durch eine chirurgische Dekompression innerhalb von 5 Stunden ein besseres neurologisches Outcome erzielen als innerhalb von 24 Stunden?

Functional outcomes in individuals undergoing very early (< 5 h) and early (5-24 h) surgical decompression in traumatic cervical spinal cord injury – analysis of neurological improvement from the Austrian spinal cord injury study

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Objective

Our study aim was to assess the neurological outcomes of surgical decompression and stabilization within 5 and 24h after injury.

Methods

We performed a multi-center, retrospective cohort study in adolescents and adults 15-85 years of age presenting cervical spinal cord injury (CSCI) at one of 6 Austrian trauma centers participating in the Austrian Spinal Cord Injury Study (ASCIS). Neurological outcomes were measured using the American Spinal Injury Association Impairment Scale (AIS) grade according to the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) form after at least 6 months of follow-up (FU).

Results

Of the 49 enrolled patients with acute CSCI, 33 underwent surgical decompression within 5 h (mean 3.2 h ± 1.1 h; very early group) after injury, and 16 underwent surgical decompression between 5 and 24 h (mean 8.6 h ± 5.5 h; early group). Significant neurological improvement was observed among the entire study population between the preoperative assessment and the FU (p=0.0002). We identified a significant difference in the AIS grade at the last FU between the groups the using Jonckheere-Terpstra test for doubly ordered crosstabs (p = 0.011) and significantly different AIS improvement rates in the early group (p=0.018). Improvement by one AIS grade was observed in 31% and 42% of the patients in the early and very early groups, respectively (p=0.54). Improvement by two AIS grades was observed in 31% and 6% of the patients in the early and very early groups, respectively (p=0.03). Improvement by three AIS grades was observed in 6% and 3% of patients in the early and very early groups, respectively (p=1.0).

Conclusion

Decompression of the spinal cord within 24 h after SCI was associated with an improved neurological outcome. No additional neurological benefit was observed in patients who underwent decompression within 5h of injury.

Wirbelsäulenzentren/*Spine centres*

V042

Klinische und radiologische Langzeitergebnisse nach chirurgischer Behandlung von lumbalen Spondylodiszitiden – eine retrospektive multizentrische Studie

Long-term clinical and radiological outcome following surgical treatment of lumbar spondylodiscitis – a retrospective multicentre study

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Objective

Spinal instrumentation for spondylodiszitis remains highly controversial. To date surgical data is limited to relatively small case series with short term follow up data. In this study, we wanted to elucidate biomechanical, surgical and neurological long-term outcomes in these patients.

Methods

We retrospectively screened the databases of two German primary care hospitals and identified 190 patients with non-specific SD over a 9-year period (2005-2014). Inclusion criteria were a) non-specific, non-tuberculous lumbar SD, b) minimum follow-up 1 year, c) Following surgical instrumentation. Clinical and radiological outcome was assessed before surgery, at discharge and at a minimum of 12 months follow up.

Results

Complete data was available in 70 patients (49 male, 21 female, age 67.0±12.1 years) with a median follow-up of 6.6±4.2 years. Follow-up data was available in 70 patients after 1 year, in 58 patients after 2 years, and 44 patients after 6 years. 35 patients underwent posterior stabilization and decompression alone, 35 were operated in a two-stage 360° interbody fusion with decompression. Pre- and postoperative angles of the affected motion segment were 16±10.8 and 14±11.3° in patients with posterior instrumentation only, 19±9.6 and 16.9±9.7° in patients with combined anterior/posterior fusion. Vertebral body subsidence was seen in 12(34.3%) and 6(17.1%) cases following posterior instrumentation and 360° Instrumentation, respectively. Non-Fusion was encountered in 22 (62.9%) and 11 (31.4%) cases following posterior instrumentation and 360° instrumentation, respectively. Length of hospital stay was 35±24.8 days. Overall surgery-associated complication rate was 18%(12/70). New neurological symptoms occurred in 7%(5/70). Revision surgery was performed in 3% (2/70) due to screw misplacement/hardware failure and in 4% (3/70) due to intraspinal hematoma. During follow-up, there were no SD-related deaths.

Conclusion

Surgical treatment of spondylodiscitis with a staged surgical approach (if needed) is safe and provides excellent long term clinical and radiological outcome.

Wirbelsäulenzentren/*Spine centres*

JM-PSN-01

Langzeitergebnisse und sagittales Alignment nach posteriorer Foraminotomie bei lateralem Bandscheibenvorfall der Halswirbelsäule

Long-term results and sagittal alignment after posterior foraminotomy for unilateral cervical radiculopathy

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Objective

Cervical posterior foraminotomy (PF) provide direct decompression of the nerve root, while maintaining cervical mobility by the avoidance of fusion. On the other hand, the posterior approach carries a risk of postoperative segmental instability due to partial facetectomy. The aim of the study was to evaluate the clinical outcomes in correlation with cervical sagittal balance in long term follow up after PF.

Methods

A prospective evaluation of a retrospective cohort of 48 consecutive patients operated on in 2005–2016 was performed. Clinical status was assessed by the Numerical Rating Scale (NRS) and Neck Disability Index (NDI). Sagittal balance was evaluated preoperatively and in follow up by the modified Toyama method, expressed as lordotic, straight or kyphotic alignment. The mean follow-up period was 8.3 years (range: 4.6–14.7 years).

Results

Surgery was performed on one cervical level in 44 (92%) cases, and on two levels in 4 (8%) cases. The mean preoperative NRS for arm and neck pain, and NRS was 8.13 (range: 6 - 10), 5.65 (range: 0 - 10) and 36.58 (range: 12 - 48), respectively. The mean postoperative NRS for arm and neck pain, and NRS was 1.38 (range: 0 - 7), 1.58 (range: 0 - 8) and 11.63 (range: 0 - 34), respectively. The Minimal Clinically Important Difference (MCID) was achieved in 94% of cases for NRS arm pain, 77% for neck pain, and 98% for NDI. None of the follow up flexion–extension radiograms showed spinal instability. According to the modified Toyama method satisfactory radiological results, defined as stable pre- and postoperative lordosis or straight spine or change toward lordosis were found in 37 (80%) patients in our series. Unsatisfactory results, defined as stable pre- and postoperative kyphosis or change toward kyphosis were found in 8 (17%) patients. This group included 3 patients with pre- and postoperative stable kyphosis, 3 patients who worsened their cervical alignment towards kyphosis after surgery, and 2 kyphotic cases despite subsequent ACDF on the same level. Multilevel degenerative disk disease (mcDDD) were found in all 8 (100%) cases with unsatisfactory radiological result, and only in 3 (8%) cases out of satisfactory group (p=0.001). Follow-up NDI scores, but not MCIDs, were significantly worse in patients with preoperative kyphosis (18.75 vs. 10.20; p=0.03) or mcDDD (17.17 vs. 9.78; p=0.024) compared to other patients.

Conclusion

Patients with preoperative kyphosis or mcDDD had worse NDI outcomes, but they also benefitted from PF. The mcDDD may play more important role than preoperative sagittal balance as a predictor for kyphosis persistence in long term after PF.

Wirbelsäulenzentren/*Spine centres*

V043

Inzidenz, Risikofaktoren und Therapie von iatrogenen Durotomien während lumbaler Dekompression
Incidence, risk factors, and treatment of incidental durotomy during lumbar decompression of the spinal canal

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Objective

The purpose of this study was to identify independent risk factors for incidental durotomy (ID) during one of the most common lumbar spine procedures and describe its treatment.

Methods

The presented study is a retrospective review of all patients who underwent lumbar decompression of the spinal canal at a tertiary institution between January 2015 and October 2019. Data collection was obtained through one independent researcher with respect to demographic data, admission charts, surgical details, and postoperative reports. In addition, preoperative magnetic resonance imaging (MRI) datasets were reviewed to evaluate potential risk factors for ID.

Results

The incidence rate of ID was 12.6% (88 of 698 cases). The most common reason for admission was disc herniation (63.2%), followed by vertebral stenosis (22.1%). ID was significantly associated with longer operation time (p=0.0001) and length of hospitalization (p=0.0001). A correlation between ID and patient"s diagnosis (p=0.0078) as well as the chosen type of surgery (p=0.0404) with an odds ratio to cause ID of 1.9 for laminectomy and 1.6 for undercutting compared to microdiscectomy were found. However, age, sex, surgeon experience, lumbar level, revision surgery, multilevel surgery as well as preoperative MRI findings were not significantly correlated with the incidence of ID. Dural tears were closed with TachoSil® (47.2%), polyester 4-0 sutures (11.1%) or a combination of both (37.5%) and the majority of patients had bed rest of at least two days (55.2%). By usage of these treatment methods no patient needed reoperation.

Conclusion

In lumbar spine procedures, vertebrostenosis and its treatment, are identified as risk factors for ID. In our cohort, dural closure procedure followed by bed rest, led to complication free postoperative courses. Nevertheless, ID should not be underestimated as it leads to prolonged operating times and postoperative hospitalization.

Wirbelsäulenzentren/*Spine centres*

V044

Erhöht eine vorausgegangene Operation die chirurgischen Komplikationen bei PLIF-Operationen im Index-Segment?

Does prior spinal surgery increase the surgical complication rate for PLIF procedures at the index segment?

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Objective

Posterior lumbar interbody fusion (PLIF) surgery is used widely in the treatment of various degenerative pathologies of the lumbar spine. Its combination with dorsal pedicle screw fixation increases the construct rigidity and provides earlier stability. However, PLIF surgery necessitates mobilization of the dural sac to introduce the cage into the intervertebral space. The approach to a segment which was operated before (disc surgery or laminectomy) is usually more demanding because of scar tissue and the adherent dura, which makes the insertion of the PLIFS more risky. Here we examined whether a prior surgery increases the risk for intraoperative complications during PLIF surgery.

Methods

Over a time period of 8 years, 213 patients underwent PLIF surgery of the lumbar spine in our department. Group A consisted of 82 patients who had prior surgery (33 had a discectomy and 61 had a dorsal spinal canal decompression), while the 131 patients in group B had no prior surgery at the index segment. The clinical and operative data were collected from the patients´ record and the occurrence of operative complications was compared between both groups.

Results

There were 96 men and 117 women. The median age in group A and B was 53 vs. 54, respectively. The median surgery time was longer in group A than B (277 vs. 260 minutes , p = 0,026). In group A, the incidence of postoperative epidural hematomas (5 vs. 1, p = 0,022) and immediate neurological deficits (8 vs. 0, p = 0,001) was significantly higher. At discharge, deficits were improved in six out of eight patients. Dural tears (11 vs. 8, p = 0,068) tended to occur also more frequently in group A. There was no significant difference regarding the time of hospital stay between both groups (median values: 8 vs.7 days, p = 0,240).

Conclusion

Although the risk for dural tears and postoperative neurological deficits is higher in patients with prior surgery, our results suggest that PLIF surgery is also safe in this group of patients. Meticulous preparation of the dural sac and the spinal nerve roots may avoid dural or neural injury.

Wirbelsäulenzentren/*Spine centres*

V045

Stellt Adipositas ein Risikofaktor für die minimalinvasive transforaminale lumbale Spondylodese (TLIF) dar?
Is obesity a significant risk factor for minimally invasive transforaminal lumbar interbody fusion?

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Objective

Percutaneous pedicle screw placement can be challenging in obese patients. The objective of this study was to compare complication rates, patient-reported outcomes and quality of life between obese and non-obese patients that underwent minimally invasive transforaminal lumbar interbody fusion (MIS-TLIF) for degenerative spine disease.

Methods

This is a review of consecutive patients that were treated by MIS-TLIF at a single center between 2011 and 2014. According to their body mass index (BMI), patients were classified as obese (BMI ≥30 kg/m2) or non-obese (BMI <30 kg/m2). Primary outcome measures were surgical complications, numerical rating scale (NRS) scores for back and leg pain, Oswestry Disability Index (ODI) and quality of life as determined by the Short-form 36 (SF36) scores.

Results

A total of 71 patients were included, of which 24 were obese (34%, 35 ± 4 kg/m2) and 47 were non-obese (66%, 25 ± 3 kg/m2). Regarding complication rates, no significant differences were observed among instrumentation failures (14% vs. 17%, p=0.07), dural tears (17% vs. 4%) and revision rates (17% vs. 19%). There were no significant differences in postoperative improvements in back pain (4.3 vs. 5.4 points, p=0.07), leg pain (3.8 vs. 4.2 points, p=0.6) and ODI (13.3 vs. 22.5 points, p=0.5), both postoperatively and at long-term follow-up. Obese patients had worse postoperative physical component SF36 scores than non-obese patients (36.4 vs. 42.7 points, p=0.03), while the mental component scores were statistically indifferent (p=0.09).

Conclusion

Obese patients can achieve similar improvement of the pain intensity and functional status even at long-term follow-up. In patients with appropriate surgical indications, obesity should therefore not be considered a contraindication for MIS-TLIF surgery.

Wirbelsäulenzentren/*Spine centres*

V046

Auftreten von Anschlussfrakturen nach chirurgischer Versorgung einer osteoporotischen Wirbelkörperfraktur – ein Vergleich zwischen zwei verschiedenen Therapiemethoden

Occurrence of adjacent segment fractures after surgical treatment of an osteoporotic vertebral fracture – a comparison between two different treatment methods

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Objective

Osteoporotic vertebral fractures are a major healthcare problem. A vertebral cement augmentation (VCA) could be used as a minimally invasive surgical approach to manage symptomatic fractures. However, there is a potential risk for an adjacent segment fracture (ASF), which may require second surgery. The addition of transcutaneous screw-fixation with cement-augmentation superior and inferior to the fracture (Hybrid transcutaneous screw-fixation HTSF) may be a good, minimally invasive alternative to reduce the incidence of ASF.

Methods

We have investigated the duration of surgery, hospital stay, intraoperative complication rate and ASF with the need for a surgical therapy in a cohort of 100 consecutive patients receiving either VCA or HTSF in our academic neurosurgical department during the period 2013 to 2018. The median follow-up was 1 year.

Results

During study period, 50 patients received VCA and 50 HTSF. Altogether 68 women (35 VCA; 33 HTSF) and 33 men (15 VCA; 17 HTSF) have been treated. The median-age was 76.5 years (76y VCA; 77 y HTSF). The median duration of surgery was 33.5 min in VCA-group and 99.9 min in the HTSF-group ($p < 0.0001$). No surgery related complications occurred in the VCA-group with just 1 in the HTSF-group ($p = 1$). The median hospital stay was 9.5 days in the VCA-group and 11 days in the HTSF-group ($p = 0.02$). Thirteen patients (26%) in the VCA-group, whereas just four patients (8%) in the HTSF-group developed an adjacent segment fracture in the follow-up ($p = 0.031$). Ten patients from the VCA-group (10%) und 3 patients (6%) in the HTSF-group received further surgery after the first operation owing to ASF ($p = 1$).

Conclusion

Based on this single-center cohort, HTSF appears to be a safe and effective option for the treatment of osteoporotic vertebral compression fractures. The duration of surgery was longer than in the HTSF-group, but the rate of ASF can be significantly reduced with the HTSF approach. Further prospective studies are required to address whether HTSF results in a lower revision rate or better postoperative quality of life.

Fig. 1

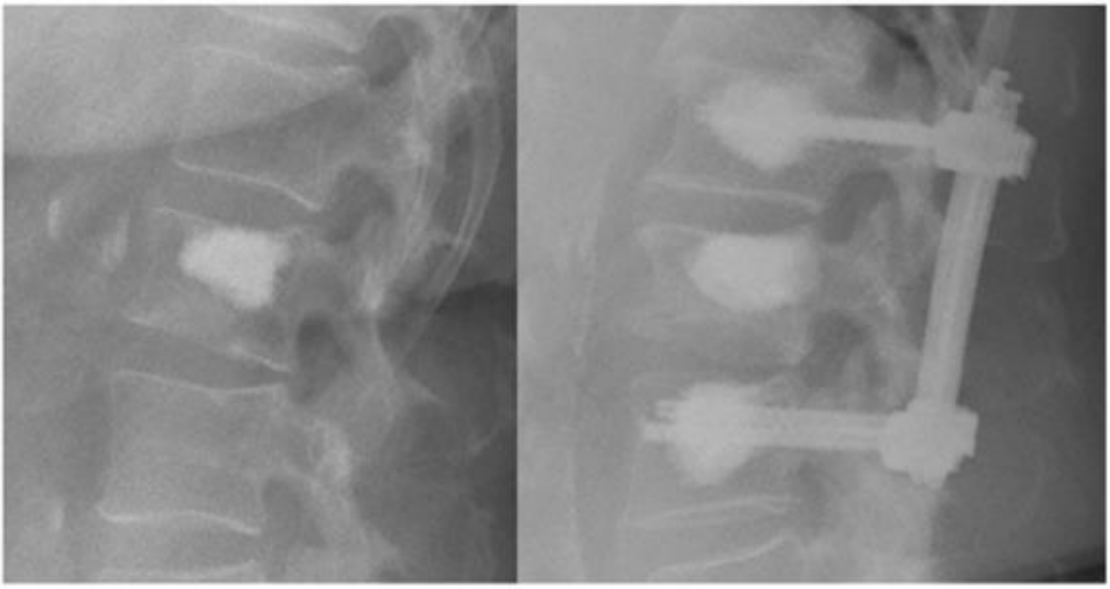

Fig. 1: Sagittal X-ray of the lumbar spine. Left: Vertebral cement-augmentation (VCA); Right: Transcutaneous cement-augmented screw-fixation with vertebral cement-augmentation (HTSF)

Wirbelsäulenzentren/*Spine centres*

V048

Gibt es Faktoren, die den Erfolg der Spinal Cord Stimulation (SCS) bei Patienten mit chronischen Beinschmerzen beeinflussen?

Are there any influence factors on the benefit of spinal cord stimulation (SCS) in patients with chronic neuropathic leg pain?

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Objective

Spinal cord stimulation (SCS) is an established and effective minimally invasive surgical method for the treatment of neuropathic leg pain. This retrospective study aims to explore factors that may influence the benefit of SCS in patients with chronic leg pain.

Methods

Between 2009 and 2018 40 patients with chronic neuropathic leg pain were treated with SCS. Charts were reviewed regarding personal data including sex, age, Body-Mass-Index, education, regular use of pc and smartphone, medical comorbidities, morbidity, ASA score, previous spinal surgery, time to last surgery, and presurgical pain medication. Furthermore pain intensity (NRS), test for neuropathic pain (DN4), generic health status (EQ-5D-5L), Oswestry Disability Index (ODI), Pain Disability Index (PDI), and Becks Depressions Inventary (BDI) were assessed for the pre- and postoperative status as well as 6 and 12 months postoperatively. Statistical analysis was performed using ANOVA and depended t-test.

Results

The 40 patients (19 females, 21 males) with a median age of 59 years (IQR25-75 54-68) had a significant improvement of NRS ($p<0.001$), DN4 ($p<0.001$), EQ-5D-5L ($p<0.001$), ODI ($p<0.001$), PDI ($p<0.001$) and BDI ($p=0.003$) one year after the SCS treatment compared to baseline.

Factors like sex, age, Body-Mass-Index, education, regular use of pc and smartphone, diagnoses, medical comorbidities, morbidity, ASA score, previous spinal surgery, time to last surgery, and presurgical pain medication had no influence on improvement of SCS treatment.

Conclusion

The treatment benefit of SCS is not affected by any factors. We conclude that SCS is a minimally invasive and effective surgical procedure, which can be applied in patients with chronic leg pain, regardless their personal characteristics and co-morbidity.

Patientensicherheit/*Patient safety*

V049

ACKT – ein neuer Score zur Vorhersage einer postoperativen invasiven Beatmung nach chirurgischer Behandlung von geriatrischen Meningeompatienten

ACKT – a novel score to predict prolonged mechanical ventilation after surgical treatment of meningioma in geriatric patients

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Objective

Indication for surgical treatment in patients with intracranial meningioma must include both clinical aspects and an individual risk-benefit stratification, especially in geriatric patients. Prolonged mechanical ventilation (PMV) has not been investigated for its potential effects in patients with meningioma. We therefore have analyzed the impact of PMV on mortality in geriatric patients that had undergone meningioma resection.

Methods

Between 2009 and 2019, 261 patients aged ≥ 70 years were surgically treated for intracranial meningioma at our institution. PMV was defined as postoperative invasive ventilation of > 7 days.

Results

Postoperative PMV was present in 17 of 261 geriatric meningioma patients (7%). 25 geriatric patients (10%) died within 1 year after surgery. Multivariate analysis identified "postoperative PMV" ($p<0.0001$) and "preoperative corticosteroid medication" ($p=0.03$) as independent predictors for 1-year-mortality. A scoring system ("ACKT") based on the variables **A**ge, **C**RP-value, **K**arnofsky performance scale and **T**umor size supports prediction of postoperative PMV (sensitivity 73%, specificity 84%).

Conclusion

PMV is a significant and independent predictor for increased mortality after surgical treatment of meningiomas in geriatric patients. Furthermore, we suggest a novel score ("ACKT") to preoperatively estimate the risk of PMV occurrence which might help to guide future risk-benefit assessment and patient counselling in the geriatric meningioma population.

Patientensicherheit/*Patient safety*

V050

Entwicklung der aseptischen Knochennekrose nach autologer Kranioplastik anhand einer computertomographisch-basierten Analyse
Development of aseptic bone flap necrosis after autologous cranioplasty based on CT-scan analysis

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Objective

Aseptic bone necrosis is still a common long-term complication after bone flap reinsertion following initial decompressive craniectomy. Aim of the study was to monitor the structural changes of the bone flap after cranioplasty as well as to determine the impact of an additional liquor shunt.

Methods

Thirty-four (22 male, 12 female) patients, who received a cranioplasty between September 2004 and April 2010, have been included. The medium age was 47 years at the time of cranioplasty. Reasons for the initial craniectomy were a subarachnoid haemorrhage (n = 10), a subdural or epidural haemorrhage (n = 11), a malignant cerebral infarction (n = 11) and an intracerebral haemorrhage (n=2).

We retrospectively analysed the first post-operative and follow-up CT scans and measured the bone density in Hounsfield units (HU), bone thickness (measurement at different defined points), the development of a bone bridge and a modification of the Lakshmanan score based on the trabecular pattern (Fig.1). The median follow-up was 44 months.

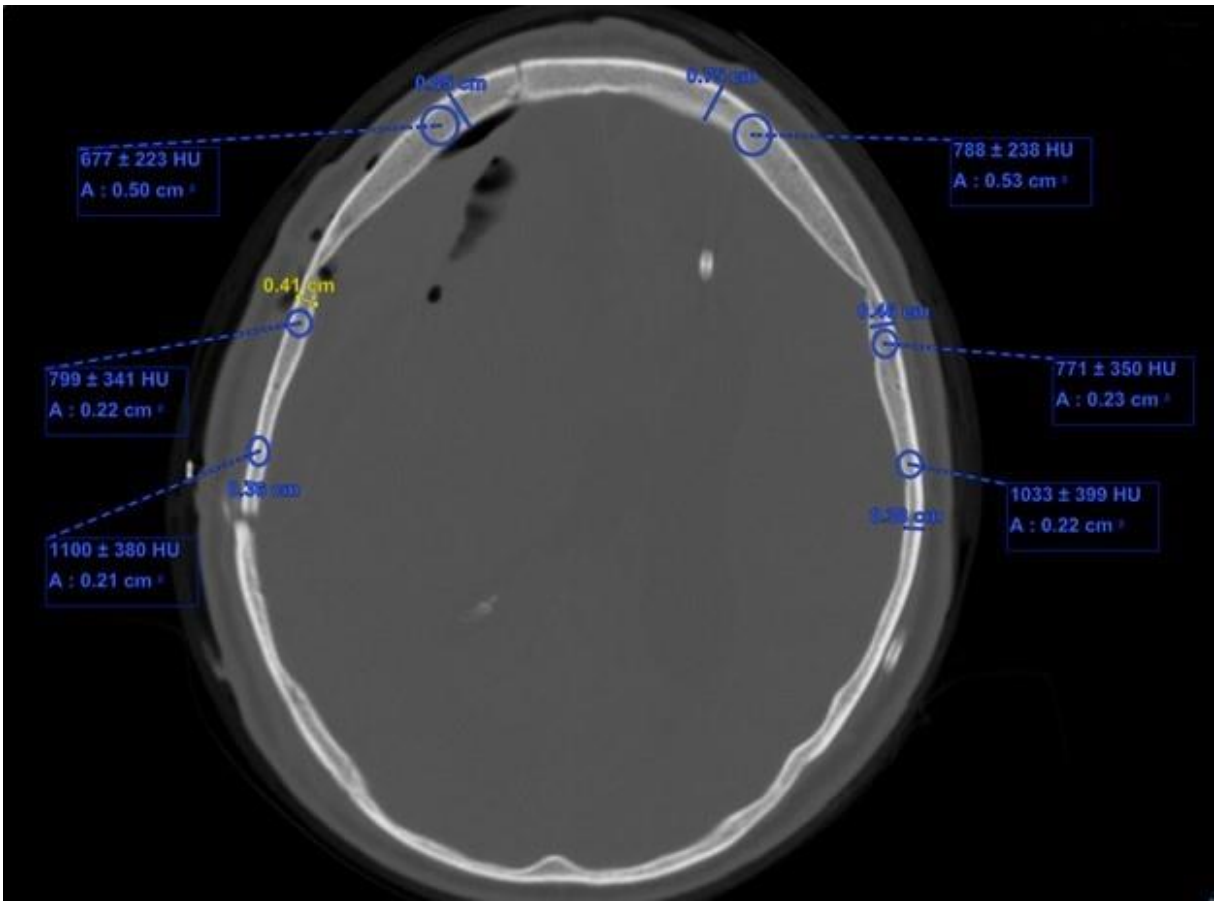
Results

A significant loss of bone density with an average decline of 22.5 % ($p<0.001$) occurred in 29 patients (85.3%). Decline of bone density within the first 6 months was statistically relevant with a mean decrease from 1066 HU to 900 HU ($p<0.001$). 31 patients (91.2%) had a decrease in the bone thickness with an average loss of 1,62 mm. A decrease of the trabecular pattern was noticed in 24 (70.6%) patients. In 12 cases (35.3 %; 6 with shunt (17.7%), 6 without (17.7%) a surgery caused by the aseptic necrosis was indicated. Patients with a ventriculoperitoneal shunt (WS) had a slightly higher bone density than those without shunt (WOS), (WS: 886.07 HU; WOS: 800.84 HU, $p = 0.488$).

Conclusion

Decline in bone density and bone thickness were common observations in this study. The decrease seems to be relevant especially in the first 6 months. For this reason, patients should be monitored particularly closely during this time. Further patients should be analysed to investigate, whether there is a significant difference between patients with or without a ventriculoperitoneal shunt.

Fig. 1


677 ± 223 HU
A : 0.50 cm
788 ± 238 HU
A : 0.53 cm
0.41 cm
799 ± 341 HU
A : 0.22 cm
771 ± 350 HU
A : 0.23 cm
1100 ± 380 HU
A : 0.21 cm
1033 ± 399 HU
A : 0.22 cm

Patientensicherheit/*Patient safety*

V051

Einfluss von Komorbiditäten und Frailty auf frühes Shuntversagen bei geriatrischen Patienten mit Normaldruck-Hydrozephalus

Impact of comorbidities and frailty on early shunt failure in geriatric patients with normal pressure hydrocephalus

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Objective

Older patients are considered to bear a higher perioperative risk. Since idiopathic normal pressure hydrocephalus (NPH) predominantly concerns older patients, identifying risk factors for early shunt failure for preoperative risk/benefit assessment is indispensable for indication and/or consultation of patients for ventriculoperitoneal shunting (VPS).

Methods

We performed a retrospective study design, including data acquired from two university hospital neurosurgical institutions between 2012 and 2019. Overall, 211 consecutive patients with clinical/radiological signs for NPH who additionally showed alleviation of symptoms after lumbar cerebrospinal fluid (CSF) drainage, received VPS and were included for further analysis. Frailty was measured using the Clinical Frailty Scale (CFS). Main outcome was early shunt failure or postoperative complications within 30 days after initial VPS surgery.

Results

The overall complication rate was 14%. Patient-related complications 35 were observed in 13 patients (6%) and procedure-related complications in 16 patients (8%). Early postoperative complications resulted in a significantly prolonged length of hospital stay 6.9 ± 6.8 vs. 10.8±11.8 days (p=0.03). Diabetes mellitus with end-organ damage (OR 35.4, 95% CI 6.6-189.4, p<0.0001) as well as preexisting Parkinson"s disease were associated with early patient-related postsurgical complications after VPS for NPH.

Conclusion

Patients comorbidities but not frailty were associated with early postoperative patient related complications in patients suffering NPH. While frailty may deter patients from other (neurosurgical) procedures, VPS surgery might contribute to treating NPH in these patients at a tolerable risk.

Patientensicherheit/*Patient safety*

V052

Einfluss von Dexamethason auf die frühe metabolische Rekompensation auf der Intensivstation bei neuroonkologischen Patienten
Impact of dexamethasone on early metabolic recompensation on intensive care unit in neurooncological patient

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Objective

The aim of this study is to evaluate the impact of pre- and intraoperative steroid administration on the metabolic recompensation in the early postoperative intensive care unit phase of patients undergoing neurosurgical removal of intracranial tumors, such as gliomas and meningiomas.

Methods

In total, we included 674 patients which underwent neurosurgical resection and were followed up on ICU. Tumor histology included glioblastoma (IDHwt, n = 284), astrocytoma (IDHmut, n = 184), 142 oligodendroglioma (n = 142), and meningioma (n = 100). Basic parameters, such as gender, age, pre- and perioperative dexamethasone administration, tumor location, Ki67 index, WHO grade, surgery lengths, as well as 17 postoperative metabolic and basic blood parameters recorded while in intensive care were analyze using a LMER and a linear statistic approach. Patients were subsequentially stratified into high (>4mg) and low (<4mg) cumulative dexamethasone application pre- and intraoperatively. This retrospective study of anonymized data sets was performed in concordance with the local ethic guidelines.

Results

Multivariate analysis showed that patients receiving high doses of dexamethasone displayed strong metabolic alterations, as they had a significantly higher pH, with increased base excess and HCO3 levels, accompanied by a steadily increased lactate level (all $p<0.001$), never reaching the same level in the early postoperative phase (24h) on ICU. In addition, systolic and diastolic blood pressure levels ($p<0.01$) were significantly increased in the high dexamethasone group. As expected, increased blood pressure levels inversely correlated with a reduced heart frequency, which was on average 10bpm lower throughout the whole ICU stay in the high dexamethasone group. After the first 10h on the ICU, patients receiving high dose dexamethasone displayed a reduced body core temperature (mean reduction -0.3°C, $p<0.001$). The effect on the glucose metabolism was significant in the early phase (hours 0-5), and increased after 20h ICU stay, showing significant glucose derangements (>200mg/dl; $p<0.05$). No differences were found between different tumor entities.

Conclusion

We found that pre- and intraoperatively administration of high doses of dexamethasone had significant impact on the metabolic recompensation of neurooncological patients undergoing neurosurgical resection and may have to be used more cautiously in the future.

Patientensicherheit/*Patient safety*

V053

Engpässe bei der Heparinversorgung – der sichere Einsatz von Tinzaparin und Fraxiparin in der Neurochirurgie
In times of heparin shortage – Tinzaparin vs. Fraxiparin safety and efficacy in neurosurgery

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Objective

An outbreak of African swine fever (ASF) in China has led to an unprecedented shortage of heparin. Most patients, especially those kept in hospital for surgery, are currently treated with prophylactic anticoagulation (AC). Should swine fever continue to reduce heparin availability, hospitals all over the globe might have to rethink and reorganize their supply. We compared tinzaparin of non-Chinese origin as an alternative to fraxiparin concerning adverse events (bleeding versus thromboembolic events) in neurosurgical patients.

Methods

Between 2012 and 2018, 517 neurosurgical patients with benign and malignant brain tumors as well as 297 patients with subarachnoid hemorrhage (SAH) were treated in the Department of Neurosurgery, University Hospital Leipzig receiving prophylactic anticoagulation within 48 hours. In 2015, prophylactic anticoagulation was switched from fraxiparin to tinzaparin throughout the university hospital. In a retrospective manner, the frequency and occurrence of adverse events (rebleeding and thromboembolic events) in connection with the substance used was analyzed. Statistical analysis was performed using Fisher"s exact test and the chi-squared test.

Results

Rebleeding rates were similar in both fraxiparin and tinzaparin cohorts in patients being treated for meningioma, glioma, and SAH combined (8.8 vs 10.3%). Accordingly, the rates of overall thromboembolic events were not significantly different (5.5% vs 4.3%). The severity of rebleeding did not vary. There was no significant difference among subgroups when compared for deep vein thrombosis (DVT) or pulmonary embolism (PE).

Conclusion

In this retrospective study, tinzaparin seems to be a safe alternative to fraxiparin for AC in patients undergoing brain tumor surgery or suffering from SAH.

Patientensicherheit/*Patient safety*

V054

Arzneimitteltherapiesicherheit in der Neurochirurgie – Einbindung von Stationsapothekern zur Reduktion von arzneimittelbezogenen Problemen im stationären Medikationsprozess

Regular clinical pharmacist medication review on a neurosurgical unit – a valuable contribution to improving patient safety

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Objective

Medication errors (MEs) are common among the inpatient population and overall 2% of patients admitted to hospitals are harmed as a result of MEs. Prescribing errors (PEs) are the most common type of ME and affect 2–15% of medication orders. Various interventions and strategies have been proposed to reduce the frequency of Pes, one of which is clinical pharmacist (CP) medication review. This study sought to determine the annual prevalence and nature of PEs in an academic neurosurgical department including its high-dependency unit (HDU). Moreover, the impact of weekly prescribing drug review by a CP and a combined surgeon-CP ward round was characterised.

Methods

During the observation period, weekly CP medication review and a combined surgeon-CP ward round took place on the 38-bed standard-care neurosurgical ward and the 10-bed HDU. PEs were determined by the CP following discussion with the surgical team. The focus of the evaluation was on drug dosing (therapeutic range, dosing interval, dose adjustment in cases of organ dysfunction). In addition, a comprehensive medication interaction check flagged interactions, which were evaluated for severity and clinical relevance. Time trends were evaluated to explore whether the CP intervention led to overall improved surgeon prescribing patterns and reduced PE rates over time.

Results

The CP identified 995 PEs across the 1795 neurosurgical patients (1370 normal ward, 425 HDU) over the 12 months. On the HDU ward, there were 0.68 PEs per patient, compared to 0.52 PEs on the normal ward. PE types identified were similar in both the normal ward and HDU settings. The most frequent PE was unclear or no longer relevant indication (17%) followed by drug interaction (12%), double prescribing (9%) and incorrect dosing interval (10%). The drugs most commonly associated with PEs were pantoprazole (5%), amlodipine (3%) and ciprofloxacin (3%).

Conclusion

Errors in drug prescribing and administration are common and arise from multiple interacting causes. The routine involvement of a clinical pharmacist for medication review led to prompt identification of a range of PEs in the normal ward and HDU environments, seemed to enhance surgeons' knowledge and prescribing skills and has the potential to impact on the safety of neurosurgical care.

Patientensicherheit/*Patient safety*

V055

suPAR als neuartiger, inflammatorischer Biomarker für die DCI-Vorhersage bei aSAB-Patienten
suPAR as a novel, inflammatory biomarker for DCI prediction in aSAH patients

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Objective

Delayed cerebral ischemia (DCI) prediction in aneurysmal subarachnoid hemorrhage (aSAH) is still an unsolved mystery, the solution of which could contribute significantly to the individualization and optimization of therapy. Soluble urokinase plasminogen activator receptor (suPAR) is a novel and pivotal inflammatory marker. High suPAR serum levels (suPAR-SL) have been associated with poor outcome in traumatic brain injury and stroke patients, but its importance is unclear in the context of aSAH. We aimed to characterize the role of circulating suPAR in both serum and CSF in aSAH patients.

Methods

All patients between 18 and 90 years of age admitted for aSAH to a tertiary care facility between 2014 and 2019 were screened for eligibility. Demographic data, the occurrence of DCI and clinical outcome (GOSE) were recorded. A healthy control group was included for comparison. suPAR was analyzed on the day of admission (all patients) and on the day of DCI or day 8 in aSAH patients without DCI. One- and two-sample t-tests were used for simple difference comparisons within and between groups. Two regression analyses were constructed to assess the influence of suPAR levels on outcome.

Results

A total of 36 aSAH patients and 32 healthy volunteers were included for analysis. Significantly elevated suPAR serum levels (suPAR-SL) were found for aSAH patients compared to healthy controls ($p < .001$). In aSAH patients, suPAR-SL increased daily by 4%, while suPAR CSF levels (suPAR-CSFL) showed a significantly faster daily increase by an average of 22.5 % ($p = .01$). Logistic regression analysis showed significant power in DCI prediction for suPAR-SL at admission ($p = .04$). Each increase of the suPAR-SL by one ng/ml more than tripled the odds of developing DCI (OR = 3.06). While admission suPAR-CSFL were not predictive of DCI, we observed a significant correlation with the dynamics of deterioration (time between admission and DCI: $p = .04$): each increase of suPAR-CSFL by one ng/ml accelerated clinical deterioration by almost an entire day. Concerning the outcome, elevated suPAR-SL at admission showed statistical significance for lower GOSE at discharge ($p = .04$).

Conclusion

We demonstrated that an initial increase in suPAR-SL is associated with the development of DCI and poor outcome. Higher suPAR-CSFL were associated with a more rapid DCI appearance. Biomarkers such as suPAR may help to further clarify the role of inflammation in the context of SAH.

Patientensicherheit/*Patient safety*

V056

Der Nutzen von Serumbiomarkern zur Optimierung der Sicherheit von intra-hospitalen Transporten cerebral verletzter neurochirurgischer Intensivpatienten

The potential of serum biomarkers for improving safety of intra-hospital transport in brain-injured neurosurgical intensive care unit patients

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Objective

Intra-hospital transport (IHT) of neurosurgical intensive care unit (NICU) patients can be hazardous. The potential of serum biomarkers for risk assessment of IHT-associated complications in brain-injured patients treated on NICU remains unknown. The present study was conducted to investigate the value of several serum biomarkers on IHT-associated complications in brain-injured NICU patients.

Methods

Prospective analysis of 523 IHTs in 223 NICU patients from 05/2019 to 05/2020. Demographic data, cranial computed tomography (CCT) scan on admission, Acute Physiology and Chronic Health Evaluation II (APACHE II) before IHT, modified Rankin Scale (mRS) at discharge as well as indications and consequences of all IHTs were analyzed. Alteration of ICP/CPP, hemodynamic and pulmonary events were defined as complications. Furthermore, hemoglobin, hematocrit, serum sodium, and albumin levels were evaluated as serum biomarkers. The study population was dichotomized into: IHTs with complications and IHTs without complications.

Results

The entire study population consisted of 98 women (43.9%) and 125 men (56.1%) with a mean age of 62.9 ± 14.9 years. At least one IHT-associated complication was identified in 58.7% of all IHTs and 60.1% of all IHTs had no direct therapeutic consequence. No significant difference was found between the two groups with regard to median GCS score on admission ($p=0.21$), APACHE II score before ($p=0.56$) and mRS score ($p=0.09$) at discharge. Furthermore, IHT for emergency CCT was not associated with a higher complication rate compared to IHT for routine control CCT ($p=0.8$) and postoperative CCT ($p=0.66$). In patients with lower hemoglobin levels before IHT, significantly higher rates of elevated intracranial pressure (ICP) ($p<0.0001$), decreased cerebral perfusion pressure (CPP; $p=0.03$) and more hemodynamic ($p<0.0001$) and pulmonary events ($p=0.01$) were observed. In addition, lower hematocrit levels prior to IHT were associated with a higher complication rate concerning hemodynamic ($p<0.0001$), pulmonary ($p=0.006$), ICP ($p<0.0001$), and CPP ($p=0.01$) events.

Conclusion

IHTs should be carried out on a restricted basis due to their risk for pulmonary and hemodynamic complications. Hemoglobin and hematocrit levels should be checked before IHT, as lower levels of these biomarkers are associated with a higher risk for ICP, CPP, hemodynamic and pulmonary events during transport.

Funktionelle Neurochirurgie und Schmerz I/*Functional neurosurgery and pain I*

V058

Können bilaterale zentrale Fußheberparesen durch beidseitig implantierte Peroneusstimulatoren behandelt werden?
Can bilateral central drop foot be treated by bilaterally implanted peroneal nerve stimulators?

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Objective

Peroneal nerve stimulation using implantable devices was shown to be highly effective in patients with central drop foot caused by stroke or multiple sclerosis (MS). The devices lead to a significant better improvement of the dynamic gait pattern than foot orthosis or surface stimulation. Here, we describe for the first time the long-term outcome after bilateral implantations.

Methods

Between 2014 and 2016 two MS patients and one hereditary spastic paraplegia (HSP) patient were bilaterally treated with implantable peroneal nerve stimulators. Each stimulation system consisted of an external control unit, a heel switch, and an implantable 4-channel nerve stimulatorwith a 12-contact electrode cuff around the peroneal nerve. The heel switch, which is worn in a sock, triggers the initiation and termination of each stimulation sequence by a radiofrequency wireless signal to the external control unit. Extensive gait analysis including video documentation and evaluation of quality of life (QoL) was performed prior to surgery and after 6, 12, 48 months.

Results

All three patients showed an impressive improvement of their gait pattern including a mean improvement of 19% in the 20-m gait test, 29% in the 6-minute walking test, and 26% in the timed up-and-go test. QoL showed a marked improvement in all patients. One MS patient was wheelchair dependent and finally managed to walk with walking aids, the HSP patient impressively improved especially in gait endurance, and one MS patient developed a much better gait safety with an almost normal gait pattern.

Conclusion

We herewith show for the first time that bilateral drop foot can be successfully treated by bilateral peroneal nerve stimulators. The stimulator systems work independently and are separately triggered by the respective heel switch of the foot that is lifted from the ground. The bilateral implantation led to an impressive improvement of the gait pattern in all three patients with marked improvements in gait analysis and QoL assessment. With a follow-up of more than 4 years without technical and surgical complications bilateral implanted peroneal nerve stimulators seem to be a good treatment option for patients with bilateral drop foot.

Funktionelle Neurochirurgie und Schmerz I/*Functional neurosurgery and pain I*

V059

Chirurgisches Langzeit-Management von Patienten mit Tiefer Hirnstimulation zur Behandlung psychiatrischer Erkrankungen

Deep brain stimulation for psychiatric disorders – long-term surgical management

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Objective

Deep Brain Stimulation (DBS) has implemented itself as a hallmark in movement disorder therapy and has been explored for psychiatric disorders in clinical trials as an adjunct treatment. Data on how to surgically manage these patients long after the clinical trial has ended is currently lacking.

Methods

A single center database analysis was performed to identify all cases of DBS for psychiatric indications. Epidemiologic data, number and type of follow-up surgeries after initial implantation, rate of complications, success in long-term therapy and documented stimulation parameters were analyzed.

Results

Over 17 years n=103 patients were implanted with a DBS system for a psychiatric indication (excluding dementias) with a mean follow-up of 106 months. Mean age was 43.1 years with two thirds being female. Indications were major depression (n=66), bipolar disorder (n=6), OCD (n=6), anorexia nervosa (n=22) and Tourette"s syndrome (n=3). The predominant target structure was the subgenual cingulate gyrus (CG25, 91% for depression, bipolar disorder and anorexia. The interthalamic peduncle (ITP, 6%) and the centromedian-parafascicular nucleus of the thalamus (CM-Pf, 3%). 48.5% of all patients still had an active DBS system with a mean follow-up of 94 months at the time of the study. 21.4% of patients had the system explanted with lack of efficacy being the most common one (77% of explants). IPG replacements were the most common scheduled surgery with an average of 2.3 replacements per patient. IPGs lasted for an average of 24.0 months with average stimulation parameters of 130Hz, 85µs and 5.3V. N=42 patients were switched to a rechargeable IPG with 24% being switched back to a non-rechargeable IPG later on. 37% of patients had unscheduled surgeries for wound-related complications (15.5% of patients), hardware related issues (10.6%) or suboptimal electrode placement (1.0%).

Conclusion

Patients with DBS for psychiatric disorders represent a separate entity compared to movement disorder patients. The rate of explants and unscheduled surgeries is higher. High stimulation parameters demand frequent IPG replacements generating a considerable rate of wound-related complications. Strategies to reduce the number of IPG replacements (optimization of stimulation parameters, use of rechargeable IPGs) could help to increase the rate of long-term responders in the future. When conceiving trials, strategies on how to enable long-term therapy for these patients should be considered.

Funktionelle Neurochirurgie und Schmerz I/*Functional neurosurgery and pain I*

V060

Tiefe Hirnstimulation des Nucleus accumbens im Adipositas Mausmodell
Deep brain stimulation of nucleus accumbens in obese mice

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Objective

According to WHO the worldwide obesity has nearly tripled in the past 50 years; almost 2 billion adults were overweighed in 2016. In order to provide a novel approach in the therapy of obesity, we investigated in this experiment the effects of Deep Brain Stimulation (DBS) in Nucleus Accumbens (NAc) on the metabolism of mice.

Methods

We put B6 mice on high fat diet and performed surgery to implant DBS electrodes in bilateral NAc. Subjects were divided in either a high frequently stimulated group (N=10) or a sham stimulated one (N=10). After a short period of acute stimulation, animals were chronically stimulated for 6 weeks. Body weight has been monitored during the complete experiment. Energy expenditure and locomotor activity have been measured with calorific cages, once during the acute stimulation phase and once again after the chronic stimulation phase. Behavioral tests (social interaction and openfield) have also been performed during acute and after chronic stimulation.

Results

Energy expenditure and locomotor activity showed a parallel course in both groups. Also in the body weight development, we could see no significant difference. The results of the behavioral tests showed no significant difference in the behavior of the animals in both groups.

Conclusion

These results suggest that BDS of NAc might not be efficient in the therapy of obesity. This confirms the difficulties in modulating metabolic parameters, especially in obesity. Nevertheless our results suggest the safety of DBS of NAc by showing no significant depressive effects in the stimulated group.

Funktionelle Neurochirurgie und Schmerz I/*Functional neurosurgery and pain I*

V061

Bestimmung der räumlichen Ausrichtung segmentierter Elektroden nach stereotaktischer Implantation zur Tiefen Hirnstimulation mit Hilfe von intraoperativem stereotaktischen Röntgen
Deviation of lead orientation angle of dDBS leads on intraoperative STX-XR

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Objective

Due to multiple programming options of directional deep brain stimulation (dDBS) in movement disorder patients knowledge of the lead orientation angle is useful for effective programming. A recent study demonstrated deviations of up to 90° from the intended orientation angle on postoperative cCT-scans (Dembek et al. 2019). In the actual study we examined the deviation of dDBS-lead orientation on intraoperative stereotactic (STX) x-ray images.

Methods

Two blinded investigators determined retrospectively on intraoperative 2D-stereotactic x-ray images the orientation of the stereotactic marker of dDBS-leads for 64 consecutive patients. The leads were stereotactically implanted with the spatial marker in rostral direction. X-ray Images were taken routinely after implantation of the first and the second lead enabling the determination of the spatial orientation of the first lead at two different time points.

Results

The mean deviation between intended and final spatial orientation was 40,8° ± 46,08° for all examined leads (N=128). The spatial orientation of the first lead did not significantly change within an average observation time of 60 minutes (N=64, Z=-0.11, p=0,916, Wilcoxon-Signed-Rank-Test). Also, the degree of deviation did not differ significantly between two lead manufacturers (group A (N=44), group B (N=84); Man-Whitney-U-Test, U=1629,500, Z=-1,098, p=0,272).

Conclusion

Our results showed deviations from the intended orientation angle due to electrode rotation immediately after the insertion of dDBS leads independent from the manufacturer. The initial spatial orientation remained stable for approximately one hour. This observation suggests that spatial deviations are a consequence of intraoperative manual manipulation so that a standardized orientation of dDBS leads is difficult to achieve.

Funktionelle Neurochirurgie und Schmerz I/*Functional neurosurgery and pain I*

V062

Dielektrische Eigenschaften von intrakraniellen Tumoren
Dielectric properties of intracranial tumours

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Objective

Recently, tumor treating fields (TTFields) were established for the treatment of newly diagnosed glioblastoma (GBM). One of the most crucial parameters defining the treatment efficacy of TTFields is the electric field intensity, which depends on the dielectric properties of the tumor tissue. In this study we determined the dieclectric properties of brain tumors by analyzing resected tissue following a fast acquisition protocol. To account for the intratumoral heterogeneity, different regions of the tumor were analyzed separately. In addition, sensitivity analyses for specific parameters (tissue hydration, temperature, and saline irrigation) were conducted.

Methods

A cohort of 130 patients with tumors of different histology and malignancy grade have been recruited (meningioma: n=36; brain metastases n=29; low grade glioma n=7; anaplastic glioma = 12; glioblastoma n=39; other= 7). Tissue samples were placed into a cylindrical cell with a known diameter. The impedance was recorded at frequencies 20Hz-1MHz using a software specifically developed for this study. The measured impedance was translated into dielectric properties of the sample (conductivity and relative permittivity) based on the parallel plate model. Each tissue probe was fixed and analyzed histologically. To assess the impact of tissue conditions on the measurements, probes were warmed to 35 degree Celsius, dehydrated or irrigated with 0.9% saline solution.

Results

We found significant differences between the conductivity of different types of tumors with meningiomas showing the lowest and GBM tissue exhibiting the highest conductivity values. Consistently, the perinecrotic areas of tumors displayed lower conductivity values compared to the solid tumor compartments. Also, we found a significant intratumoral heterogeneity within individual tumors. While tissue temperature had no detectable effects on the dielectric properties in GBM, saline irrigation tissue hydration significantly affected the results.

Conclusion

The dielectric properties of intracranial tumors appear to be depending on histological class and malignancy grade and show significant intratumoral heterogeneity. Dehydration and saline irrigation are important influencing factors. These results may allow a more precise modelling of electric field intensity distribution within the tumor.

Funktionelle Neurochirurgie und Schmerz I/*Functional neurosurgery and pain I*

V063

Dorsalganglienstimulation (DRGS) reduziert chronische neuropathische Schmerzen unter gleichzeitiger Abnahme der kortikalen Gammabandaktivität

Dorsal root ganglion stimulation (DRGS) relieves chronic neuropathic pain along with a decrease in cortical gamma power

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Objective

Gamma band oscillations reflect ongoing pain intensity in chronic pain patients. It was or hypothesis that dorsal root ganglion stimulation (DRGS) relieves chronic neuropathic pain along with a decrease in the broadband cortical gamma power.

Methods

We examined 9 patients (2 females, mean age 56.8 years; range 36 to 77 years) who were diagnosed with CNP and received DRGS therapy. We used the numeric rating scale (NRS) on the painful limb and simultaneously recorded electroencephalography (EEG) to measure broad-band gamma power. Measurements were taken on day 1 and 7.

Results

The resting state gamma power after DRGS revealed a significant decrease (p = .012) in the low gamma power between 30 – 45 Hz, recorded from the central electrodes from day 1 (M = 0.48, SD = 0.24) to day 7 (M = 0.31, SD = 0.12). High gamma-band power (55-95Hz) recorded from the frontal electrodes also decreased (p = .047) significantly from day 1 (M = 0.40, SD = 0.29) to day 7 (M = 0.23, SD = 0.11). We found a positive correlation between the low (rs = 0.528, p = .024) and high (rs = 0.292, p = .24) gamma power with CNP rating.

Conclusion

A decrease in the broadband gamma power may be considered as further evidence in favor of a reduction of the hyperexcitability of the nociceptive system in response to DRGS therapy. This is another important neurophysiological proof of the efficacy of DRGS.

Fig. 1

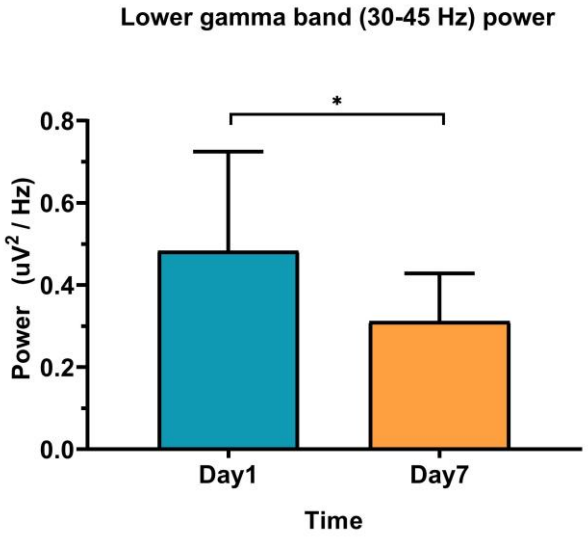
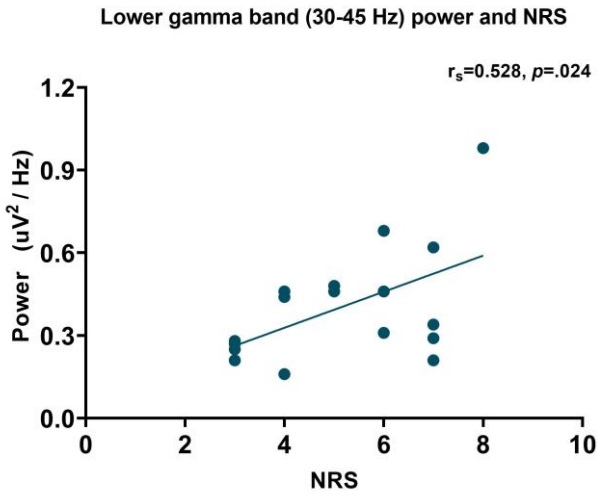

Lower gamma band (30-45 Hz) power
*
0.8
0.6
0.4
0.2
0.0
Power (uV² / Hz)
Day1
Day7
Time

Fig. 2


Lower gamma band (30-45 Hz) power and NRS
rs=0.528, p=.024
1.2
0.9
0.6
0.3
0.0
Power (uV² / Hz)
0
2
4
6
8
10
NRS

Funktionelle Neurochirurgie und Schmerz I/*Functional neurosurgery and pain I*

V064

Einflussfaktoren auf kortikospinale Erregbarkeit gemessen mit transkranieller Magnetstimulation (TMS)
Factors influencing corticospinal excitability measured with navigated transcranial magnetic stimulation (nTMS)

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Objective

Navigated transcranial magnetic stimulation (nTMS) is increasingly used in neurosurgical preoperative diagnostics and explored as a therapy option. Most of these applications rely on the resting motor threshold (RMT), a measure of cortical excitability, to scale intensity of stimulation sequences and evaluate treatment outcomes. Consequently, accurate measurement of the RMT is crucial and understanding of its confounders needs to be improved. The aim of this study was to validate findings on the impact of coil-to-cortex distance (CCD), age, cortical grey matter volume, hemisphere and functional connectivity between motor areas on the RMT.

Methods

35 healthy right-handed subjects (38.7 ± 13.7 years, 19 females) without any neurological or psychiatric condition were investigated using navigated TMS and their RMT was assessed. CCD, age, grey matter volume and resting-state functional connectivity between various motor areas were assessed. Additionally, the effect of the hemisphere was investigated. The effect of these predictors on the RMT was assessed with a linear mixed model to account for non-independence of observations within the same subjects.

Results

The RMT varied between 23 and 51% of stimulator output (mean 34.0%, standard deviation 6.1%). The model tested in this study explained 44% of variability in the RMT. CCD was positively associated with the RMT ($b = 1.46$, $t(34)=5.51$, $p < .001$) and we obtained strong evidence ($BF10 = 1.8*104$) for this effect. None of the other investigated factors influenced the RMT significantly. The absence of these effects was further moderately supported by Bayes Factors.

Conclusion

Our results are in line with previous studies showing an effect of CCD on the RMT. In contrast to our hypothesis, we did not see an impact of any of the other investigated factors. Thus, the variance explained by the model remained low. This highlights the need for a more through investigation of factors potentially influencing the RMT and contributing to changes in corticospinal excitability.

Funktionelle Neurochirurgie und Schmerz I/*Functional neurosurgery and pain I*

V065

Gebrechliche Patienten mit idiopathischem Normaldruckhydrozephalus profitieren gleichermaßen von Shunt-Operationen
Frail patients with idiopathic normal pressure hydrocephalus equally benefit from shunting

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Objective

Multiple studies have shown a strong correlation between frailty and perioperative outcome in different surgical disciplines. In this study, we evaluated frailty in patients with idiopathic normal pressure hydrocephalus (iNPH) and the possible associations it could have with overall perioperative response and outcome.

Methods

We retrospectively evaluated patients older than 65 years of age with iNPH who underwent ventriculoperitoneal shunt (VPS) surgery for the first time between 2010 and 2020. The diagnosis of iNPH was made radiologically as well as clinically with a trial of cerebrospinal fluid (CSF) drainage (either lumbar tap test or lumbar drain) in all cases. We evaluated every patient's frailty with the clinical frailty score (CFS) and dichotomized them in "frail" (CFS>4) and "non-frail" (CFS<5). The severity of iNPH was objectivized with the NPH Score by Sorteberg et al preoperatively, postoperatively, and at last follow-up. Our primary endpoint was the need for valve pressure adjustment due to worsening of NPH symptoms. Secondary endpoint was overall benefit from VPS, as objectivized by an improvement of >2 points in the NPH Score at last follow-up.

Results

One hundred forty-four patients were included in this study. Mean age at surgery was 75 years. In our cohort, 46 (32%) patients were considered frail. Mean NPH Scores pre- and postoperatively were 10 and 12, respectively, showing a statistically significant improvement of NPH symptoms postoperatively in a paired-samples t-test ($p<.001$). CFS had a statistically significant correlation with the severity of NPH symptoms at presentation ($p<.001$). Valve readjustment was necessary in 70 (49%) patients, with worsening of NPH symptoms being the cause in 48 of them. Frailty did not predict the need for readjustment ($p=.898$), and frail and non-frail patients benefited equally from VPS ($p=.920$). Furthermore, frail individuals were not at an increased risk for overdrainage ($p=.632$).

Conclusion

Frailty is increasingly used to select elderly patients for surgical treatment or best supportive care. While frailty predicts greater impairment from iNPH symptoms preoperatively, frail iNPH patients also benefit from VPS. Thus, frail individuals should not be dismissed from surgical therapies for iNPH.

Funktionelle Neurochirurgie und Schmerz I/*Functional neurosurgery and pain I*

V066

Veränderungen der Herzfrequenzvariabilität nach Tiefen Hirnstimulation des vorderen Thalamuskerns bei Epilepsiepatienten

Interictal heart rate variability changes of patients undergoing anterior thalamic nuclei deep brain stimulation for the treatment of epilepsy

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Objective

Reduced heart rate variability (HRV) is associated with maladaptive response to mental and physical stress, shortened life expectancy and increased risk of death in epilepsy, acute myocardial infarct and diabetic neuropathy. HRV changes after resective epilepsy surgery / vagus nerve stimulation were reported. We aimed to examine the effects of anterior thalamic nuclei (ANT) deep brain stimulation (DBS) on HRV parameters in 30 patients underwent DBS implantation at 2 Hungarian epilepsy centers between 2011 and 2019.

Methods

We retrospectively analyzed data of 30 drug resistant patient"s charts and collected ECG epochs recorded during video-EEG monitoring both in awake and N1 or N2 stage sleep at 3 timepoints: T1) before DBS implantation, T2) after surgery without stimulation and T3) after stimulation was started. ECG epochs were analyzed using HRV Kubios Premium Software. Statistical analysis was carried out by factorial one-way repeated measures Anova.

Results

Among time domain parameters mean RMSSD (square root of the mean squared differences between successive RR intervals) and SDNN (standard deviation of RR intervals) values significantly ($p < 0.05$) differed between timepoints, showing an increase in HRV after surgery. Frequency domain parameters LF (low frequency: 0.04 - 0.15 Hz), HF (high frequency 0.15-0.4Hz) in sleep, LF/HF ratio in awake and VLF (very low frequency: < 0.04Hz) also significantly ($p < 0.05$) changed suggesting improved autonomic regulation after surgery.

Conclusion

ANT DBS implantation might positively influence autonomic regulation reflected by increased HRV in drug resistant epilepsy patients undergoing DBS implantation. Prospective studies are needed for further evidence.

Fig. 1

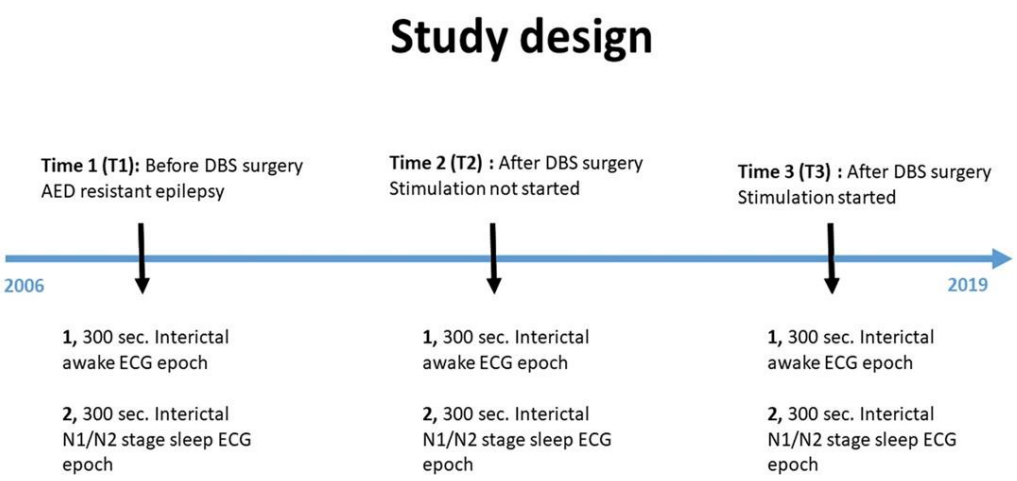

Fig. 2

HRV time and frequency domain parameters	N1-N2 Sleep/ Awake	Statistically significant change (P≤ 0,05)			Statistically not significant change (P> 0,05)		
RMSSD (ms)	Sleep	T1 <	T2 <	T3	-	-	-
	Awake	T1 <	T2 <	T3	-	-	-
	Sleep / awake	-	-	-	T1 >	T2 >	T3
LF pow.AR.nu (0,04-0,15 Hz)	Sleep	T1 >	-	T3			
	Awake	T1 >	T2	T1 > T3	-		
HF pow.AR.nu (0,15-0,4 Hz)	Sleep	-	-	-	T1 <	T2 <	T3
	Awake	T1 <	-	T3			
LF/HF ratio	Sleep	-	-	-	T1 <	T2 >	T3 T1 < T3
	Awake	T1 >	T2	T1 > T3	-		
VLF AR log. (<0,04 Hz)	Sleep Awake	T1 < T1 <	- -	T3 T3	T1 < T1 <	T2 < T2 <	T3 T3

Neurointensivmedizin/*Neurointensive care*

V067

Hämoglobin im Liquor als Driver für sekundären Hirnschaden nach aneurysmatischer Subarachnoidalblutung
Cerebrospinal fluid haemoglobin drives subarachnoid haemorrhage-related secondary brain injury

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Objective

Secondary brain injury (SBI) is an important driver of mortality and morbidity in patients with aneurysmal subarachnoid hemorrhage (aSAH). The lag time between aneurysm rupture and aSAH-related SBI (SAH-SBI) provides a potential window of opportunity for therapeutic interventions; however, diagnostic biomarkers and novel drug targets represent an unmet need. Prior experimental evidence has suggested that cell-free hemoglobin in the cerebrospinal fluid (CSF-Hb) is an upstream pathophysiological driver of SAH-SBI that promotes vascular and neuronal toxicity. The aim of our study was to investigate the clinical and pathophysiological association between CSF-Hb and SAH-SBI.

Methods

We prospectively enrolled 47 consecutive patients with aSAH and collected daily CSF samples and clinical data between days 1 and 14 after aneurysm rupture.

Results

Using a generalized additive model, we found very strong evidence for a positive association between CSF-Hb and SAH-SBI. The diagnostic accuracy of CSF-Hb for SAH-SBI markedly exceeded that of other biomarkers as well as radiological and clinical scores (area under the curve: 0.89 [0.85-0.92]). LC-MS/MS analysis of the temporal changes in the levels of 757 CSF proteins demonstrated that erythrolysis accompanied by an adaptive macrophage response are the two dominant biological processes occurring in the CSF space after aSAH. To further investigate the pathophysiological association between CSF-Hb and SAH-SBI, we explored the vasoconstrictive and lipid peroxidation activities of Hb ex vivo within the CSF-Hb concentration range defined by our patient cohort. These experiments revealed critical inflection points overlapping CSF-Hb concentration thresholds in patients with SAH-SBI. Selective Hb depletion and in-solution neutralization by the hemoglobin-scavenger haptoglobin or the heme-scavenger hemopexin efficiently attenuated the vasoconstrictive and lipid peroxidation activities of CSF-Hb in patient CSF.

Conclusion

Collectively, the clinical association between high CSF-Hb levels and SAH-SBI, the underlying pathophysiological rationale, and the favorable effects of haptoglobin and hemopexin in ex vivo experiments position CSF-Hb as a highly attractive biomarker and potential drug target.

Fig. 1

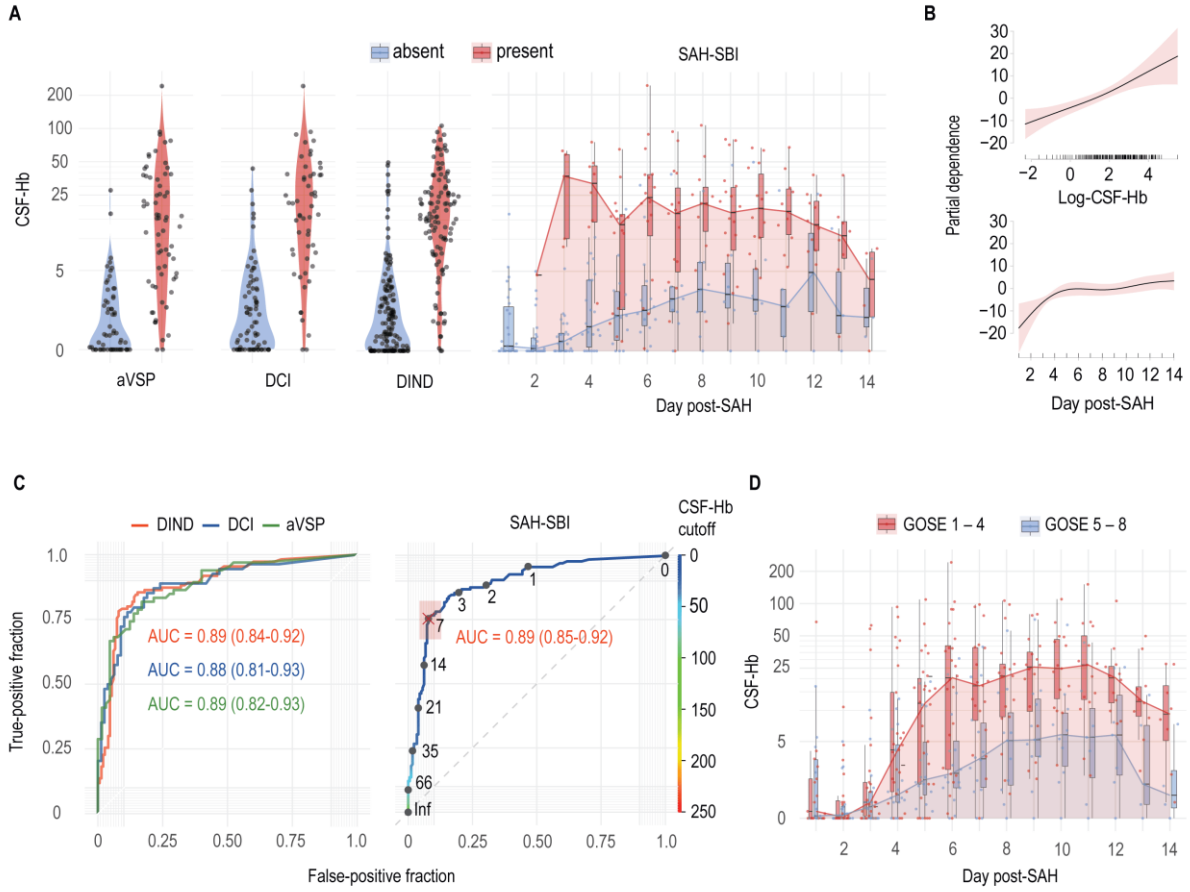
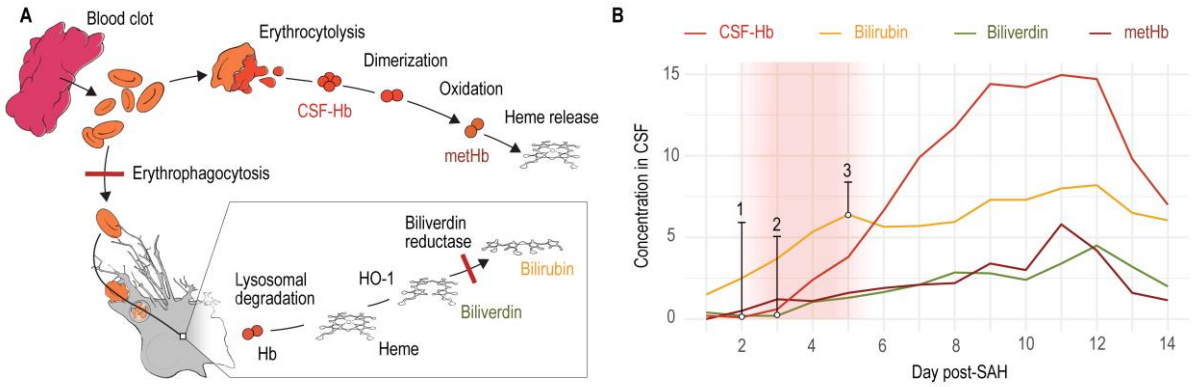

A
absent
present
SAH-SBI
CSF-Hb
aVSP
DCI
DIND
Day post-SAH
B
Partial dependence
Log-CSF-Hb
Day post-SAH
C
DIND
DCI
aVSP
AUC = 0.89 (0.84-0.92)
AUC = 0.88 (0.81-0.93)
AUC = 0.89 (0.82-0.93)
True-positive fraction
False-positive fraction
SAH-SBI
AUC = 0.89 (0.85-0.92)
CSF-Hb cutoff
D
GOSE 1 – 4
GOSE 5 – 8
CSF-Hb
Day post-SAH

Fig. 2


A
Blood clot
Erythrocytolysis
Dimerization
Oxidation
CSF-Hb
Heme release
metHb
Erythrophagocytosis
Biliverdin reductase
Bilirubin
Lysosomal degradation
HO-1
Biliverdin
Hb
Heme
B
CSF-Hb
Bilirubin
Biliverdin
metHb
Concentration in CSF
Day post-SAH

Neurointensivmedizin/*Neurointensive care*

V068

Verzögerte Ischämien nach aneurysmatischer Subarachnoidalblutung sind assoziiert mit Unterschreitung des optimalen zerebralen Perfusionsdrucks (CPP_{opt})

Delayed cerebral ischemia after aneurysmal subarachnoid haemorrhage is preceded by failure to meet optimal cerebral perfusion pressure (CPP_{opt})

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Objective

Delayed cerebral ischemia (DCI) after aneurysmal subarachnoid hemorrhage (aSAH) has frequently been associated with poor cerebral autoregulation and outcome. However, means to improve autoregulation have been lacking so far. A new concept has been introduced where an "optimal" cerebral perfusion pressure (CPP_{opt}) can be identified at which autoregulation may function best. The relationship between CPP, CPP_{opt} and the incidence of DCI is yet unclear.

Methods

We prospectively recruited patients with aSAH treated at a single tertiary center between 04/2014 and 09/2020. The well-known pressure reactivity index (PR_x) and associated CPP_{opt} were retrospectively calculated for patients with available high frequency ICP/CPP data in the early phase after aSAH. Daily means were calculated during the first seven days after hemorrhage and for 6-hour intervals prior to the occurrence of DCI (neurological deterioration, territorial or watershed hypoperfusion on CT perfusion imaging). Blood pressure management was liberal with a lower CPP limit > 60 mmHg. Deviation of CPP from CPP_{opt} (ΔCPP, defined as actual CPP-CPP_{opt}) was recorded.

Results

Data of n=45 patients (DCI n=24, no DCI n=21) were analyzed and a large variability of individual CPP_{opt} was observed for the first seven days (range 65.9-115.7mmHg). CPP_{opt} increased continuously from day 0-1 to day 2-4 to day 5-7 (77.3±11.8 to 84.4±9.5 to 87.2±7.5mmHg, repeated measures ANOVA $p<0.05$). This dynamic was matched by spontaneously higher levels of CPP (75.7±9.9 to 81.3±11.9 to 84.7±9.4mmHg, $p<0.01$), observed both in patients with and without DCI (all intervals DCI vs. no DCI $p>0.05$). In the two days before DCI, CPP_{opt} was relatively stable (85.7±8.9mmHg). However, in the 6 hours preceding DCI diagnosis, actual CPP decreased significantly (CPP 48-6h before DCI: 85.4±10.1mmHg, 6-0h: 79.5±8.5mmHg, $p<0.05$), which was associated with negative ΔCPP (48-6h: -0.5±4.3mmHg, 6-0h: -4.8±8.3mmHg, $p<0.01$) and worsening of autoregulation status (PR_x 48-6h: 0.10±0.21, 6-0h: 0.18±0.29, $p<0.01$).

Conclusion

Patients with aSAH may upregulate their individual CPP in the early post-bleeding phase to compensate for the increasing cerebral demand. Spontaneous decreases below calculated CPP_{opt} may be associated with development of DCI. Bedside calculation of CPP_{opt} and fine-tuning CPP accordingly could assist in avoiding such episodes, and the effect on DCI and outcome should be investigated in prospective trials.

Neurointensivmedizin/*Neurointensive care*

V069

Ist eine intensiv-medizinische Überwachung nach einer elektiven Kraniotomie im Rahmen eines epilepsiechirurgischen Eingriffs notwendig? Zeit für einen Paradigmenwechsel

Is there a need for routinely intensive care unit admission after elective craniotomy for epilepsy surgery? Time to re-think the paradigm

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Objective

Traditionally, patients undergoing elective craniotomy for epilepsy surgery are monitored postoperative in an intensive care unit (ICU) overnight in order to quickly recognize a potential postoperative complication. In this study, the authors investigated the frequency postoperative events required ICU setting in patients who had undergone elective craniotomy for epilepsy surgery. Furthermore, we aimed to evaluate whether routine postoperative admission to a step-down unit is safe in this patient population.

Methods

A cohort study was performed assessing patients with medically intractable epilepsy who underwent elective craniotomy for epilepsy surgery between 2012 and 2019 at the authors" institution (n=273). The recorded data included age, relevant accompanying conditions, type of surgical approach, intraoperative surgical and anesthesiological events as well as adverse events requiring ICU settings. A multivariate analysis was performed to identify independent pre- and intraoperative risk factors for postoperative adverse events requiring ICU care.

Results

Overall, 256 out of 273 patients (93.8%) who underwent elective craniotomy for epilepsy surgery required no ICU setting or intervention during the postoperative course. The univariate analysis revealed that patients with planned functional hemispherectomy ($p < 0.0005$), ASA-Score ≥ 3 ($p=0.027$), diabetes mellitus ($p=0.047$), BMI ≥ 30 ($p=0.02$), intraoperative surgical abnormalities and tissue vulnerability ($p=0.032$), prolonged surgery length ($p=0,025$), and intraoperative blood loss > 325ml ($p<0.0005$) were more likely to develop an adverse event, which necessitated an ICU intervention. The multivariate analysis only found planned functional hemispherectomy (OR=33; $p<0.0005$), intraoperative blood loss > 325ml (OR=4.7; $p=0.012$), intraoperative surgical abnormalities and tissue vulnerability (OR=4.2; $p=0.047$) and diabetes mellitus (OR=9.33; $p=0.025$) as independent predictors for postoperative ICU admission.

Conclusion

Our results show that routinely step-down ward admission for patients undergoing elective craniotomy might be feasible and safe. However, attention should be paid to patients with planned functional hemispherotomy, increased intraoperative blood loss (>325ml) and diabetes mellitus, who should be monitored postoperatively on ICU.

Neurointensivmedizin/*Neurointensive care*

V070

PCO2-Management im Rahmen der intensivmedizinischen Therapie bei aneurysmatischen Subarchnoidalblutungen

PCO2-management in the neuro-critical care of patients with aneurysmal subarachnoid haemorrhage – seeking the optimal values

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Objective

The partial pressure of the carbon dioxide (PCO2) in the arterial blood is a strong vasomodulator affecting the cerebral blood flow. In the acutely injured brain, the risk of cerebral edema and ischemia depends on the alterations of the PCO2 values. Both complications are related to poor outcome in patients with aneurysmal subarachnoid hemorrhage (aSAH). We aimed to analyze the effect of PCO2 levels on the course and outcome of aSAH.

Methods

All patients of a single institution that were treated for aSAH over a 13.5-year period were included (n=633). The assessed PCO2 values were based on the daily arterial blood gas measurements and recorded for up to 2 weeks after ictus. The study endpoints were: delayed cerebral ischemia (DCI), refractory intracranial pressure (ICP) necessitating decompressive craniectomy, in-hospital mortality, and functional disability at 6 months after aSAH (modified Rankin scale >2). In the multivariate analysis, the association between the PCO2 and the study endpoints were adjusted for the patients" age, radiographic and clinical severity of aSAH, premorbid and acute respiratory conditions, duration of mechanical ventilation and the need for conservative ICP therapy.

Results

Using the receiver operating characteristic curve, the clinically relevant cutoff for the PCO2 was set at <38 mmHg. The patients with the daily mean PCO2 values <38 mmHg were at lower risk for sustained ICP requiring decompressive surgery (7.3% vs. 13.8%; aOR 0.49, p=0.048), but not for the DCI risk (18.6% vs. 27.5%; aOR=0.45, p=0.084). Finally, PCO2 <38 mmHg was independently associated with the risk of in-hospital mortality (8.1% vs. 17.9%; aOR 0.40, p=0.002) and functional disability (38.5% vs. 56.1%; aOR 0.64, p=0.043).

Conclusion

Patients with aSAH might profit from low-normal PCO2 values during the first weeks after aneurysm rupture. This effect is most likely attributed to the reduction of cerebral edema and associated ICP increase. In addition, despite the known vasoconstrictor effect of a low PCO2, aSAH patients with PCO2 <38 mmHg showed rather a trend to a lower risk of DCI.

Neurointensivmedizin/*Neurointensive care*

V071

Der Herniations-WFNS Score, zur Prognoseabschätzung von Patienten mit schwerer aneurysmatischer Subarachnoidalblutung – eine prospektive Multicenter-Studie

The herniation WFNS score, to predict outcome in poor grade aneurysmal subarachnoid haemorrhage patients – a prospective multicentre study

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[4]Universitätsspital Zürich, Department of Neurosurgery, Zürich, Switzerland
[5]Kantonsspital Aarau, Neurosurgery, Aarau, Switzerland
[6]Kantonsspital St. Gallen, Klinik für Neurochirurgie, St. Gallen, Switzerland
[7]Maimonides Medical Center, Neurosurgery, New York, NY, United States
[8]Universitätsspital Basel, Neurochirurgie, Basel, Switzerland
[9]Centre Hospitalier Universitaire Vaudois, Neurochirurgie, Lausanne, Switzerland
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Objective

Incorporation of signs of brainstem dysfunction into the current World Federation of Neurosurgical Societies (WFNS) classification might improve outcome prediction in patients with aneurysmal subarachnoid hemorrhage (aSAH).

Methods

We performed an international prospective multicenter study in poor grade aSAH patients to compare the WFNS classification with a modified WFNS classification - the herniation WFNS score (hWFNS). Here, only patients that showed signs of brainstem dysfunction were assigned hWFNS V. Outcome was assessed by modified Rankin score 6 months after hemorrhage. The primary endpoint is the difference of specificities of the WFNS and hWFNS with respect to poor outcome at 6 months after initial hemorrhage.

Results

250 patients were included. 237 reached the primary endpoint. Comparing the pre-resuscitation and post-resuscitation WFNS and hWFNS score the specificities increased from 0.35 to 0.84 and from 0.19 to 0.93. The positive predictive value increased from 65.9 to 80.5 and 61.9 to 88.3, respectively.

Conclusion

The hWFNS score improves outcome prediction for poor grade aSAH patients by implementing signs of brainstem dysfunction into the current WFNS grading. This has major impact for daily clinical practice and decision-making and interpretation of scientific data.

Neurointensivmedizin/*Neurointensive care*

V072

Die Rescue-Therapie mittels lokaler intraarterieller Applikation von Nimodipin hat einen positiven Effekt auf das klinische Outcome von Patienten mit aneurysmatischer Subarachnoidalblutung und verzögert auftretender Durchblutungsstörungen

Rescue therapy with local intraarterial administration of nimodipine positively affects clinical outcome in patients with aneurysmatic subarachnoid haemorrhage and delayed cerebral ischemia

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Objective

Development of vasospasm after aneurysmatic subarachnoid hemorrhage (aSAH) is closely linked to the development of delayed cerebral ischemia (DCI), which is a major contributor to unfavorable outcome after aSAH. Despite having been available for more than a decade, the effect of local intraarterial administration of nimodipine as a rescue measure on clinical outcome remains understudied; therefore, we evaluated it`s effect on short and long term functional and neuropsychological outcome after aSAH.

Methods

A total of 107 consecutive patients treated for aSAH on the neurosurgical intensive care unit of our university hospital according to the local standard of care were recruited. Follow-up was conducted at three, twelve and 24 months after the hemorrhage. At follow-up visits, functional outcome was assessed by extended Glasgow Outcome Scale (GOSE) and mRS, while neurocognitive function was evaluated using the screening module of the Neuropsychological Assessment Battery (NAB-S). Outcome of patients, who received rescue therapy (intervention group, n=37), and those, who were treated conservatively (control group, n=70), was compared.

Results

Even though significantly more patients in the interventional treatment group suffered from high grade aSAH (WFNS Grade IV + V) compared to the control group (54.1% vs. 31.4%, p=0.04), significant differences in functional outcome were present only at discharge and three months after the bleeding (GOSE >4 in 8.1% vs. 41.4% and 28.6% vs. 72.7%, p<0.001 and p=0.01, respectively). Thereafter, group differences were no longer significant. The same temporal pattern of recovery could be seen when assessing severe neuropsychological deficits and the ability to return to work: While significantly more patients in the intervention group had severe neuropsychological deficits (76.3% vs. 36.0% and 66.7% vs. 26.1%, p=0.04 and 0.03, respectively) and were unable to work (5.9% vs. 40.0%, p=0.02 at twelve months) at three and twelve months after the hemorrhage, no significant differences between the two groups could be detected at long term follow up. The presence of moderate neuropsychological impairments did not significantly differ between the groups at any timepoint.

Conclusion

Intraarterial administration of nimodipine as a rescue measure to treat vasospasm moderately improves functional as well as neuropsychological outcome and professional reintegration after aSAH.

Neurointensivmedizin/*Neurointensive care*

V073

Quantifizierung des cerebralen Glucosemetabolismus im Rattenhirn nach experimenteller Subarachnoidalblutung unter Anwendung eines MRT-Vorlage basierten Analysetools

Quantification of cerebral glucose metabolism in rat brain after experimental subarachnoid haemorrhage using an MRI-template based analysis tool

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Objective

Data analysis and medical imaging are two essential requirements for diagnosis and treatment of neurologic diseases. Despite sustained progresses in the last decade, analysis of in vitro acquired data still remains challenging, especially in molecular imaging using positron emission tomography (PET). The present interdisciplinary study describes and tests a semi-automated data analysis tool, which should be able to analyze imaging data independently from the administrated radiotracer or imaging modality. As proof of principle, we evaluated the cerebral glucose metabolism by PET with [^{18}F]flourodeoxyglucose (^{18}FDG-PET) in a subarachnoid hemorrhage (SAH) rat model.

Methods

The uptake of [18F]fluordeoxyglucose was evaluated in different brain regions in 18 male Sprague-Dawley rats (weighing 250-300g) which were randomly assigned into one of two groups: (1) SAH induced by the endovascular filament model and (2) sham operated controls. Serial ^{18}FDG-PETs were performed 3 hours following SAH/sham, as well as on day 1, day 4 and day7 after SAH/sham operation. Data analysis was performed by uptake ratio using a self-developed data analysis tool, implemented in Matlab.

Results

In data analysis, multiple significant differences between sham and SAH experimental groups were determined in various brain regions using uptake ratio (UR), which could not be observed when analyzing the data using the standardized uptake value (SUV). The SAH group showed a significant higher tracer accumulation in the grey matter compared to the sham group (day 0 $p<0.001$, day 1 $p<0.01$, day 4 $p<0.05$, day 7 $p<0.01$), while the white matter region showed a significant reduced tracer accumulation in SAH animals (day 0 $p<0.001$, day 1 $p<0.01$, day 4 $p<0.05$). Significant URs in the neocortex could also be shown, but haven"t been as significant as the differences in the basal forebrain region or the olfactory system region.

Conclusion

Our interdisciplinary study on glucose metabolism in an experimental rat SAH-model could provide important insights into brain metabolism changes following SAH via ^{18}FDG-PET in separation of different brain regions. Using a self-developed analysis instrument it could be shown that the extended evaluation methods allow a more flexible data evaluation, especially with regard to the preclinical evaluation of novel (PET) tracers.

V074

Autologe tumorlysat-beladene dendritische Zellvakzinierung verändert den Phänotyp von tumor-infiltrierenden Lymphozyten in neudiagnostizierten Glioblastompatienten

Autologous tumour-lysate loaded dendritic cell vaccination alters the phenotype of tumour-infiltrating lymphocytes in newly diagnosed glioblastoma patients

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Objective

In an on-going phase II clinical trial (GlioVax), patients with newly diagnosed glioblastoma (GBM) are treated with dendritic cell vaccination as add on to the standard radio-/chemotherapy. To assess the impact of the vaccination on tumor immunity, tumor-infiltrating lymphocytes (TILs) in recurrent tumor tissue were analyzed in vaccinated and control patients as well an in primary samples at initial diagnosis.

Methods

Patients with newly diagnosed GBM were treated either with standard radio-/chemotherapy alone or combined with DC vaccination. In the event of MRI-suspected tumor recurrence, patients were subjected to surgery, when medically indicated. Infiltrating lymphocytes in the resected tissue were analyzed using flow-cytometry for T cell subset and activation markers, IFNγ-production as well as the expression of immune checkpoint regulators.

Results

After diagnosed tumor recurrence via MRI, 17 patients (10 vaccinated; 7 control) received additional ^{18}FET-PET imaging. In cases of congruent imaging findings, surgery was performed in 10 patients (5 vaccinated; 5 control). In 2 vaccinated patients neuropathological diagnoses revealed treatment-induced changes in the absence of tumor cells and the isolated TILs showed high frequencies of CD69$^+$IFNγ-producing CD4$^+$ (17.65%) and CD8$^+$ (35.91%) T cells, indicating an infiltration of reactive T cells, while in the 3 vaccinated and 5 control patients vital tumor cells were detected and a minor T cell infiltration and IFNγ-production. The T cells of the 2 pseudo-progressed vaccinated patients showed lower levels of Foxp3 expression but a simultaneous expression of PD-1 and Tim3 together with a T-bet^{high}Eomes^{high} phenotype.

Conclusion

Here, we report the presence of immunoreactive effector T cells in vaccinated patients. These cells produce high amounts of IFNγ, but may be in an exhausted state. These findings might add valuable insights for the understanding of treatment-related changes following multimodal therapy including dendritic cell vaccination.

Neuroonkologie II/*Neurooncology II*

V075

Charakterisierung des heterogenen Antigenexpressionsmusters in Glioblastomen und ihren Rezidiven als Voraussetzung für das CAR-T Zell-Design

Characterisation of the heterogenous antigen-expression pattern in matched samples of primary and recurrent glioblastoma as a prerequisite for CAR-T cell engineering

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Objective

Recent studies showed promising progress in the treatment of glioblastoma patients with CAR-T cells. Antigen escape mechanisms of malignant gliomas still constitute major obstacles and are reasons for non-response or relapse. Here, we present data for the surface expression of the ten *in vitro* and *in vivo* most targeted antigens in CAR-T cell therapy in primary and recurrent glioblastoma patients, their local distribution within the tumor and changes in relapse.

Methods

Tissue samples of 35 patients with glioblastomas and their respective relapses were analysed for expression of HER2, EGFRvIII, CD70, B7H3, Il13Rα2, NY-ESO1, GD2, CD133, CSPG4 and EphA2 by immunohistochemistry. In order to determine antigen expression in normal brain, slides of three healthy specimens (cerebrum, cerebellum, brain stem) were stained for the same antigens. To specify intrapersonal heterogeneity, five representative areas per patient and slide were evaluated.

Results

Interestingly, some antigens like EGFRvIII and NY-ESO1 showed a rather low expression in primary and recurrent glioblastoma while others like GD2, CD70, CD133 and EphA2 were expressed moderately. Three antigens were significantly increased in relapse relative to the tissue primarily obtained: HER2 (p=0.005, Cohen"s r=0.48), EGFRvIII (p=0.042, Cohen"s r=0.344), and GD2 (p=0.013, Cohen"s r=0.42). There were significant intrapersonal expression differences detectable for each antigen. However, none of the ten antigens was found in healthy brain tissue.

Conclusion

Thus, inter- and intrapersonal heterogeneity is one of the major obstacles to be overcome in order to implement targeted therapies for the treatment of glioblastoma.

Neuroonkologie II/*Neurooncology II*

V076

Zirkulierende extrazelluläre Vesikel als eine neue Methode zur Verlaufskontrolle bei Hirntumorpatienten
Circulating extracellular vesicles as a novel tool for therapy monitoring of brain tumour patients

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Objective

Extracellular vesicles (EVs) represent a population of lipid bilayer nanoparticles released by all cell types, including tumor cells, and have recently garnered attention as mediators of intercellular communication. Emerging evidence supports their key function in modulating the tumormicroenvironment and tumorprogression, as they are capable of horizontal transfer of pro-oncogenic cargo to recipient cells. To date, MRI-Images are the established method to monitor treatment efficacy in brain tumor patients. Given the critical need for a reliable biomarker in the therapy monitoring of glioblastoma patients, EVs are of translational interest as they harbor tumor-specific nucleic acids and proteins, transgress the blood-brain-barrier and thus may serve as a noninvasive resource for liquid biopsy. The aim of this study was to investigate the potential of circulating EVs to mirror therapy efficacy and tumorprogression

Methods

We collected plasma samples from glioblastoma (n=40) and meningioma patients (n=25) before, as well as on the first and fourth day after, microsurgical tumorresection. Follow-up samples were obtained every 3 months. Additionally, we analyzed a group of healthy donors (n=18). EVs were isolated by Ultracentrifugation and the plasma concentration was measured by Nanoparticle Tracking Analysis (NTA). Tumor burden was measured on T1-weighted and FLAIR MRI images

Results

Prior to surgery, the level of circulating EVs in glioblastoma and meningioma patients is elevated, distinguishing them from healthy controls (2-fold increase in meningioma, 5-fold increase in GBM; $p < 0.0001$). After surgery, the concentration of EVs per ml plasma decreased significantly. In the group of glioblastoma patients, the number of circulating plasma EVs dropped by a factor of 7 until the fourth day after tumor resection ($p < 0.001$) In meningioma patients, EV concentration decreased by a factor of 3 ($p < 0.05$), while it was most distinct in who grade 2. A massive drop in EVs was associated with a more radical surgical resection ($p < 0.05$). Interestingly, at the time of tumor recurrence, the number of circulating EVs increased again in all patients during a follow-up period of 9 months

Conclusion

Our findings highlight the potential of circulating extracellular vesicles as a resource for monitoring treatment response of glioblastoma patients, as they seem to reflect the presence of a tumor mass and thus may assist in clinical decision making.

Neuroonkologie II/*Neurooncology II*

V077

Die Entwicklung und externe Validierung eines klinischen Prädiktionsmodells für die Überlebenszeiten von Patienten mit Glioblastomen

Development and external validation of a clinical prediction model for survival in glioblastoma patients

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Objective

Glioblastoma survival prognostication has become more refined by the molecular reclassification into isocitrate dehydrogenase (IDH) wild-type and IDH mutant tumors. We aimed to provide an updated prediction model that predicts individual survival prognosis in IDH wild-type glioblastoma patients.

Methods

Data from existing databases from Germany and The Netherlands provided data on de novo diagnosed glioblastoma patients treated between 2012 and 2018. The prediction model considered recent glioblastoma biology markers in addition to well-known classical prognostic variables which were updated and refined with additional categories. The clinical prediction model was developed with Cox proportional hazards regression. Performance was evaluated according to calibration (calibration plots, calibration slope) and discrimination (c-statistic) in a cross-validation procedure to assess external validity.

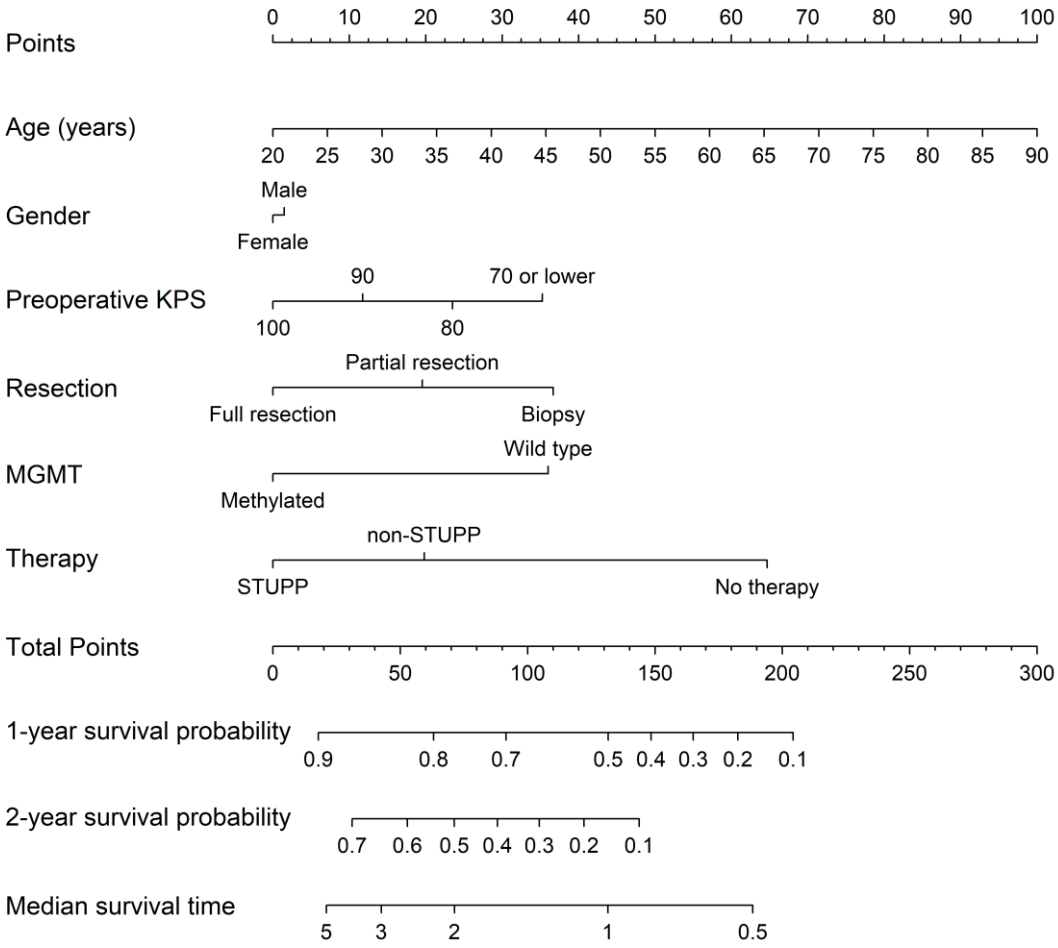
Results

The German patient cohort consisted of 710 patients of whom 511 (72%) had died. Median follow-up was 11 months. The Dutch patient cohort consisted of 326 patients of whom 308 (94.5%) had died. Median follow-up was 10 months. Cohorts (n=1036) were combined to develop three models in order of increasing complexity. The final model considering age, gender, preoperative Karnofsky performance status, extent of surgical resection, MGMT promoter methylation status, and adjuvant therapeutic regime showed an optimism-corrected c-statistic of 0·73 (95% confidence interval 0·71 – 0·75). Cross-validation between the national cohorts yielded comparable results. Moderate miscalibration was observed.

Conclusion

The prediction model reliably predicts individual survival prognosis in newly diagnosed IDH wild-type glioblastoma patients, although additional validation—especially for long-term survival—may be desired. The nomogram and web application support shared decision making.

Fig. 1


Points
0 10 20 30 40 50 60 70 80 90 100
Age (years)
20 25 30 35 40 45 50 55 60 65 70 75 80 85 90
Gender
Male
Female
Preoperative KPS
90
70 or lower
100
80
Resection
Partial resection
Full resection
Biopsy
MGMT
Wild type
Methylated
Therapy
non-STUPP
STUPP
No therapy
Total Points
0 50 100 150 200 250 300
1-year survival probability
0.9 0.8 0.7 0.5 0.4 0.3 0.2 0.1
2-year survival probability
0.7 0.6 0.5 0.4 0.3 0.2 0.1
Median survival time
5 3 2 1 0.5

Neuroonkologie II/*Neurooncology II*

V078

Kombination von Tumor Treating Fields und Radiotherapie in humanen Glioblastomzellen – Spielt die zeitliche Reihenfolge eine Rolle?

Combination treatment of tumor treating fields and irradiation in human glioblastoma cells – Does the temporal sequence make a difference?

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Objective

Recent studies are investigating the concurrent application of tumor treating fields (TTFields) during radiochemotherapy in glioblastoma (GBM) patients. An influence on the repair mechanisms after irradiation (IR) in GBM cell lines in vitro was described, when TTFields were applied after IR. Nevertheless, whether TTFields have radiosensitizing effects on human GBM cells, when applied before IR, is an important question. The aim of our study is to compare the effects on cell proliferation when TTFields were applied before and after IR.

Methods

A172 and U87 GBM cells were plated on cover slips. After 24 hours one group received photon-beam IR at a dose of 4Gy and immediately afterwards TTFields at a frequency of 200Hz and a field intensity of 1.26 V/cm for 24 hours. The other group received the same treatment combination in the reverse order. 24h after treatment cells were harvested, and survival fractions (SF) were determined performing automatic cell count and clonogenic cell assays.

Results

IR alone decreased the number of surviving cells to 30.09% (95%CI: ±13.42%) in U87 cells and to a survival fraction of 34.57% (95%CI: ±8.66%) in A172 cells. After 24 hours treatment with TTFields alone U87 cells showed a survival fraction of 48.35 (95%CI: ±43.01%) while in A172 46.97% (95%CI: ± 16.57%) of cells were still viable. The survival rates after TTField treatment followed by IR were 33.5% (95%CI: ± 19.82%) in U87 and 26.56% (95% CI: ± 7.26%) in A172 cells. When IR was applied before TTFields 17.27% (95%CI: ± 9.82%) of U87 and 15.96% (95%CI: ± 2.48%) of A172 cells were counted as viable.

Conclusion

IR and TTFields treatment alone showed antiproliferative results on human GBM cells. The treatment with TTFields before IR had an additive effect on the survival of both GBM cell lines. However, only the sequence of IR followed by TTFields reached the cutoff for a synergistic effect in A172 cells and almost in U87 cells. These results imply that TTFields have an impact on the repair mechanisms after IR and a radiosenzitizing effect.

Radiochirurgie/*Radiosurgery*

V079

Stereotaktische Radiochirurgie von Hirnstammmetastasen
Stereotactic radiosurgery for brainstem metastases

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Objective

Surgical options for treating brainstem metastases (BSM) are limited. As an alternative to local or whole brain radiation therapy, stereotactic radiosurgery (SRS) can be applied for the treatment of BSM. However, especially in brainstem the applied dose has to be balanced between toxicity and efficacy of treatment. Therefore, we evaluated safety and efficacy of Cyberknife®-SRS in BSM.

Methods

In this single centre retrospective series we included all patients between 2013 and 2018 with BSM who underwent single session SRS using Cyberknife® and a minimum dose of 18 Gy. Patient data were analyzed with Kaplan-Meier estimates in terms of local control using Response Assessment in Neuro-Oncology (RANO) criteria, overall survival (OS) and progression free survival (PFS). Preexisting symptoms were rated as improved, stable and deteriorated during follow-up.

Results

A total of 35 patients (f/m =20/15, median age 58, range 33-78 years) with 39 BSM were identified. Mean tumor volume was 1.56 ± 2.1 cm3 (range, 0.03 – 8.7 cm3), median marginal dose was 19.1 Gy (range, 18-20 Gy) and the prescription isodose was 65 % in all cases. Mean follow-up was 11.7 months (range, 1-77 months).

Symptoms improved in 29%, remain stable in 68%. One patient showed deterioration of hemiparesis due to radiation induced tissue reaction.

At 6 and 12 months follow-up actuarial local control was 100%, PFS was 60% and 20%, OS was 90%, respectively.

Conclusion

Our preliminary results show that Cyberknife SRS can be applied safely and effectively in patients harbouring BSM regarding local control.

Radiochirurgie/*Radiosurgery*

V080

Radiochirurgie bei Schädelbasismeningiomen
Radiosurgery for skull base meningiomas – outcomes from over 3500 cases – update a comparative analysis with anatomical nuances

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Objective

Skull base Meningiomas are the most frequent benign tumours treated with Gamma Knife Radiosurgery (GKRS). However, the assessment of its efficacy and safety in slow growing tumours is an ongoing process, requiring analysis of long-term results. This study involves the experience of several European Gamma Knife Centres. We report on the efficacy of GKRS for the treatment of skull base Meningiomas, clinical and radiological control and side effects

Methods

From 15 participating centers, we performed a retrospective observational analysis of a cohort of 3752 benign meningiomas treated with GKRS. All were treated with Gamma Knife radiosurgery at least 5 years before assessment for this study. Clinical and imaging data were retrieved from each center and uniformly entered into a database by 1 author (A.S.). A statistical analysis is presented.

Results

3451 patients harbouring 3752 meningiomas treated in fifteen institutions recruited were evaluated. The median age was 56 years (range 6 - 89 years). The median tumour volume was 5.20 ccm (range 0.5 - 85 ccm) and tumour margin dose to the 50 % isodose line 13.5 Gy (range 3 - 45 Gy). The median radiological follow-up was 61 months, but detailed results were only available for 3259 meningiomas (86.8 %). The volume of treated tumours decreased in 1753 lesions (54 %) did not change in 1305 lesions (40 %) and increased in 200 lesions (6 %). The temporary morbidity rate after GKRS was 5.3 % and the permanent morbidity rate was 5.6 %. The actuarial control rate was 97.9 % at 5 years post GKRS.

Conclusion

GKRS is a safe and not invasive method of treatment of skull base meningiomas and the large number analysed confirms a high tumour control and low morbidity rate even after a long-term follow-up period.

Radiochirurgie/*Radiosurgery*

V081

Unterschiede bei den Risikofaktoren für Strahlennekrosen zwischen malignen und nicht-malignen intrakraniellen Neoplasien nach radiochirurgischer Behandlung

Differences in risk factors for radiation necrosis after radiosurgery of malignant vs. non-malignant intracranial neoplasms

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Objective

Radiosurgery is an interdisciplinary treatment concept for intracranial neoplasms of different biological behavior. Radiation necrosis is a possible complication, but there are still only few known risk factors for its development. The aim of this study was to compare the incidence and risk factors of radiation necrosis between malignant and non-malignant tumors after radiosurgery.

Methods

Patients treated with single staged radiosurgery between January 2004 and November 2020 were included. The clinical, imaging and medication data were gained from patient records. The largest axial diameter of the tumors was measured using MRI scans in T1 weighted imaging with gadolinium and the edema in T2 weighted imaging. Due to a similar biological behavior, acoustic neuroma (AN) and meningiomas were stratified together and compared with metastases.

Results

388 patients were included, 61 (15.7%) developed a radiation necrosis. Median follow-up was 24 (6-62) months with a median onset of radiation necrosis at 8 (6-12) months. The most frequent tumors were metastases with 47.2%, followed by AN with 32.2 % and meningiomas with 13.4%. Metastases presented with a significantly smaller diameter (p=0.038) but significantly more edema (p=0.017). Metastases were treated with a significantly higher median dose of 20 (18-20) Gy compared to meningioma and AN with a median dose of 14 (12-16) Gy (p<0.001). Compared to AN and meningiomas, metastases showed a significantly lower risk of radiation necrosis (p=0.002). However, a clear correlation between a higher dose and radiation necrosis (OR 1.745) could also be shown for all tumor entities (p<0.001), which should outweigh the lower risk of metastases per se. Age plays a significant role for radiation necrosis with an OR of 1.066 only in metastases (p=0.049). For non-malignant tumors, no significance with regard to age could be determined.

Neither surrounding edema nor the amount of cortisone given had an effect on the occurrence of radiation necrosis.

Conclusion

Although metastases demonstrated a significant lower risk of radiation necrosis, which may be explained by their smaller diameter, the higher dose for single stage radiosurgery of metastases may outweigh this benefit. For the first time, age has been shown as a risk factor for radiation necrosis in metastases.

Radiochirurgie/*Radiosurgery*

V083

Vergleich der Effektivität und des Outcomes nach CyberKnife-Radiochirurgie oder Thermokoagulation in Patienten mit therapierefraktärer Trigeminusneuralgie und neurologischer Ko-Morbidität

Comparison of treatment efficacy and outcome in patients with refractory trigeminal neuralgia and neurological co-morbidity – CyberKnife radiosurgery vs. radiofrequency thermocoagulation

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Objective

Treatment of symptomatic trigeminal neuralgia (TN) in patients with neurological co-morbidites, e.g., multiple sclerosis remains challenging. Single-fraction Cyberknife radiosurgery (CK) and retrogasserian thermocoagulation (TC) are possible therapeutic options. We aimed to compare treatment efficacy and outcome in patients with TN treated by CK or TC with respect to neurological co-morbidities.

Methods

Clinical and radiographic data of patients with TN treated with single-fraction CK or TC at a single academic institution were analyzed. Pain level was evaluated using the Barrow Neurological Institute (BNI) pain scale pre-intervention and 3,6, 12 and 24 months post-interventionally. Group comparison and multivariate statistical analysis was performed using SPSS. Data is given as mean and range. Ethical approval was granted by local authorities (EA 1/289/19).

Results

107 patients (nCK=54 and nTC=53) were treated with 158 treatments. Mean age of the cohort was 61.2 (31.7-98.1) years, male to female ratio was 38 to 69. 22 patients had multiple treatments. Left-sided pain was present in 51 patients, right-sided pain in 56 patients. 44 patients had involvement of one branch, 56 patients of two or more branches. 53 patients had neurological co-morbidities; 40 of them were diagnosed with multiple sclerosis (nMCK=17, nMTC=23). Mean BNI pre-intervention was 4.2 (range 3 to 5), mean BNI post-procedural was 3.0 (range 1-5). Pain was improved after 133, stable after 22 and worse after 3 treatments. Mean BNI improvement in the TC subcohort at 3-months-follow-up was significantly better than in the CK cohort (1.22 vs. 1.72; p=0.023). Exclusive analysis of the multiple sclerosis subgroup revealed no significant difference in mean BNI improvement between patients treated with CK or TC (1.63 vs. 1.56; p=0.071). Incidence of new-onset hypaesthesia remained relatively low after both procedures (16.4%; CK=1.8%, TK=26.4%).

Conclusion

Both therapies present valid strategies for pain improvement. BNI improvement was significantly better in patients treated with TC in the cohort. In patients with multiple sclerosis as neurological co-morbidity, there was no difference in pain improvement between the two treatment modalities.

V085

Fluoreszenzgestützte Resektion intrakranieller Meningeome mit einem neuartigen Somatostatin-Liganden-Rezeptor-Farbstoff – eine Tiermodellstudie an der Nacktmaus

Fluorescent image-guided resection for intracranial meningioma with a new somatostatin-ligands-dye – an experimental study on the nude mice

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Objective

The use of photodynamic agents in malignant cranial tumor surgery is quite common. All methods that permit intraoperative identification of residual tumor tissue may be of benefit. This study was established to investigate fluorescent image-guided resection for intracranial meningioma in the nude mice with a new designed dye.

Methods

Primary meningioma cell cultures were stereotactically implanted subdural into 20 nude mice. 90 days after inoculation of the cells, a cranial MRI with contrast material was performed for detection of tumor growth. After identification of meningioma growth in MR images, FAM-TOC5,6-Carboxyfluoresceine-Tyr3-Octreotide was injected intravenously and tumor mass was hereafter resected with fluorescent microscope and endoscope. Finally, brain dissection were performed a histologically processed for measurement of extent of resection.

Results

Tumor growth was detected in 18 of 20 mice in MRI after 90 days of inoculation. The tumor mass could be clearly identified under fluorescent view of the microscope and endoscope after injecting FAM-TOC5,6-Carboxyfluoresceine-Tyr3-Octreotide. The tumor margins could be better visualized and no remnant tumor remained in situ. The histological analysis revealed a GTR in all cases.

Conclusion

This study demonstrates the use of FAM-TOC5,6-Carboxyfluoresceine-Tyr3-Octreotide in fluorescent identification of meningioma cells in vivo for the first time. The authors were able to establish an experimental animal model for fluoesence guided meningimoa resection with a somatostatin-ligand based fluorescence dye for the first time.

Neuroonkologie II/*Neurooncology II*

V086

Funktionelle Konnektivität bei Patienten mit raumfordernden Läsionen im okzipitalen Kortex
Functional connectivity networks in patients with space-occupying lesions in the occipital cortex

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Objective

Space-occupying brain lesions as brain tumors or vessel malformations in the area of the occipital lobe have only been sparsely investigated so far, as this localization is extremely rare with only 1% of cases. It is still unclear how this affects the overall organization of the visual system. To address this issue, we wanted to investigate functional connectivity of functional networks associated with higher visual processing between patients with occipital space-occupying lesion in the occipital cortex and healthy controls.

Methods

12 patients with brain tumors and 7 patients with vascular lesions in the occipital cortex as well as 19 healthy subjects matched for age and sex were included. During functional MRI patients and subjects were instructed to strictly fixate a blue spot in the center of a grey screen while a flickering checker board spreads from the inner to the outer visual field. Data preprocessing including motion correction of functional data, a registration of functional data on the cortical surface of the anatomical image as well as functional connectivity analysis to assess temporal correlation of brain areas was done using the Statistical Parametric Mapping 12 software and CONN toolbox both based on Matlab. We used 23 Regions of Interest (ROIs) implemented in the CONN toolbox assigned to the Default Mode, Visual, Salience, Dorsal Attention, and Fronto Parietal networks. For each subject, connectivity was calculated using Fischer transformed pairwise correlations. These correlations were first considered separately for each group in one-sample analyses and then compared between the groups

Results

Compared to their assigned control subjects, the tumor patients and patients with vascular lesion showed reduced intra-network connectivity in the visual and frontoparietal network. Increased connectivity was observed within the salience network in both patient groups compared to controls. In the vascular lesion group there was additional increased connectivity within the default mode network compared to controls.

Conclusion

The results indicate that in the course of the disease, compensatory countermeasures take place in the brain against a brain tumor or a space-occupying brain lesion with the aim of maintaining the performance level and cognitive processes for as long as possible. However, more research is needed in this area to understand the mechanisms and effects of brain tumors and space-consuming brain lesions on surrounding tissue.

Neuroonkologie II/*Neurooncology II*

V087

Glykierung von beningnen Meningeomzellen führt zu einem aggressiveren Verhalten
Glycation of benign meningioma cells leads to an increased malignant potential

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Objective

In a previous study, we investigated the influence of glycation in invasiveness on two meningioma cell lines representing the WHO grade I and III. Therefore cells were treated with Methylglyoxal (MGO). We could show, that glycation leads to a more aggressive behavior of the beningn cell line and to a less aggressive behavior of the malignant cell line. In this study, we wanted to investigate the molecular mechanisms of this behaviour.

Methods

Two meningioma cell lines, representing the WHO grade I (BEN-MEN-1) and the WHO grade III (IOMM-Lee) were cultured in the absence or presence of MGO. Expression of N-Cadherin, E-Cadherin, several Integrins, RAGE (Receptor for Advanced Glycation Endproducts), NCAM (neuronal cell adhesion molecul), Tn-Antigen and GALNT (GalNAc polypeptide N-acetylgalactosaminyltransferases) were analyzed.

Results

We observed that E-Cadherin expression was increased after glycation and N-Cadherin expression was decreased in BEN-MEN-1 cells. The Cadherin expression was not affected in IOMM-Lee cells. In both cell lines, we could observe an increased RAGE expression after glycation. Tn-Antigen was increased after glycation in BEN-MEN1 cells and was not affected in IOM-LEE cells after glycation. The expression of NCAM was decreases in IOM-LEE cells after glycation. For the GALNT 10 we saw no alteration in IOM-LEE cells after glycation where it was decreased in BEN-MEN1 cells.

Conclusion

Glycation of benign meningioma cell line results in an increased E-Cadherin and RAGE expression and a decreased N-Cadherin expression, which could be an evidence for more invasiveness of the benign meningioma cell line. IOMM-Lee cells were not affected in Cadherin expression through glycation. In addition, we saw changes in the expression of Tn-Antigen and GALNT 10 in BEN-MEN1 cells after glycation.

Fig. 1

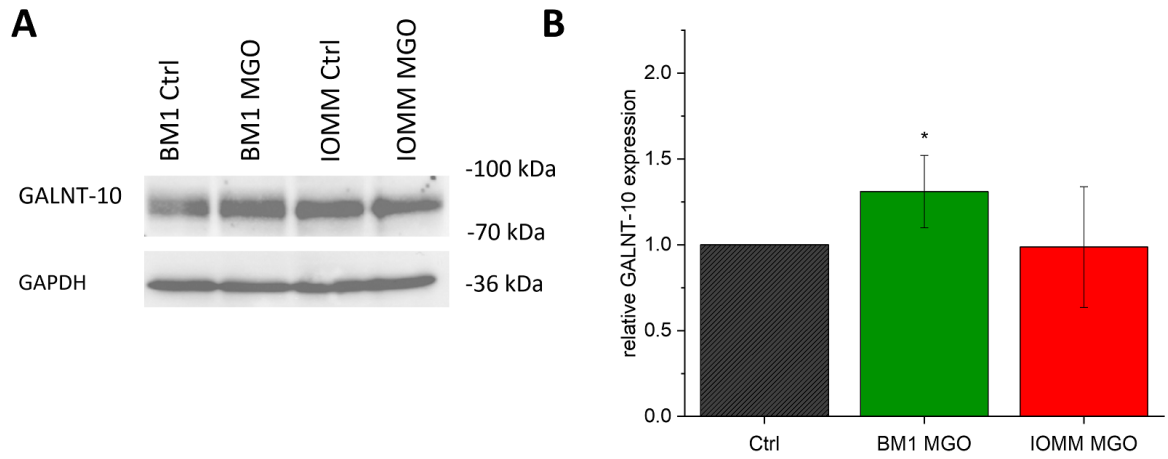
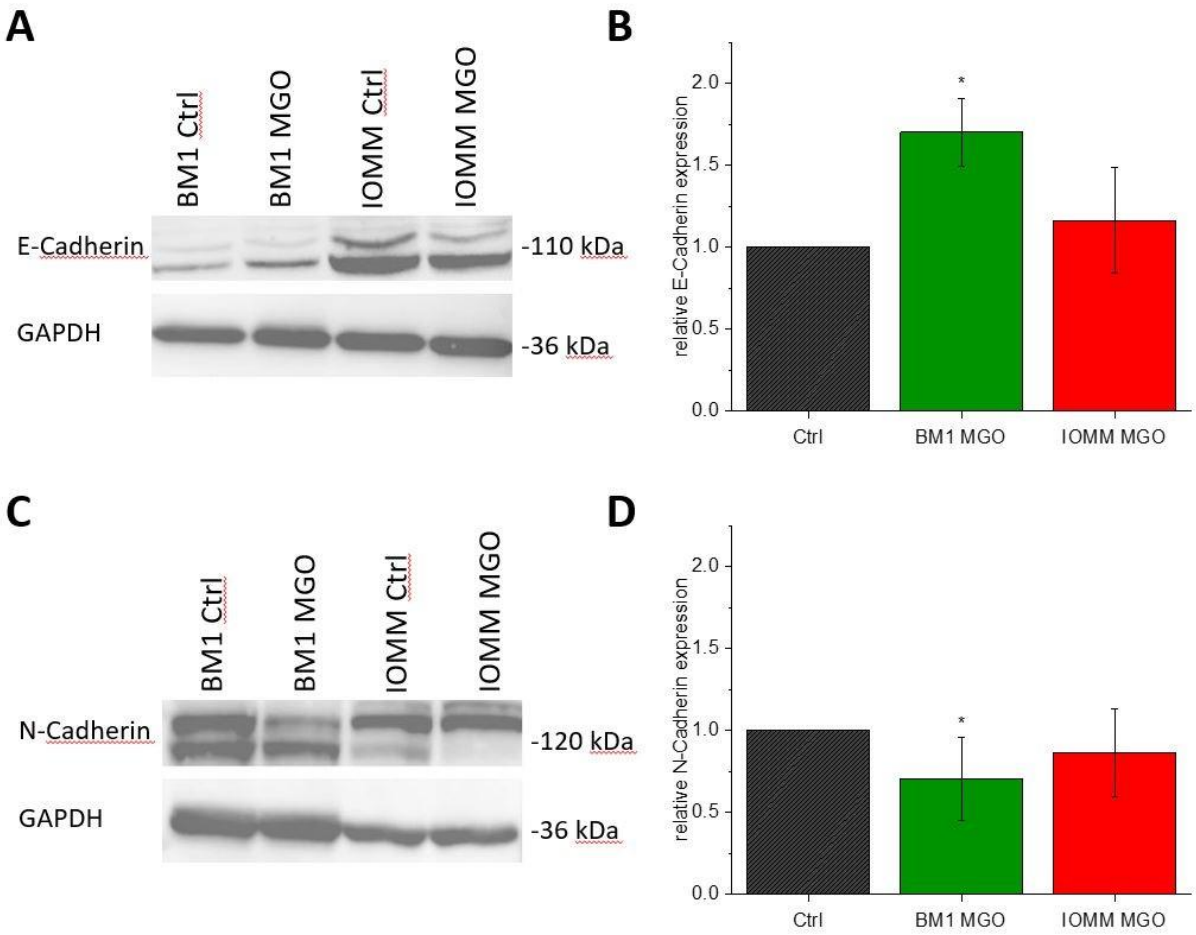

A
BM1 Ctrl
BM1 MGO
IOMM Ctrl
IOMM MGO
GALNT-10
GAPDH
-100 kDa
-70 kDa
-36 kDa
B
relative GALNT-10 expression
2.0
1.5
1.0
0.5
0.0
*
Ctrl
BM1 MGO
IOMM MGO

Fig. 2


A
BM1 Ctrl
BM1 MGO
IOMM Ctrl
IOMM MGO
E-Cadherin
GAPDH
-110 kDa
-36 kDa
B
relative E-Cadherin expression
2.0
1.5
1.0
0.5
0.0
*
Ctrl
BM1 MGO
IOMM MGO
C
BM1 Ctrl
BM1 MGO
IOMM Ctrl
IOMM MGO
N-Cadherin
GAPDH
-120 kDa
-36 kDa
D
relative N-Cadherin expression
2.0
1.5
1.0
0.5
0.0
*
Ctrl
BM1 MGO
IOMM MGO

Neuroonkologie II/*Neurooncology II*

V088

Identifizierung von Tumormarkern im Vestibularisschwannom
Identification of tumour markers in progressive vestibular schwannomas

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Objective

Vestibular schwannomas (VS) are the most common tumors of the cerebellopontine angle. Typical symptoms are vertigo, tinnitus, hearing loss and facial nerve paresis. Beside scan and wait, current therapeutic strategies are limited to tumor resection and/or radiotherapy. The molecular differences of progressive or stagnating VS are unknown. Evidence suggested that increased vascularization, secretion of macrophage activating factors or enhanced expression of inflammation or growth factors may play a role. Based on these findings, comparative expression analyses of VS with different growth characteristics and Koos classification were performed to identify tumor markers in an explorative study.

Methods

RNA was isolated from VS tissue of 141 patients with different Koos classification. Excluded were patients with neurofibromatosis, previously irradiated VS and recurrences. The mRNA was transcribed into cDNA and the expression of monocytic markers CD68, CD163 and macrophage colony-stimulating factor (M-CSF) was determined using qPCR. In addition, the transcript level of vascular endothelial growth factor (VEGF), cyclooxygenase 2 (COX2) and Ki-67 (proliferation) was measured. The relationship between marker expression, tumor cell proliferation and Koos classification was tested using the Spearman"s rank correlation coefficient, respectively.

Results

The data analysis showed a strong positive correlation of the inflammation markers CD68 and CD163 ($r=0.71$, $p<0.0001$). A moderate positive correlation was detected both between M-CSF with CD163 ($r=0.48$, $p<0.0001$) and CD68 ($r=0.47$, $p<0.0001$) as well as between the vasculatory factor VEGF and the proliferation marker Ki-67 ($r=0.42$, $p<0.0001$). Surprisingly, a weak negative correlation between the Koos classification and proliferation (Ki-67, $r=-0.39$, $p<0.0001$; COX2, $r=-0.32$, $p=0.0001$) and vacularisation (VEGF, $r=-0.26$, $p=0.002$) was found. In contrast, a weak positive correlation of the Koos classification with the inflammatory markers CD68 ($r=0.35$, $p=0.0001$) and CD163 ($r=0.21$, $p=0.02$) as well as between Ki-67 and M-CSF ($r=0.23$, $p=0.0072$) was observed.

Conclusion

The initial explorative data of our study suggest that VS with low Koos grade have higher expression of proliferation markers, whereas higher Koos grades show increased expression of inflammatory and macrophage markers. Therefore, it seems that the progression of VS is not only driven by proliferation, but could be induced by macrophage infiltration and inflammatory processes.

Neuroonkologie II/*Neurooncology II*

V090

Einfluss der Primär oder Rezidiv-Wachoperation auf den psychoonkologischen Status von neuroonkologischen Patienten

Impact of primary or recurrent planned awake brain surgery on psychooncological status in neurooncological patients

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Objective

Patients with cerebral tumours perioperatively show high rates of distress, anxiety, and depression. For several patients with eloquently located cerebral lesions awake surgery is the best surgical method for preservation of speech and motor function but might be accompanied by increased psychological stress. Aim of the present study was to find out if patients planned for awake craniotomy suffer from increased prevalence or higher scores in distress, anxiety or depression.

Methods

Data were collected perioperatively using the NCCN distress thermometer, Hospital Anxiety and Depression Scale (HADS), the SF36 as well as the European Platform of Cancer Research quality of life questionnaire brain module (EORTC QLQ-BN20). Retrospective statistical analyses for nominal variables were conducted using Chi-square-test. Metric variables were analysed using the Kruskal-Wallis-Test, the Man-Whitney-U-Test and Independent-sample T-tests.

Results

Data from 54 patients (26 male, 28 female) aged 29 to 82 years (56.07 ± 15.34 years of age) were available for statistical analyses. 37 of the patients received primary and 17 patients recurrent surgery. Awake surgery was planned for 35 patients, 19 patients were planned for non-awake surgery.There was no significant difference in awake versus non awake surgery patients regarding prevalence (has or has not) of distress (p=.695), anxiety (p=.165) or depression (p=.786). Furthermore, awake surgery had no significant influence on distress thermometer score (p=.470), anxiety-score (p=.461) or depression-score (p=.417) as well as future uncertainty (p=.436) or global health-status (p=.943). Additionally, analyses revealed that primary or recurrent surgery also did not have any significant influence on prevelance or scoring of the evaluated items.

Conclusion

Analyses of our cohort"s data suggest that planned awake surgery might not have a significantly negative impact on patients concerning the prevalence and severity of manifestation of distress, anxiety or depression in psychooncological screening. However, data only comprise a small number of patients, hence further investigation in larger patient cohorts are to be conducted.

Wirbelsäulenchirurgie I/*Spinal surgery I*

V091

Ein einfacher Score zur Beurteilung der Fusion nach dorsaler spinaler Instrumentation
A simple fusion score for dorsal spinal instrumentation

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Objective

The assessment criteria for successful fusion after spine surgery vary widely. While some authors content themselves with a lack of implant loosening, others request imaging evidence of bone bridge formation, e.g. on radiographs or even on computed tomography.

The aim of this study was to assess imaging after posterior lumbar instrumentation in order to devise a simple and reproducible system to report successful or absent fusion.

Methods

We performed a retrospective chart and imaging review of patients who underwent lumbar spinal instrumentation for degenerative disease. The analysis was based on demographic and radiographic parameters including age, sex, indication for surgery, number of operated segments. On postoperative CT scans with a mean follow-up of 30±25 months, we assessed three criteria pertaining to anterior column fusion (interbody fusion according to the Brantigan Fraser score, points 0-2), dorsolateral fusion (facet joint and laminar bridging according to the Lenke score, points 0-2) and implant stability (absent signs of loosening 2 points, halo sign < 2mm 1 point, large halo sign or implant dislocation 0 points) resulting in a composite fusion score (CFS) from 0-6 points. A higher score represents a more solid fusion, a lower score reflects lack thereof. We evaluated the predictive power of this score for implant failure requiring a second surgery.

Results

145 patients (86 female, 59%) with a mean age of 59.8±13 years undergoing posterior lumbar instrumentation in 170 segments were analyzed. Implant loosening was predicted by low bone density and absent interbody and posterolateral fusion (CFS ≤ 4 points, p≤ 0.001). Low bone density predicted absent interbody and posterolateral fusion (p≤ 0.001). Revision surgery at follow-up was lower in the group with more favorable fusion scores (OR 0.30; CI95% 0.14-0.64; p=0.002).

Conclusion

Among all studied parameters, only a high fusion score reliably predicted good (revision-free) outcome at an average of 30 months after lumbar instrumentation for degenerative disease. Based on this work, we propose an objective scoring tool to report fusion outcomes in lumbar spine surgery.

Wirbelsäulenchirurgie I/*Spinal surgery I*

V092

Adaptation des somatosensiblen Kortex bei Patienten mit degenerativer cervikaler Myelopathie
Adaptation of the somatosensory cortex in patients suffering from degenerative cervical myelopathy

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Objective

Degenerative cervical myelopathy (DCM) shows growing prevalence in industrial nations due to the demographic development. However, the surgical decision-making is still challenging due to the lack of sufficiently reliable predictors of disease progression and surgical outcome. Recently, the compensatory potential of reorganization processes within the cerebrospinal motor network has been discussed. Somatosensory impairment as an early but often overlooked symptom of DCM was not in the main focus of research so far. We, here, investigated how the primary and secondary somatosensory cortex (S1 & S2) adapt in DCM.

Methods

A cohort of 18 right-handed participants, consisting of 9 DCM patients (mean JOA score 13.3 ± 2.3) and 9 age- and gender-matched healthy control subjects, underwent an fMRI (3T) session using a block design. The fMRI procedure consisted of alternating, passive somatosensory stimulation of the subjects' hands and feet by means of a felt stick. Using MATLAB® 2019a and the SPM12 software package, a ROI-wise analysis of BOLD-response was performed at the group level using a three-way ANOVA, including the factors "group" (patients/controls), "limb" (hand/foot) and "side" (left/right).

Results

In both, patients and controls, we found a strongly left-lateralized cortical response in S1 and S2 ($p \leq 0.05$, FWE-corrected) regarding the somatosensory stimulation of the right (dominant) hand. However, activation in patients was lower than in healthy control subjects ($p \leq 0.001$, uncorrected). Regarding the other task conditions, controls showed significant responses within the somatosensory cortex ($p \leq 0.05$, FWE-corrected), including a consistent activation within the ipsilateral S2. In contrast, patients showed only weak activation in S1 ($p \leq 0.001$, uncorrected) and a much scarcer involvement of ipsilateral areas.

Conclusion

Our results imply that DCM patients show reduced cortical responsiveness to peripheral stimuli. The cortical somatosensory representation of the right (preferred) hand seems to be more robust to deviations due to DCM than the representations of the other tested limbs. It remains to be investigated whether clinical impairment is correlated with cortical somatosensory responsiveness and if the respective alterations are reversible after surgical decompression.

Wirbelsäulenchirurgie I/*Spinal surgery I*

V093

Ist die spinale Dekompression bei Patienten mit pyogener Spondylodiszitis wirklich notwendig?
Is spinal decompression necessary in patients with pyogenic spondylodiscitis?

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Objective

Patients with pyogenic spondylodiscitis might present with neurological deficits with or without epidural abscess requiring spinal decompression. The aim of this study was to investigate the role of epidural abscess and spinal decompression in the treatment of patients with pyogenic Spondylodiscitis.

Methods

We reviewed data of 218 patients who underwent surgical treatment for pyogenic spondylodiscitis at our institution between 2008 and 2018. In addition to the medical treatment, dorsal instrumentation was the standard surgical approach. Additional spinal decompression to alleviate neural impingement was performed in case of neurological deficit at admission, regardless of the presence of epidural abscess. Analysis included preoperative MRI- imaging, preoperative and last CRP values, microbiological yield, duration of hospital stay as well as relapse and wound infection.

Results

Epidural abscess was found in 68 patients (31%) at admission, while a neurological deficit requiring spinal decompression was found in 80 patients (37%) at admission. Of them, 33 patients (41%) had an epidural abscess. No correlation was found between epidural abscess and preoperative neurological deficit (OR 5-95%, 0.818 to 2.6, P = 0.257) or CRP values at admission (105 vs. 82 mg/l, P = 0.087). Patients with epidural abscess did not have a longer hospital stay (median 23 vs. 24 days, P = 0.412). Spinal decompression was associated with a higher microbiological yield (OR 5-95%, 1.101 to 3.435, P = 0.031) but did not correlate with lower last CRP values (33 vs. 31 mg/l, P = 0.644) or shorter hospital stay (median 23 vs. 24 days, P = 0.412). Neither epidural abscess nor spinal compression was associated with relapse infection (OR 5-95%, 0.486 to 4.948, P = 0.636 and OR 5-95%, 0.306 to 2.431, P = 0.984, respectively) or surgical wound infection (OR 5-95%, 0.670 to 2.816, P = 0. 497 and OR 5-95%, 0.906 to 3.641, P = 0.13, respectively).

Conclusion

Spinal decompression in patients with pyogenic spondylodiscitis might be justified in case of neurological deficit at admission but not to treat epidural abscess per se. Our data showed that neither epidural abscess nor spinal decompression influenced the course of the infection.

Wirbelsäulenchirurgie I/*Spinal surgery I*

V094

Beurteilung der Knochenqualität von Wirbelkörpern anhand von computertomographisch gemessenen Hounsfieldeinheiten

Assessment of the bone quality of vertebral bodies using computed tomography measured Hounsfield units

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Objective

Nonspecific back pain due to vertebral fractures is the most common manifestation of osteoporosis. Due to the increasing age of patients, the evaluation of bone density is becoming more and more important, especially in preparation for spinal surgery. The aim of the study is to determine bone density using computed tomography (CT). Here care should be investigated a possible correlation of Hounsfield Units (HU) of CT with bone density values of a quantitative computed tomography (QCT).

Methods

The study is a monocentric, retrospective data analysis. We examined 1000 vertebral bodies from a total of 369 patients who received a CT of the thoracolumbar transition and the lumbar spine (L1-4) in the period from January 1, 2015 to February 15, 2019 and compared the HU with the values of a QCT. Using SPSS, a linear regression, the general estimation equation and the Wald Chi square test, a general equation for the calculation of the QCT values was established. This equation includes the following influencing factors: HU, contrast medium application, sex and age of the patients.

Results

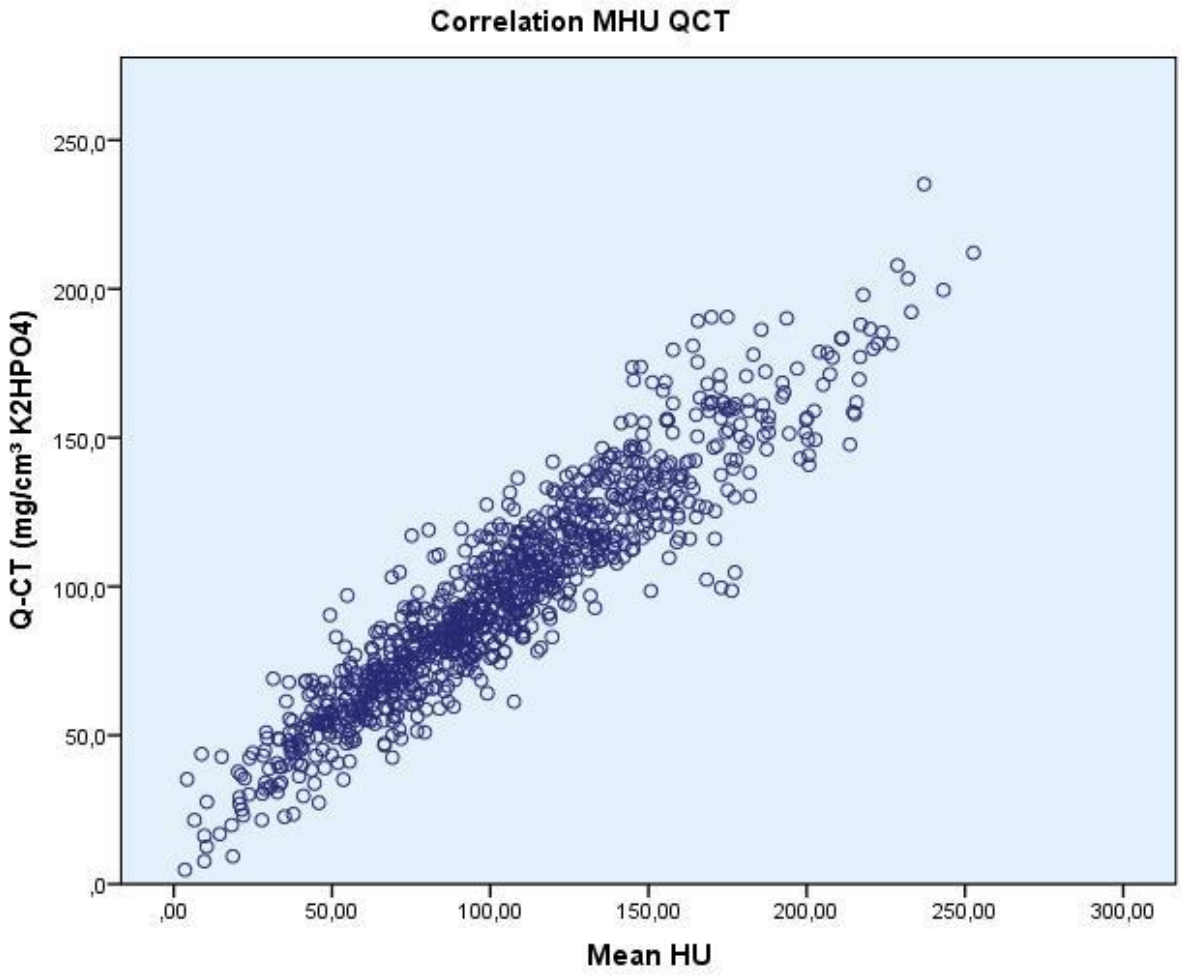
In our work we could prove a significant correlation between the Hounsfield units of a CT of the lumbar spine and the corresponding QCT values. The application of contrast agent significantly influences the correlation of the HU and the QCT values ($p < 0.001$; Fig1). We also observed that the calculated QCT values are independent of patient gender ($p < 0.942$) and that patient age has no clinically relevant influence on the calculation of QCT values (-0.2HU/year, $p < 0.003$). Furthermore, we could not demonstrate differences in the correlation of the three measured levels (axial, sagittal, coronary) to the QCT values. Since the application of contrast agent has a significant influence on the correlation, we only used native CT (N = 902) to establish the equation. According to our data we were able to establish a calculation to approximate QCT from lumbar spine QCT = 17.8+ 0.7 * HU.

Fig.1: Scatter diagram showing the values of QCT in relation to the mean values of the Hounsfield units in TH 11 to L 4, N= 1000, correlation coefficient r = 0.933

Conclusion

The conversion equation makes it possible to calculate bone density values without the need for an additional QCT, without further radiation exposure or costs, and thus to evaluate bone quality. The measuring method makes it possible to obtain additional information from computed tomography.

Fig. 1


Correlation MHU QCT
Q-CT (mg/cm³ K2HPO4)
250,0
200,0
150,0
100,0
50,0
,0
,00
50,00
100,00
150,00
200,00
250,00
300,00
Mean HU

Wirbelsäulenchirurgie I/*Spinal surgery I*

V095

Kortikale Volumenreduktion als Zeichen einer zerebralen und zerebellären sekundären Schädigung bei Patienten mit degenerativer zervikaler Myelopathie

Cortical volume reductions as a sign of secondary cerebral and cerebellar impairment in patients with degenerative cervical myelopathy

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Objective

This study investigated supra- and infratentorial structural gray and white matter (GM, WM) alterations in patients with degenerative cervical myelopathy (DCM) as an indicator of secondary harm due to chronic cervical cord compression and micro traumata.

Methods

With MRI-based anatomical assessment and subsequent voxel-based morphometry analyses, pre- and postoperative volume alterations in the primary motor cortex (MI), the primary somatosensory cortex (SI), the supplementary motor area (SMA), and the cerebellum were analyzed in 43 DCM patients and 20 controls. Disease-related symptom severity was assessed by the modified Japanese Orthopedic Association scale (mJOA). Symptom severity-based brain volume alterations were explored, as well as their association with the clinical status.

Results

Patients had lower mJOA scores (p<.001) and lower GM volume than controls in SI (p<.05) and cerebellar regions (p<.001). Symptom severity-based subgroup analyses revealed volume reductions across all investigated GM ROIs in patients with severe clinical symptoms (all p<.05), as well as already present atrophy in patients with moderate symptom severity (p<.05). Clinical symptoms in DCM were associated with cortical and cerebellar volume reduction.

Conclusion

GM volume alterations may serve as an indicator of both disease severity and ongoing disease progression in DCM and should be considered in further patient care and treatment monitoring.

Wirbelsäulenchirurgie I/*Spinal surgery I*

V096

Die Kortikospinale Reserve – die Beurteilung des Krankheitsstadiums und -dynamik bei cervikaler Myelopathie
The corticospinal reserve – evaluation of disease stage and dynamics in degenerative cervical myelopathy with navigated TMS

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Objective

In patients suffering from degenerative cervical myelopathy (DCM), conventional radiology with additional electrophysiology often fails to reliable quantify stage of disease and dynamics of disease progression. We have recently introduced the concept of "corticospinal reserve" in which severely symptomatic patients (JOA≤12) with an exhausted reserve presented with a restricted motor area, reduced recruitment curve and increased inhibition. In contrast, patients suffering from mild symptoms (JOA>12) and thus preserved corticospinal reserve, an enlarged motor area due to a higher recruitment of adjacent neuronal groups was observed. The current prospective multicenter trial has been designed to validate this new pathophysiological concept and demonstrate its diagnostic potential in DCM.

Methods

We investigated 120 patients (mean age 64.5 ± 11.8 yrs.) with DCM preoperatively and following surgical decompression from four spine centers in Germany and Switzerland. The study was sponsored by a DWG research grant. Patients were divided into three groups, based on the initial Japanese Orthopedic Association Score (JOA ≤12/13-15/>15). In addition, conventional electrophysiology (SSEP/MEP) and the "Disabilities of Arm, Shoulder and Hand Questionnaire" (DASH) were recorded. For the assessment of corticospinal excitability, we measured the resting motor threshold (RMT), motor area, recruitment curve (RC) and cortical silent period (CSP) by means of navigated transcranial magnetic stimulation (nTMS).

Results

In patients with moderate symptoms (JOA >15) we encountered a compensatory increased motor cortex activation (motor area: p≤12: 225.7 ± 159.5) and maintained corticospinal excitability (RC slope p=0.4, JOA 13-15: 10.6 ± 6 vs. JOA >15: 11.1 ± 5.2). In contrast patients with severe symptoms (JOA≤12) presented a reduced excitability of cortico-cortical axons reflected by an elevated RMT (p≤12: 43.8 ± 11.4 vs. JOA >15: 39.2 ± 8.4) and reduced corticospinal excitability expressed by a lower RC slope (p≤12: 8.4± 4.8 vs. JOA >15: 11.1± 5.2). The conventional electrophysiology revealed only 73.3% pathological SSEPs for patients with a severe impairment (JOA ≤12), 65.8% for moderate symptoms (JOA 13-15) and 27,3% for mild symptoms (JOA >15).

Conclusion

In summary, our prospective multicenter trial has confirmed our concept for functional reorganization in patients suffering from DCM i.e. the "corticospinal reserve capacity". Based on our findings it became apparent that conventional diagnostics often fail to demonstrate clinical impairment and disease progression. The corticospinal reserve might be able to overcome the diagnostic gap in DCM and serve as an objective and valuable tool for future treatment strategies in these patients.

Digitale und KI-basierte Anwendungen I/*Digital and AI-based implementations I*

V097

Pedikelschraubenplatzierung mit dem OP Roboter – potentielle Vorteile und Auswirkungen auf die Zukunft der Wirbelsäulenchirurgie

Accurate pedicle screw placement using navigated robotic guidance – potential advantages and implications in the future of spine surgery

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Objective

Since the introduction of modern spine robots spine surgeons are persuaded that a paradigmatic shift in spine surgery regarding reliability, safety innovation, simulation, training and radiation exposure is happening. The aim of this study is to see wether these systems can perform efficently.

Methods

Retrospective study from a prospectively collected database in a German spine center of patients who underwent navigated robot-guided spine surgery. From October 2018 to November 2019, 250 Patients underwent pedicle screw instrumentation with navigated robotic guidance. 90 Patients received traditional open lumbar fusion with pedicle screw system (594 screws) with intraoperative imgae adquisition. 140 patients underwent MIS TLIF and thoracic instrumentation procedures with percutaneous pedicle screw system (609 screws). 20 Patients underwent dorsal cervical instrumentation with lateral mass and pedicle screws (94 screws). Intraoperative CT scans were taken if robotic system did not validate complete set of screw placement based on the planned trajectory. Using intraoperative CT scans deviations from the planned screws were measured from the middle of the actual pedicle screw placement to the middle of the pedicle. The measurement of the screws was adjudicated as: perfect (<1.5mm deviation), good (1.5-3mm deviation) and fair (3-5 mm deviation) in relation to the planned trajectory.

Results

90% of all screws received the intraoperative checkmark from the navigation software. All those screws adjudicated as correct by the verification algorithm where in the range of < 1.5 mm. From the total of 129 screws not adjudicated as correct by the software algorithms, 65 were still in the range < 1.5 mm, whereas 50 were in the range 1,5 - 3 mm and only 14 screws ranged 3 - 5 mm. 6 screws required intraoperative revision, none of them in the cervical spine.

Conclusion

Robotic guided screw placement seems to be safe, efficient and reliable. Training and preoperative simulation seem to be translate into clinical workflow and outcome. Further Investigation is required to compare prospectively different workflows and competing systems.

Digitale und KI-basierte Anwendungen I/*Digital and AI-based implementations I*

V099

Differenzierung von Multipler Sklerose und Gliomen WHO II° / III° anhand von AI-basierten 18F-FET-PET Untersuchungen

Artificial intelligence for the differentiation between multiple sclerosis and glioma II° or III° using 18F-FET-PET imaging

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Objective

To evaluate the diagnostic significance of ^{18}F-FET-PET imaging for the differentiation between multiple sclerosis (MS) and World Health Organization (WHO) grade 2/3 glioma (glioma II°/III°).

Methods

We retrospectively screened for patients in whom 18F-FET-PET imaging was performed for the diagnostic workup of newly-diagnosed lesions evident on magnetic resonance imaging (MRI) and suspicious for glioma. Among those, we identified patients with histologically confirmed glioma II°/III° and those who later turned out to have multiple sclerosis pursuant to the revised McDonald criteria from 2017. For each group, the mean and maximum tumor-to-brain ratio (TBR) of 18F-FET were determined. Moreover, we used a support-vector machine (SVM) based machine learning algorithm trained on a development and evaluated on a validation subgroup. Receiver operating characteristic (ROC) analysis with area under the curve (AUC) metric was used to assess model performance.

Results

A total of n=33 patients met inclusion criteria. Subsequent diagnostics confirmed MS in n=7 and glioma II°/III° in n=26 patients. TBRmean and TBRmax were significantly higher in the glioma group (TBRmean glioma group: 2.16±0.93, MS group: 1.33±0.14, p = 0.03; TBRmax glioma group: 2.01±0.79, MS group: 1.23±0.19, p = 0.02). In a subgroup analysis, TBRmean and TBRmax significantly differentiated between MS and oligodendroglioma (OG) II°/III° (TBRmean OG group: 2.75±0.91, MS group: 1.33±0.14, p = 0.002; TBRmax OG group: 2.47±0.71, TBRmean MS group: 1.23±0.19, p = 0.003). As shown on ROC analysis, the ability to differentiate between MS and glioma increased from 78.6% using standard TBR analysis to 93.0% using a SVM based machine learning algorithm.

Conclusion

18F-FET-PET imaging using an SVM based machine learning algorithm enhanced classification performance for the differentiation of MS from glioma. Future studies with larger sample sizes are needed to confirm this observation.

Digitale und KI-basierte Anwendungen I/*Digital and AI-based implementations I*

V101

Automatisierte Erkennung und Segmentation von fokalen kortikalen Dysplasien (FCDs) – Vorstellung eines neuartigen künstlichen neuronalen Netzwerks und dessen prospektiver klinischer Validierung

Automated detection and segmentation of focal cortical dysplasias (FCDs) – presentation of a novel artificial neural network with a prospective clinical validation

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Objective

Focal cortical dysplasias (FCDs) are highly epileptogenic lesions frequently accounting for pharmaco-resistant focal epilepsy. Although MRI techniques have improved significantly over the past years, FCD detection remains challenging, as FCDs vary in location, size, and shape and commonly blend into surrounding tissues without clear definable boundaries. We developed a novel convolutional neural network for FCD detection and segmentation and validated it prospectively on daily-routine MRIs.

Methods

The neural network was trained on 201 T1 and FLAIR 3T MRI volume sequences of 158 patients with at least one FCD, regardless of type. Non-FCD MRIs, drawn from 100 normal MRIs and 50 MRIs with non-FCD pathologies, were added to the training. We applied the algorithm prospectively on 100 consecutive MRIs of patients with focal epilepsy from daily clinical practice. The results were compared with associated neuroradiological reports and morphometric analyses evaluated by an experienced epileptologist.

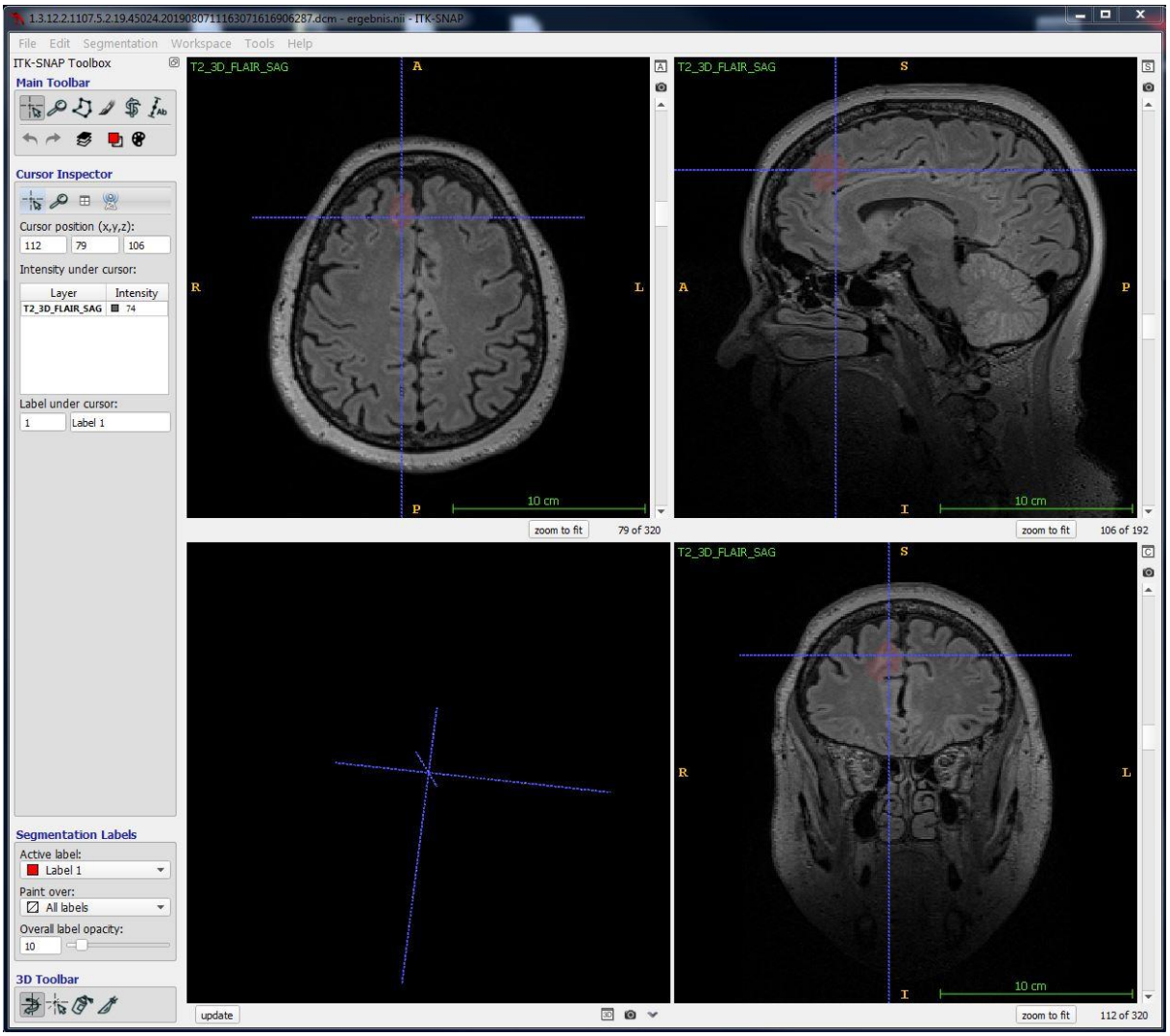
Results

Best training results reached a sensitivity (recall) of 70.1% and a precision of 54.3% for detecting FCDs. Applied on the daily-routine MRIs, 7 out of 9 FCDs were detected and segmented correctly with a sensitivity of 77.8% and a specificity of 5.5%. The results of conventional visual analyses were 33.3% and 94.5%, respectively (3/9 FCDs detected); the results of morphometric analyses with overall epileptologic evaluation were both 100% (9/9 FCDs detected) and thus served as reference.

Conclusion

We developed a 3D convolutional neural network with autoencoder regularization for FCD detection and segmentation. Our algorithm employs the largest FCD training cohort to date consisting of 201 MRIs with various types of FCDs. The higher sensitivity in detecting and segmenting FCDs compared to visual analyses allows our algorithm to be used as a convenient FCD pre-screening tool. However, its current low specificity, leading to a high rate of false positive predictions, still calls for validation by visual and morphometric analyses as well as the need for further algorithm training.

Fig. 1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File Edit Segmentation Workspace Tools Help
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Label under cursor:
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Pädiatrische Neurochirurgie/*Paediatric neurosurgery*

V102

Schaffung eines nationalen Zentrums für Kinderneurochirurgie in der Slowakischen Republik – Ist eine zentralisierte Spezialversorgung in der Kinderneurochirurgie erforderlich?

Creating a national centre of paediatric neurosurgery in the Slovak Republic – Is there a need for a centralised special care in paediatric neurosurgery?

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Objective

The high need for a national centre in our country was stated according to insufficient care in paediatric neurosurgery and growing number of patients undergoing their neurosurgical care abroad. A new neurosurgical department with neuropaediatric expertise was established in Bratislava with a catchment area of about 2 million inhabitants for regular procedures and 5.5 million (nationwide) for specialised procedures.

Methods

The facts from the official and medical records are summarized and compared with the historical records and with the reminiscences of participants. We analysed the procedures during the first 18 months after establishing the new departement.

Results

Team consisting of 3 neurosurgeons, 1 paediatric surgeon, 3 neurosurgical residents, 3 part-time neurosurgeons, 1 neurologist (electrophysiologist) and 1 part-time psychologist. There were 551 surgeries during the first 18 months. The spectrum range is wide: tumours (83), vascular (9), developmental disorders and cysts (45), hydrocephalus (166), cranial trauma (23), spinal trauma (16), peripheral nerves (10), functional (39) and minor precedures (160). We established successful and growing interdisciplinary cooperation with paediatric anaesthesiology, neurology, neonatology, surgery, radiology, oncology, ENT, ophtalmology and paediatrics in the National Children´s Hospital.

Conclusion

Despite the rigidity of the traditional neurosurgical service in process of founding of paediatric neurosurgical centre there seem to be significant benefits in the patient care in comparison with the historical records: 1. Introduction of up-to-date standards of the paediatric neurosurgical care, 2.Introduction of novel procedures (endoscopic surgery for craniostenosis, endoscopic surgery for tumours, cysts and hydrocephalus, neuroendoscopic lavage for neonatal hemorrhage, microsurgery for peripheral nerves, paediatric spinal instrumentation, endovascular intervention for pediatric vascular malformations and tumours, novel techniques of the intraoperative neuromonitoring), 3.Up-to-date revitalisation of historicaly performed procedures (tumour and vascular microsurgery, open surgery for developmental disorders, shunting procedures, spasticity and epilepsy), 4.Highly specialized equipment of the neurosurgical OP room, 5.Focused psychological support of the parents, 6.Shortening of the waiting period for surgery, 7.Elimination of the need for the specialized patient care abroad

Pädiatrische Neurochirurgie/*Paediatric neurosurgery*

V103

Kontroverse Aspekte in der Behandlung von Kindern mit Hydrocephalus
Controversies in paediatric hydrocephalus treatment

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Objective

Hydrocephalus in childhood is a frequent condition known for long but still there are controversies referring to diagnostic procedures and treatment strategies. This study aimed to get an overview over concepts used worldwide.

Methods

We made an inquiry dealing with questions of hydrocephalus treatment in childhood taking into account several aspects of care in different countries and continents. Data were collected using a questionnaire distributed online.

Results

We evaluated 281 replies, mostly from countries of the European Union (23,3%), Japan, South Korea and China (20,4%), Latin America (15,8%) and North America and Canada (11,5%). CT, MRI and ultrasound (US) are commonly used. 53,8% always performed US, 36,5% CT and 28,5% MRI before 1st surgery. Primary treatment procedures include - in descending order - implantation of a reservoir, external ventricular drainage systems (EVD), vp-shunts, ventriculo-subgaleal shunts, ventriculostomy (ETV) and a repeated puncturing through the fontanel. 26% desired a body weight of the child of > 2500g for primary ventriculo-peritoneal shunt placement. 1,5% accept a weight of < 1000g. Frontal approach for ventricular catheter placement is preferred in 56,7%. Standard application of intraoperative guiding systems for catheter placement is not very common (US 8,3%, navigation 2,5%). Length of the peritoneal catheter varies from > 80cm (18,2%), 60-80cm (14,9%), 40-60cm (25,8%), 20-40cm (36,4%) to < 20cm (4,7%). Distal catheter revision for routine just due to the growth of the child is not favoured by a majority of the respondents.In all forms of hydrocephalus fixed differential pressure valves are used most frequently and adjustable antisiphon valves are used least. Asked about the use of perioperative antibiotics a single shot concept is used in 51,3% when shunt surgery is performed and 35,8% when an EVD is placed. 39,9% preferred antibiotic treatment for the whole time the EVD is in place. Clinical follow up is done every 6 months (32,4%), every 12 months (52,9%), every 24 months (4,7%) or only when the patient has complaints (10,1%). After shunting 54% perform radiologic examinations in regular intervals, 46% only when the child is symptomatic.

Conclusion

We found an impressive variety in treatment concepts used in various countries with different socio-economic background. Further investigation is needed to find out about feasable treatment solutions for children with hydrocephalus worldwide.

Pädiatrische Neurochirurgie/*Paediatric neurosurgery*

V104

Neuroendoskopie bei posthämorrhagischem Hydrozephalus des Frühgeborenen
Neuroendoscopy (lavage, clot removal, septostomy) for posthaemorrhagic hydrocephalus (PHH) in newborns

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Objective

There is an on-going debate about the optimal treatment strategies for posthemorrhagic hydrocephalus (PHH) in premature infants. Recent studies show a reduction of shunt dependency after endoscopic lavage and clot removal. To determine the role of endoscopic lavage, clot removal combined with septostomy, followed by temporizing methods (ventricular reservoir, subgaleal shunting) in order to provide a lower shunt complication rate or even to reduce shunt dependency. We demonstrate our single center experience.

Methods

We performed 17 endoscopic lavages in 11 preterm infants (gestational week: 23-36 (mean 27), birth weight: 595-2400 g (mean 971)) and 1 term neonate (41 wks, 3155 g) suffering from intraventricular hemorrhages (grade II-III+). Initial surgery was done 13-118 (mean 38) days after birth. Warmed Ringer solution (750-3000ml) was used. Furthermore, interventions included partial or nearly total clot removal, septostomy (n=6, incl. stent=3) followed by ventricular reservoir (all) and subgaleal shunting (n=5), followed by intermittent punctures (if necessary). The indications for operation were progressive ventricular enlargement, enlarging head circumference combined with symptoms of intracranial hypertension.

Results

Endoscopic procedures could be safely performed (LOTTA-Ventriculoscopic System, Storz, Tuttlingen). No direct secondary hemorrhage or endoscopy related morbidity/mortality occurred. One second hemorrhage of the other side occurred after 4 days. One premature infant died due to pulmonary insufficiency. Permanent shunting (incl. stent to fourth ventricle (n=1)) was performed after 14 -112 (mean 57) days after first operation. No avoidance of shunting was possible in this small cohort. Afterward, shunt revision was needed in only one patient due to a suspected shunt obstruction during the follow-up period of 15-76 (mean 55) months. One intraventricular cyst occurred and could be endoscopically fenestrated. No CSF infection occurred.

Conclusion

Neuroendoscopic interventions are safe treatment options for PHH in premature infants, and might reduce later shunt complications. Earlier referral/intervention and more complete clot removal may even reduce shunt dependency. Further prospective evaluations with larger cohorts and longer follow-up are needed in view of the most important point: functional outcome.

Pädiatrische Neurochirurgie/*Paediatric neurosurgery*

V105

Langzeit Anfallsfreiheit nach resektiver Temporallappenchirurgie in eine pädiatrischen Kohorte – eine Single-Center retrospektive Studie

Long-term seizure outcome after resective temporal lobe surgery in a paediatric cohort – single-centre retrospective study

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Objective

In therapy resistant focal epilepsy the seizure onset zone is most often located in the temporal lobe. Resective surgery has emerged as a curative option, however the extent of resection remains at the surgeons discretion. While extensive resections might impair cognitive development, freedom of disabling seizures is still the best predictor of later quality of life. We therefore wanted to evaluate the long term seizure outcome after different resective temporal lobe surgeries in a pediatric cohort.

Methods

We performed a retrospective analysis of all pediatric patients undergoing resective temporal lobe surgery for intractable epilepsy with a minimum follow up of one year. Surgery type, histological findings, and seizure outcome according to the ILAE classification were extracted from patient records. Surgeries were stratified into lesionectomy, anterior temporal lobectomie (TLR) and selective amygdalahippocampectomies (SAHE).

Results

In total, 104 pediatric patients were operated between 1993 and 2019. The median follow up period was 9 years (range 1 to 14 years). Forty-nine lesionectomies, 42 TLRs and 13 SAHEs were performed. One year after surgery, 73 patients (70.2%) were seizure free. Seizure freedom rates were significantly lower for SAHE patients compared to lesionectomies and TLR (46.2% vs. 65.3% vs. 83.3% respectively, p = 0.022) and patients that had generalized seizures before surgery (65.6% vs. 88.4% in patients with partial seizures only). The most frequent pathologies were hippocampal sclerosis (n=35, 33.7%), gangliogliomas (n=24, 23.1%), and low grade gliomas (n=19, 18.3%). At least one relapse occurred in 24 patients (23.1%) that were initially seizure free. Surgery had to be repeated in 12 patients (11.5%), five of whom had an ILAE class I outcome at their last follow up. With additional surgery and medication changes 79 patients (76%) were seizure free at their last follow up visit.

Conclusion

Pediatric patients undergoing temporal lobe surgery for intractable epilepsy have a good rates of seizure outcome overall. Surgery type is a modifiable prognostic factor for later seizure freedom. SAHE appears to be ill suited for pediatric patients and should therefore be reserved for older patients. Re-resection after failed initial surgery can still offer a good chance at seizure freedom.

Pädiatrische Neurochirurgie/*Paediatric neurosurgery*

V106

Prädiktoren für die postoperative Anfallsfreiheit in 50 pädiatrischen Patieten mit fokal-kortikalen Dysplasie Typ II – retrospektive Single-Center-Studie

Predictors of postoperative long-term seizure in 50 paediatric patients with focal cortical dysplasia type II – retrospective single-centre study

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Objective

Focal cortical dysplasia (FCD) is the most common reason for early-onset intractable epilepsy among children. Surgical resection is growing overtime to become highly sufficient treatment option. This study provides a retrospective analysis of preoperative and postoperative factors and their impact on postsurgical long-term seizure outcome.

Methods

Fifty pediatric patients with mean age of 8 years (SD: ±4.49) with histologically proven FCD type II were retrospectively analyzed regarding the long-term postsurgical outcome. Furthermore, the impact of demographic data, imaging characteristic and surgical outcome on the long-term seizure outcome was analyzed. The patients underwent clinical examinations and short-term EEG at 6 months and 12 months after surgery. The seizure outcome was evaluated based on the ILAE-Classification.

Results

Complete resection of FCD was achieved in 74% (n=37). One year after surgery ILAE class I was achieved in 72% (n=36) and the long-term outcome improved to 74% (n=37) class I. A reduction of anti-epileptic drugs (AED) to monotherapy or complete discharge of AED was achieved in 37% (n=19). Eighteen percent (n=9) had late seizure recurrence, 14% (n=7) occurred after reduction of AED. Younger age at time surgery ($p<0.001$), shorter duration of epilepsy ($p<0.001$), lower number of taken AED prior to surgery ($p=0.023$) and completeness of resection were positive prognostic factors for a better long-term seizure outcome.

Conclusion

Duration of epilepsy, completeness of resection, number of AED and younger Age at time of surgery serve as predictors for the postsurgical long-term seizure outcome. The factors help in the selection process of surgical candidates as well as provide a better presurgical patient counseling. An earlier evaluation for surgery in patients with FCD II could elevate the long-term seizure outcome.

Pädiatrische Neurochirurgie/*Paediatric neurosurgery*

V108

Neurochirurgische Operationen bei Erwachsenen nach offener Myelomeningozele
Neurosurgical interventions in adults born with open myelomeningocele

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Objective

The frequency of neurosurgical interventions in adults born with open myelomeningocele (MMC) is unknown. Transition from pediatric to adult care is often difficult due to a lack of adult interdisciplinary spina bifida centers. We have therefore analyzed the frequency and type of such interventions.

Methods

This is a retrospective single-center analysis of operations performed between 2010 and 2019 in patients ≥ 18 years of age with ICD-10-main diagnosis Q05.-, which is spina bifida. Patients with open MMC were selected and data collected from electronic records.

Results

We performed 20 operations in 13 patients (8 female, 5 male) with a mean age of 36 years (range 20 to 56), of which 6 patients had lumbar and 7 lumbosacral MMC. In 12 cases a detethering for tethered cord syndrome was performed, being symptomatic with pain (N=4), motor (N=6), sensory (N=2) or urological (N=4) deficits. In 7 cases shunt revisions were performed, being symptomatic with headache (N=5), papilledema (N=2) or abdominal pain (N=2). In one case an incidental cavernoma was removed.

Conclusion

95% of operations performed in this cohort of adults patients born with open MMC were related to the primary disease: 60% were detetherings and 35% were shunt revisions. Neurological and urological symptoms were the presenting complaints. MMC-associated problems continue to occur in adulthood. The spectrum is similar to the pediatric age group and thus transition into interdisciplinary adult care should be achieved.

Neurotraumatologie, Radiochirurgie, Freie Themen/*Neurotraumatology, radiosurgery, free topics*

P001

Das Spektrum pädiatrischer Schädeltumoren
The spectrum of paediatric skull tumours

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Objective

Skull tumors are rare in childhood and no comprehensive data exist. Affected children may be treated by different medical specialities. This retrospective study provides an overview and recommendations for diagnostics and treatment.

Methods

This is a retrospective study of a consecutive single unit series of patients who underwent surgery for tumors affecting the skull. Patient characteristics, imaging, histopathology, treatment and prognosis were investigated.

Results

65 patients (58% female, 42% male) have been operated between March 2009 and February 2020. Mean age at time of surgery was 5.4 years (0.17-20.83). 64 patient had visible or palpable masses, one was suffering from diabetes insipidus (multilocular Langerhans hostiocytosis, LCH). All patients received CT- or MRI imaging. Histology: dermoid cyst (29;44.6%), dermoid cyst with dermal sinus (2;3.1%), LCH (8;12%), fibrous dysplasia (4;6.2%), aneurysmatic bone cyst (3;4.6%), ossifying fibroma (2;3.1%) and osteoma (2;3.1%). The remaining cases suffered from rare entities (fasciitis, myofibroma, hemangioma etc). 2 patients developed a 2nd malignant tumor manifestation (sarcomas) in the skull region after treatment for primary brain tumors (secondary glioblastoma, anaplastic meningioma). 3 patient received chemotherapy alone, 2 radio-chemotherapy. All others have been cured with surgery alone. Skull base tumors have been treated by an interdisciplinary surgical team. Radiological diagnosis was not conclusive in cases other than dermoid cysts. A blinded radiological evaluation was performed by 2 independent radiologists. Typical tumor related locations and age groups have been identified.

Conclusion

Nearly one half of skull tumors are dermoid cysts, which can easily be diagnosed and operated. The other half represents a broad variety of different pathologies, which cannot be predicted by imaging. It is recommended to manage all skull tumors surgically and an oncological team should always be involved, since skull tumors can be part of a systemic or malignant disease. In complex tumors of the skull base an interdisciplinary surgical team provides best results. CT and/or MRI is necessary in all cases.

Neurotraumatologie, Radiochirurgie, Freie Themen/*Neurotraumatology, radiosurgery, free topics*

P002

Minimal invasive Evakuation von intrazerebralen Hämatomen – Liquor augmentiert oder nicht?
Minimal invasive evacuation of intracerebral haematomas – CSF-augmented or not?

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Objective

Surgical treatment of spontaneous intracerebral haematomas (ICH) located in the basal ganglia or/and thalamus (BG/T) is challenging. Our study aims to analyze the effect of a minimal invasive method, namely the implantation of an Intraclot Drainage through the Ventricles (IDV), on the radiological and clinical course of patients with non-traumatic ICH of above-mentioned location.

Methods

We analyzed 62 patients with spontaneous supratentorial ICH demonstrating an ICH volume > 15 ml treated in our neuroICU between August 2019 and October 2020. 24 ICH were located in BG/T, whereas 28 ICH were depicted in remaining brain parenchyma (15 eloquent; 13 non-eloquent). Minimal invasive ICH evacuation plus rtPA was performed according to MISTIE protocol. ICH volumetry was estimated via Brainlab software smartbrush 2x (Brainlab, Inc.,Chicago, USA). Favorable radiological and clinical outcome were defined as ICH volume reduction of >30% at third postoperative day and GOS at discharge of 4&5, respectively. Statistical analysis was performed using SPSS v. 26 (IBM Corp. Armonk, USA).

Results

Median age of our cohort war 72 years; 31 (50%) patients were male. Median GCS at admission and discharge, were 9 and 12, respectively. Median ICH volume, median Hemphill"s ICH score and median Charlson comorbidity score at admission were 26,1 ml, 3 and 3, respectively. IDV was performed in 14 patients, whereas 9 patients underwent a non CSF-augmented minimal invasive implantation of intraclot drainage (ID); the remaining cohort was treated either surgically (decompressive craniectomy or microscopical ICH evacuation) or conservative. Patients who underwent IDV plus rtPA demonstrated a more favorable radiological outcome compared to patients treated with ID plus rtPA (p=0.021). No differences of clinical outcome at discharge as well as of complications rate were observed between IDV and ID.

Conclusion

IDV plus rtPA was associated with greater ICH volume reduction compared to non CSF-augmented ID plus rtPA. This method may appear as a safe and effective alternative of minimal invasive ICH evacuation located in basal ganglia or/and thalamus.

Neurotraumatologie, Radiochirurgie, Freie Themen/*Neurotraumatology, radiosurgery, free topics*

P003

Danger-scooter – das unterschätzte Risiko von schweren Elektroroller-assoziierten Schädelhirntraumata
Danger-scooter – the underestimated risk of severe electric scooter associated traumatic brain injury

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Objective

Since the approval of electric scooters (e-scooters) for road use in Germany in 2019, they have become increasingly popular. In our experience, patients treated after e-scooter accidents often have particularly severe traumatic brain injuries (TBI). Aim of this observational study was characterization of frequency, injury patterns, severity, and outcome of e-scooter accidents as literature on this topic remains very limited.

Methods

We performed a retrospective observational analysis of all consecutive e-scooter accident associated TBI in our center between June 2019 and September 2020. Analysis included basic demographic data, use of helmets, ethanol blood levels, accident-mechanism, injury patterns, surgical treatment, and outcome.

Results

A total of 63 patients with e-scooter accidents were admitted in the observation period. Thirteen patients (12 male, 1 female, mean age 24, age range15-79y) suffered TBI of which 7 had a severe trauma requiring craniotomy/craniectomy. Additionally, 5 patients had craniofacial and midface injuries requiring interdisciplinary surgical treatment. None of the patients wore helmets and 3 had elevated blood ethanol levels on admission. Of the 7 patients with severe trauma, only 3 have recovered well (GOS 7), 2 suffer from hemiparesis and impairing psychomotor deficits (GOS 4), 1 has retained a complete unilateral paresis of the oculomotor nerve, and 1 remained in a state of minimal awareness (GOS 3). During the observation period, bicycle accidents were treated approximately 7-fold more often with a significantly lower proportion of severe TBI (n=7) requiring neurosurgical treatment.

Conclusion

E-scooter accidents seem to be disproportionately often associated with severe TBI and often have devastating consequences for those affected. The refusal of most users to wear helmets presumably contributes to the poor outcome after these accidents. In light of these alarming findings, the current legislation should be reconsidered.

Neurotraumatologie, Radiochirurgie, Freie Themen/*Neurotraumatology, radiosurgery, free topics*

P004

Präoperative zervikale Traktion mit Garner-Wells-Zange – Wer profitiert am meisten?
Preoperative cervical traction with Gardner-Wells Tongs – Who profits most?

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Objective

Preoperative traction with the Gardner-Wells Tongs (PTGWT) is a valuable option for cervical spine injuries with malalignment. The aim of this study was to analyze the factors related to the treatment success of PTGWT.

Methods

All consecutive cases with PTGWT due to cervical spine injury with malalignment treated in our hospital between January 2010 and September 2020 were eligible for the study. Patients" records were reviewed for demographic and clinical characteristics. Treatment success was evaluated upon the angle correction in the sagittal plane using the computed tomography scans before and after completing the PTGWT. Statistical analysis was conducted using R version 3.6.0.

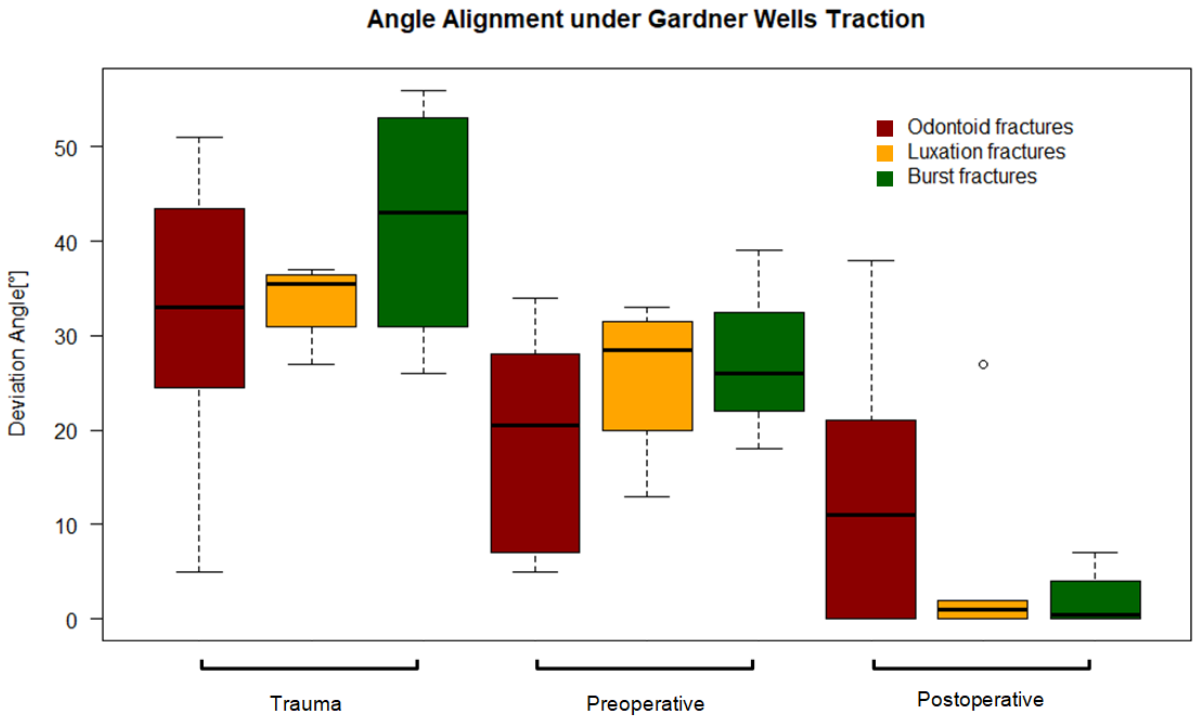
Results

Of 24 patients in the final analysis (mean age: 67.8±18.0 years; 13 females [54.17%]), 14 individuals were treated for the type II odontoid fracture, the remaining cases presented with luxation (n=5) or burst (n=5) fractures between C 3 and 7. There were no PTGWT-related complications and no incompliance cases in the series. Patients" demographic characteristics and previous medical history, the time passed since the injury (p=0.59), as well as the duration of the PTGWT (p=0.76) were not associated with the correction of the deviation angle. The duration of PTGWT for the burst fractures was longer (5.0±3.7 days, p=0.02), as compared to the luxation (2.4±1.1 days) and odontoid (2.1±1.5 days) fractures. PTGWT resulted in a significant improvement of the angular deviation for the odontoid (13.1°±12.4°, p<0.01), but not for the luxation (8.0°±10.9°, p=0.17) and burst injuries (9.7°±1.5°, p=0.18). Vice versa, intraoperative reposition resulted in significant improvement of the angular deviation for the luxation (18.3°±14.7°, p=0.02) and burst (25.3°±14.0°, p=0.04) fractures, but not for the odontoid fractures (5.4°±8.6°, p=0.19).

Conclusion

PTGWT is an effective, safe, and well-tolerable treatment for cervical spine injuries with malalignment. The patients with the odontoid fracture might particularly profit from the PTGWT. In turn, there is a high capacity for intraoperative correction for the luxation and burst fractures of the cervical spine.

Fig. 1


Angle Alignment under Gardner Wells Traction
Deviation Angle[°]
0
10
20
30
40
50
Odontoid fractures
Luxation fractures
Burst fractures
Trauma
Preoperative
Postoperative

Neurotraumatologie, Radiochirurgie, Freie Themen/*Neurotraumatology, radiosurgery, free topics*

P005

Chronische Subduralhämatome – eine retrospektive Analyse ihrer internen Architektur und Erhebung von neuen Risikofaktoren im Hinblick auf Rezidive nach operativer Behandlung

Chronic subdural haematomas – a retrospective analysis of the internal architecture and evaluation of new risk factors for recurrences after surgical therapy

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Objective

Chronic subdural hematoma (cSDH) is a common disease which is increasing due to aging population and the use of anticoagulation and antiplatelet medication. Aim of this study is to investigate new risk factors for recurrent cSDH after surgery and for developing cSDH in first place. Furthermore, was the aim to analyze the internal structure of cSDH using cranial CT-imaging and to investigate potential associations between the type of cSDH and the recurrence rate. The aim is to better understand the disease patterns and to maximize treatment options.

Methods

This retrospective study evaluated data of 189 patients that were treated surgical between 2014-2018 at our department. Recorded were demographic-, clinical-, surgical treatment-, cCT-imaging-, neurological status- and follow up data. The outcome was assessed clinically and with follow-up cCT imaging 3-4 weeks after surgery. Coronar-cCT images were used to measure the thickness of haematomas, hyperdens areas, chronic parts and membranes. Complications and outcome was defined using modified Ranking scale (mRS) 4 weeks after the treatment.

Results

After surgical treatment patients showed a significantly higher BMI (p<0,001, 61,6%), arterial hypertension (p<0,001, 68,3%) and the intake of anticoagulant therapy (p<0,001, 58%). The patients were initially symptomatic in 48,6 % with a paresis, in 33,7 % with an aphasia and in 41,6% with a dizziness. In 35 cases was a recurrent cSDH found after 3-4 weeks. The frontoparietal convexity-typ was in 70 % the most represented. In 60 % the internal structure of cSDH was septated, 66,7% had an architectural change of the hematoma. After univariable and multivariable analysis, the initial hemispheric typ (p=0,019, HR: 3,191; p=0,012, HR: 3,810) and the increasing preoperative midline shift (p=0,028, HR: 1,114; p=0,041, HR: 1,107) in CT-imaging increase are independent predictors for recurrence. In 5,8 % was a revision surgery due to recurrence cSDH necessary. Complications were found in 6,3 % with secondary hemorrhage and 1,6 % wound healing deficit. 70,3 % of the patients with recurrence cSDH had a mRS of 0-2.

Conclusion

Increasing midline shift before surgery as well as hemispheric typ of haematoma were independent predictors for recurrence according to our data. The most of patients achieved an excellent outcome with low risk profile.

Neurotraumatologie, Radiochirurgie, Freie Themen/*Neurotraumatology, radiosurgery, free topics*

P006

Intraoperativ-geformte- vs. CAD-CAM-Kranioplastik nach dekompressiver Kraniektomie – eine retrospektive Single-Center-Analyse von 258 Fällen im Hinblick auf perioperative Modalitäten, sowie kurz- und langfristige Komplikationen und ästhetische Ergebnisse

Intraoperative-moulded- vs. CAD-CAM-cranioplasty after decompressive craniectomy – a retrospective single-centre analysis of 258 cases with regard to perioperative modalities as well as short- and long-term complication rates and aesthetic results

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Objective

Cranioplasty (CP) after decompressive craniectomy (DC) restores the functionality and aesthetic of the patients cranial vault. Although it is a routine procedure, high complication rates have been described, partly related to the type of implant material used. Among many others, PMMA has been in clinical use for many years. It is available as intraoperative-molded (e.g. Palacos®) or computer-assisted/computer-manufactured (CAD-CAM) implants, which differ in the manufacturing and insertion process. We conducted this study to compare both implants in patients underwent DC with regard to perioperative modalities, short- and long-term complication rates and aesthetic results.

Methods

This retrospective single-center-analysis was conducted on 258 cases that underwent CP after DC. Palacos® patients (87/258) were observed from 01/2005-12/2012, whereas CAD-CAM patients (171/258) from 01/2010-12/2018 were included. Patients were followed based on medical, operative and digital records. Postoperative complications were divided into short-term (>30 days) and long-term (<30 days). Aesthetic results were evaluated via telephone interview.

Results

CAD-CAM patients had a significantly shorter surgery time ($p < 0.001$) and significantly lower intraoperative blood loss ($p < 0.001$) than Palacos® patients. Further surgical treatment after CP had to be carried out at 12.8% of patients. In the short term, the main reason for re-operation was epidural hematoma (6.2 %). Overall, Palacos® patients had significantly more implant dislocations ($p < 0.05$) compared to CAD-CAM. Implant infections occurred in 2.3% of Palacos® cases and 1.8% of CAD-CAM cases on the long-term view. Wound healing disorders occurred more frequently in CAD-CAM patients, which was associated with an increased number of previous operations. Regarding minor complications, Palacos® implants showed significantly more CSF pads ($p < 0.05$). Also, Palacos® leads to a significantly longer postoperative hospitalization ($p < 0.005$) than CAD-CAM. Although without statistical significance, CAD-CAM patients reported a better aesthetic result compared to Palacos® patients according to the results of our telephone interview.

Conclusion

This largest single-center-study on CP after DC shows superior peri- and postoperative results for CAD-CAM-implants compared to Palacos®. Further studies are needed to evaluate long-term complication rates, especially for CAD-CAM implants, and to increase the sample size to prove the observations in aesthetic results.

Neurotraumatologie, Radiochirurgie, Freie Themen/*Neurotraumatology, radiosurgery, free topics*

P007

Ergebnisse der chirurgischen Behandlung von Liquorlecks bei spontaner intrakranieller Hypotension – eine Frage der Zeit

Outcome after surgical treatment of cerebrospinal fluid leaks in spontaneous intracranial hypotension – a matter of time

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Objective

Spinal cerebrospinal fluid (CSF) leaking causes spontaneous intracranial hypotension (SIH). Surgical closure of spinal CSF leaks is a mainstay in the management of these patients. Despite surgical closure of the leak, some patients suffer from residual symptoms. Aim of the study was to assess predictors for favorable outcome after surgical treatment of SIH.

Methods

We included consecutive patients with SIH treated surgically from January 2013 to May 2020. Subjects were surveyed by a specifically designed questionnaire at a mean of 2.1 years after treatment. Primary outcome was resolution of symptoms rated by the patient as complete, partial or unchanged. Secondary outcome was postoperative headache intensity on the numeric rating scale 0-10. Association between variables and outcome was assessed using univariate ordinal logistic regression for the primary and univariate linear regression for the secondary outcome. Any variable with a p-value ≤ 0.15 was integrated into a multivariate model. We converted symptom duration to a logarithmic scale, since the data had a right skew. In order to define a cut-off value for continuous variables, we performed an ROC analysis using complete resolution of symptoms as a positive result.

Results

Eighty-six patients were identified, of which 69 (80.2%) returned the questionnaire and were analyzed. Mean age was 46.7 years and 65.2% of the patients were female. Mean pre- and postoperative headache intensity was 8.33 and 1.45 on the numeric rating scale. Neither sex, age, type of pathology (ventral vs lateral leak), lumbar opening pressure, nor initial presentation were associated with the primary outcome. A significant association with the primary outcome was found only for symptom duration (p=0.001), whereby a shorter symptom duration was associated with better outcome. Symptom duration remained the only significant predictor in a multivariate model (p=0.011). Similarly, only symptom duration was associated with the secondary outcome (p<0.001). ROC analysis of symptom duration yielded 9.1 weeks as reasonable cut-off with a false positive rate of 0.192.

Conclusion

Shorter duration of preoperative symptoms is the most powerful predictor of favorable outcome after surgical treatment of SIH. While an initial attempt of conservative treatment is justified, we advocate early surgical treatment within 9.1 weeks in case of persisting symptoms and a proven spinal CSF leak.

Neurotraumatologie, Radiochirurgie, Freie Themen/*Neurotraumatology, radiosurgery, free topics*

P008

Pterionale Orbitadekompression bei endokriner Orbitopathie mit Optikusneuropathie
Pterional orbit decompression in Grave's disease with dysthyroid optic neuropathy

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Objective

The choice of surgical technique in sight-threatening Grave"s orbitopathy remains controversial. Available data are mostly derived from mixed cohorts with multiple surgical indications and techniques. The authors assessed predictors for visual outcome after standardized pterional orbital decompression for dysthyroid optic neuropathy (DON).

Methods

Retrospective analysis of 62 pterional orbital decompressions performed on 40 patients with DON.

Results

Visual acuity improved by an average of 3.8 lines in eyes with preoperative visual impairment (95% confidence interval [CI]: 1.8 – 5.8 lines, $p < 0.001$) and remained stable in eyes without prior visual impairment (95% CI -1.3 – 1 lines, $p = 0.81$). Proptosis was reduced by an average of 3.1 mm (95% CI 1.8 – 4.3 mm, $p < 0.001$). Higher degrees of proptosis were predictive of worse visual outcomes ($p = 0.017$). New-onset diplopia developed in two patients, while previous diplopia resolved after surgery in six patients.

Conclusion

This cohort is the largest series of pterional orbit decompressions, and the first to focus exclusively on dysthyroid neuropathy. Complication rates were low. Decompression surgery was highly effective at restoring and maintaining visual acuity in patients with dysthyroid optic neuropathy.

Neurotraumatologie, Radiochirurgie, Freie Themen/*Neurotraumatology, radiosurgery, free topics*

P009

Rapid Closure Technik in suboccipitaler Dekompression
Rapid closure technique in suboccipital decompression

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Objective

Aim of this study was to examine the differences between fibrin sealant patch and dural reconstruction in suboccipital decompression for acute mass-effect lesions.

Methods

We retrospectively analyzed data of patients who underwent suboccipital decompression due to spontaneous cerebellar hemorrhage, cerebellar infarction and acute traumatic subdural hematoma between 2010 and 2019 at our institution. Two different dural reconstruction techniques were performed according to the attending neurosurgen: 1) fibrin sealant patch (FSP) and 2) dural reconstruction (SR) including the use of dural patch. Complications, operation time, functional outcome and the necessity of venticuloperitoneal shunting were assessed and further analyzed.

Results

Overall, 87 patients were treated at the author´s institution (44 in the FPS group and 43 in the SR group). Glasgow coma scale on admission and preoperative coagulation state did not differ between the groups. Moreover, we found no difference in cerebrospinal fluid leakage or chronic hydrocephalus rates between the groups ($p=0.47$). Revision rates were 2.27% (1/44 patients) in the FPS group, compared to 16.27% (7/43) in the SR group ($p<0.023$). Operation time was significantly shorter in the FPS group (90.3 ± 31.0 min vs. 199.0 ± 48.8 min, $p < 0.0001$).

Conclusion

Rapid closure technique in suboccipital decompression was associated with low postoperative complication and shorter operation time.

Neurotraumatologie, Radiochirurgie, Freie Themen/*Neurotraumatology, radiosurgery, free topics*

P010

Wundheilungsstörung während COVID-19 – Hat der Paradigmenwechsel bei den Hygienemaßnahmen die Häufigkeit von Wundheilungsstörungen bei neurochirurgischen Patienten beeinflusst?

Surgical site infection during COVID-19 times – Did the paradigm shift of the hygiene measures affect the rate of SSI in neurosurgical patients?

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Objective

Hygiene measures were intensified when the COVID-19 pandemic began. Patient contacts were limited to a minimum. Visitors were either not allowed for a certain period or limited for the rest of the time. The hospital staff began to wear masks and gloves continuously. Clinical examinations and routine wound controls were also performed under intensified hygiene standards. These circumstances result in a limitation of direct physical interactions between the nursing staff, the physicians and the patients. We analyzed to what extent the intensification of hygiene measures affect the rate of surgical site infections (SSI) after neurosurgical procedures.

Methods

The rate of SSI during the six month interval of COVID-19 measures was compared with the SSI rate before. The numbers of the period before COVID-19 were analyzed as mean values resulting from the analysis of two separate time periods each consisting of six months. The spectrum of surgical procedures was compared. Patient related risk factors for SSIs were noted. Microorganisms were analyzed. We focused on SSIs occurring at maximum 60 days after the primary surgery.

Results

Overall, in the respective six months periods before COVID-19, a mean of 1379 patients were surgically treated in our institution. After the beginning of COVID-19 (starting from 03/2020) our surgical numbers only dropped by 23, resulting in a total number of 1356 patients being operated after 03/2020 until 09/2020. The SSI rate was 3.6% (03/2019 – 09/2019, 50 SSIs) and 2.1% (09/2019 – 03/2020, 29 SSIs), resulting in a mean of 2.9% before COVID-19 began. After the beginning of COVID-19 hygiene measures this rate dropped to 1.2% (17 SSIs). Risk factors for development of SSI were present in 67% of all patients. Comparison of pre- and post COVID-19 groups revealed no difference (p=0.15). The site of SSIs did not differ regarding cranial and spinal procedures comparing the time intervals pre- and post COVID-19 (p=0.08). Comparing the number (p=0.36) and the species (p=0.47) of microorganisms (MO) causing SSI, we found a similar distribution.

Conclusion

Despite equal demographics and characteristics of SSI, the rate of SSI dropped dramatically. This argues for an effective reduction of postoperative SSI resulting from the implementation of strict hygiene measures being established after the beginning of the COVID-19 pandemic. We therefore advocated continuing with the strict hygiene measures in the future.

Neurotraumatologie, Radiochirurgie, Freie Themen/*Neurotraumatology, radiosurgery, free topics*

P011

Klinische und radiologische Ergebnisse gewrappter Aneurysmen im Langzeitverlauf in einem neurovaskulären Zentrum

Clinical and radiological outcomes of wrapped aneurysms in the long term follow up in a neurovascular centre

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Objective

Few cerebral aneurysms are not completely clippable or even unclippable due to small size and/or difficult morphology. In some cases, the aneurysm can be clipped partially and the remnant is wrapped with muscle, cotton and glue (clip-wrapping), or, the aneurysm is wrapped solely. In this study we aimed to assess the clinical and radiological outcomes of patients with aneurysms wrapped or clip-wrapped in our department over more than 20 years.

Methods

This retrospective study included 51 patients (39 women, 6 men; mean age 63 years) between 1993 and 2019. We reviewed pre- and postoperative charts, surgical reports, wrapping technique, and radiographic data for demographics, co-morbidities, radiographic features, Neurological Performance Scale (MRC) and the Karnofsky Performance Index (KPI).

Results

47 (94%) of those aneurysms were located in the anterior circulation, and 22 patients (44%) presented with subarachnoid hemorrhage . Most frequently, wrapping was performed with autologous muscle or cotton, additionally fixed with fibrin glue.15 aneurysms were fusiform (30%), 14 aneurysms incorporated a bifurcation. 41 aneurysms were wrapped (82%), and 9 (18%) were clip-wrapped. At discharge the MRC score was 0 in 41 patients (82%), 1 in 7 patients (14%), and one patient died. The mean follow-up was 4.8 years (range, 2–19 y). 2 patients (1%) experienced further SAH from a wrapped aneurysm during follow-up. Due to the available radiographic data, we did not detect any change in size or morphology of a wrapped or clip-wrapped aneurysm.

Conclusion

Wrapping or clip-wrapping of small and/or fusiform intracranial aneurysms is rare but it seemingly provides protection against aneurysmal growth or (re-)rupture.

On the one hand, our data support the feasibility of wrapping and clip-wrapping in small and fusiform aneurysms, but on the other hand, the risks and benefits have to be compared to the natural course of this selected subgroup of vascular malformations.

Neurotraumatologie, Radiochirurgie, Freie Themen/*Neurotraumatology, radiosurgery, free topics*

P012

Assessment des Rupturrisikos von multiplen intrakraniellen Aneurysmen – warum es nicht notwendig ist, Dutzende von klinischen, morphologischen und hämodynamischen Parametern zu bestimmen

Rupture risk assessment for multiple intracranial aneurysms – why there is no need for dozens of clinical, morphological and haemodynamic parameters

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Objective

For rupture risk assessment of intracranial aneurysms, a multitude of approaches have been postulated. However, the amount of potential predictive factors is not applicable in clinical practice and they are rejected in favor of the more practical PHASES Score. For the subgroup of multiple intracranial aneurysms (MIA), the PHASES Score might severely underestimate the rupture risk, since only the aneurysm with the largest diameter is considered for risk evaluation.

Methods

In this study, we investigated 38 patients harboring a total number of 87 MIA with respect to their morphological and hemodynamical characteristics. For the determination of the best suited parameters regarding their predictive power for aneurysm rupture, we conducted three phases of statistical evaluation. The statistical analysis aimed to identify parameters, which differ significantly between ruptured and unruptured aneurysms, show smallest possible correlations among each other and have a high impact on rupture risk prediction.

Results

Significant differences between ruptured and unruptured aneurysms were found in 16 out of 49 parameters. The lowest correlation were found for gamma, aspect ratio (AR1), aneurysm maximal relative residence time (Aneurysm_RRT_max) and aneurysm mean relative residence time. The data-driven parameter selection yielded a significant correlation of only two parameters (AR1 and the Aneurysm_RRT_max) with rupture state (area under curve = 0.75).

Conclusion

A high number of established morphological and hemodynamical parameters seem to have no or only low effect on prediction of aneurysm-rupture in patients with MIA. For best possible rupture risk assessment of patients with MIA, only the morphological parameter AR1 and the hemodynamical parameter Aneurysm_RRT_max need to be included in the prediction model.

Seltene Erkrankungen/*Rare diseases*

P013

Aggressive Hypophysenadenome im Kontext des Lynch-Syndroms – ein Fallbericht unter Berücksichtigung der Literaturlage zu diesem seltenen Phänomen

Aggressive pituitary adenoma in the context of Lynch syndrome – a case report and literature review on this rare coincidence

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Objective

Lynch Syndrome is a cancer-predisposing condition resulting from hereditary mutation of one or more genes involved in DNA mismatch repair mechanisms. Especially gastrointestinal, urogenital, and endometrial carcinomas are well-known to predominantly occur in patients with this condition. In contrast, there are only few reports on brain tumours in the context of Lynch Syndrome and to date intracranial tumour manifestation appear to be rather coincidental despite the known predisposition of these patients for all kinds of malignomas.

Methods

We present the case of a 56-year-old female developing aggressive lactotroph pituitary adenoma following a history of multiple Lynch-associated malignomas and having a confirmed *MSH2* mutation. Furthermore, we performed a literature review via PubMed using the search terms "Lynch Syndrome", "HNPCC", "MMR mutation" in combination with "intracranial tumour", "sellar tumour", "pituitary adenoma", or "pituitary carcinoma", focusing on other reported cases and treatment regimens.

Results

A handful of studies have indicated an increased frequency of associated brain tumours in the context of Lynch Syndrome, predominantly glioblastoma and less frequently astrocytoma, oligodendroglioma or other brain tumours. However, a Swedish study also presented 3 cases of pituitary adenomas in patients suffering Lynch Syndrome. Importantly, there is strong indication that common recommendations for treatment of aggressive pituitary adenoma or carcinoma might be insufficient in these patients, calling for adaption in consideration of the underlying MMR mutations.

Conclusion

Combined with our case, there is a growing body of evidence that intracranial tumours and in particular those of the sellar region might be more prevalent in Lynch Syndrome patients than previously assumed, with their genetic profile substantially affecting viability and efficacy of treatment options. Clinical signs of aggressive tumour growth in combination with irresponsiveness to standard treatment in case of recurrence should lead to further diagnostic measures, because revelation of germline MMR mutations would call for an extended screening for other neoplastic manifestations and would markedly influence further treatment.

Seltene Erkrankungen/*Rare diseases*

P014

Zerebrales Amyloidom – intraoperativer Befund und Literaturrecherche
Cerebral amyloidoma – intraoperative findings and review of the literature

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Objective

Primary cerebral amyloidomas represent a benign but rare condition with about thirty published cases. Most published studies focus on radiological and histological characteristics. Here, we present the case of a 66-year old woman with an infiltrative process of the parietal lobe who underwent an open biopsy and show intraoperative findings.

Methods

Case Report and Literature Review

Results

Cerebral amyloidomas are a subtype of marginal cell lymphomas or lymphomas of the B-cell line, characterized by deposits of amyloid light chains. They mostly have a subcortical location and have been associated with neurodegenerative processes in the past. A review of the literature shows that most cases undergo a stable clinical course, but represent a certain risk for intracerebral hemorrhaging.

A 66-year old female presented initially with a pulsating noise in her left ear. Besides a hysterectomy for multiple myomas at an earlier age and an autoimmune thyroiditis, there were no other preexistent conditions. MRI showed a diffuse process of the left parietal lobe with moderate contrast enhancement and signal enhancement in the T2-Flair-sequences. Upon biopsy, the intraoperative aspect was one of a well vascularized process consisting out of diffusely spread follicular structures throughout the white matter, reaching to the left ventricle. Histology showed a massive protein agglutination among lymphocyte infiltrates and k- light- chain- mRNA-restriction, consistent with the diagnosis of amyloidoma.

Conclusion

Cerebral amyloidomas are easily misdiagnosed as neoplastic processes. A better knowledge of the characteristics of this entity is necessary to guide specific therapies.

Seltene Erkrankungen/*Rare diseases*

P015

Zervikale Facettengelenkszysten – klinische Symptomatik und funktionelles 'Outcome' – eine Single-Center-Studie
Cervical Juxta-facet cysts – clinical presentation and functional outcome in a single-institution experience

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Objective

Cervical juxta-facet cysts (JFC) are rare but important differential diagnosis in spinal degenerative diseases. Patients' demographic features, clinical and imaging characteristics, treatment options and outcomes are important variables, which have been discussed through few numbers of publications. This study aims to report our institute experience with cervical JFC, hoping to better define these variables and increase the literature knowledge.

Methods

This study retrospectively reviewed cases of 11 patients with JFC, treated in our institute from 2005 to 2020. Patients' age, sex, cervical level, clinical presentation, imaging, intraoperative findings, treatment strategy and outcomes were obtained from medical reports and analyzed. This cohort study was approved by the local ethical committee.

Results

Out of 378 patients with JFC who had been treated in our institute, there were 11 patients (2.9 %) (6 men and 5 women) having JFC in the cervical region. Patients' age ranged from 54 - 84 years. The most common cervical level was C7-T1 (72.7 %). Only 9% of cases had bilateral cysts. The most frequent clinical presentations were: Radiculopathy (100%), sensory deficit (90.1%), motor deficit (63.6%), while axial neck pain and myelopathy occurred in 45.5% and 36.4%, respectively. The follow up period ranged from 6 - 72 months. Surgery was the main treatment strategy in 90.9 % (10 pt.). Only 1 patient had conservative treatment Fusion was required in 70% of cases (60% initial and 10% delayed), while microsurgical excision alone was enough in 30%. All cases had complete clinical improvement after surgery. Cyst recurrence occurred in one patient. Patients' satisfaction on Macnab classification was excellent and good in 90 % of cases.

Conclusion

This study advocates for early surgery rather than prolonged conservative treatment. Dynamic imaging is very important before and after surgery to identify instability. High fusion rate in cervical region reflects hypermobility of this region, especially the junctional level C7-T1 (where most cases occur).This study also reflects the rarity of these lesions (only 11 patients over a time period of 15 years), so further prospective studies with longer follow up are needed to corroborate these findings.

Seltene Erkrankungen/*Rare diseases*

P016

Kollisionstumore und intratumorale Metastasen – eine retrospektive Analyse zu einer seltenen Erkrankung
Collision tumours and tumour-to-tumour metastases – a retrospective analysis on a rare disease

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Objective

With roughly 200 cases published world-wide since 1930, combination tumours such as collision tumours and tumour-to-tumour metastases (TTM) pose rare constellations of neoplastic disease with their clinical relevance still being a matter of debate.

Methods

Among all patients operated on intracranial or spinal glioma, meningioma, hematoma, or hemangioblastoma between 2009 and 2020 in our hospital we selected those with concomitant neoplastic disease (primarily high-grade glioma, lymphoma, or carcinoma) and retrospectively evaluated all diagnostic and surgical reports to identify cases of combination tumours, which we then aggregated into a descriptive analysis.

Results

In our cohort of 665 patients, we have identified 8 patients with combination tumours (1.2 %). In all cases, the benign "host" tumour was a meningioma, whereas the malignant tumour mostly derived from adenocarcinomas of the breast, lung, or prostate (62.5 %) on the one hand, or B-cell lymphoma and glioblastoma (12.5 % respectively) on the other hand. The patients' age ranged from 48 to 81 years (ratio female/male 1:1). In 62.5 % of cases, the malignant tumour was previously known with a median latency of 9 years (range: 7 months to 14 years) until manifestation of the combination tumour. Hence, 50.0 % of patients had already received chemotherapy. However, none of them had received previous cranial radiotherapy. Notably, in 3 patients identification of a concomitant tumour was first achieved in the context of a collision tumour or TTM. Following re-evaluation of preoperative MRI reports, a combination tumour had been considered in only 25.0 % of cases.

Conclusion

With regard to the current literature, we provide one of the largest clinical series of combination tumours from one single institution. Our cohort supports the notion that meningiomas are common hosts in combined tumours, indicating the existence of permissive features regarding the growth of malignant entities, especially metastases of adenocarcinoma, but also glioblastoma or hematopoietic tumours. This series cannot conclusively answer the question, whether collision tumours or TTM are more than a random coincidence, but considering our comparably short time window for analysis and the focus on only one institution, there might be evidence for an underestimation of the phenomenon. Either way, diagnosis of such a combined tumour leads to relevant therapeutic consequences, which may largely contribute to the patient"s long-term prognosis and treatment.

Seltene Erkrankungen/*Rare diseases*

P017

Embolisation vor der Resektion von Hämangioblastomen – In welchen Fällen ist dies ratsam?
Embolisation prior to haemangioblastoma surgery – In which cases is it advisable?

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Objective

Hemangioblastomas are highly vascularized tumors and can be associated with von Hippel-Lindau (VHL) disease. Preoperative embolization has been proposed to occlude tumor-feeding vessels and thus reduce the perfusion of the tumor. However, preoperative embolization is not an established standard, and the available evidence is mainly based on uncontrolled retrospective small case series. In this context, the safety and efficacy of preoperative embolization for central nervous system (CNS) hemangioblastomas are not well characterized. We share the experience of our interdisciplinary VHL center with preoperative embolization and subsequent microsurgical removal of CNS hemangioblastomas.

Methods

We reviewed all resected CNS hemangioblastomas over a period of six years (2014 - 2020) in our VHL center. We examined radiographic and clinical criteria such as imaging tumor characteristics, extent of devascularization and tumor resection, complications, intraoperative blood loss, transfusion requirements, and the neurological status according to the modified Rankin Scale and modified McCormick Scale.

Results

In total, 131 patients had surgery for removal of up to six hemangioblastomas. Preoperative embolization was performed for 8 spinal and 6 intracranial hemangioblastomas in 14 patients (10.7 %). The volume of tumors selected for embolization was 7.4 ± 8.4 cm^3; intraoperative blood loss was 605 ± 485 ml. Two of these patients (14.3 %) experienced embolization-related complications, including femoral artery dissection and permanent cranial nerve dysfunction. Subsequent hemangioblastoma surgery did not lead to permanent neurological deficits.

Conclusion

Preoperative embolization should not be considered standard of care for CNS hemangioblastomas, as it harbors a potential for neurological deterioration. Smaller CNS hemangioblastomas can usually be safely removed without the need for preoperative embolization. For larger hemangioblastomas, however, preoperative embolization may be advisable. This additional intervention should be carefully indicated on a personalized basis and should be reserved for specialized interdisciplinary centers.

Seltene Erkrankungen/*Rare diseases*

P018

Einfluss des Von-Hippel-Lindau-Syndroms und der Tumor-Morphologie auf Hämangioblastome des Zentralnervensystems
Influence of Von Hippel-Lindau syndrome and the tumour morphology on central nervous system haemangioblastoma

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Objective

This study examines the influence of Von Hippel-Lindau syndrome (VHL) and the tumour morphology on central nervous system (CNS) Haemangioblastoma (HB).

Methods

We retrospectively analysed patients who underwent surgery for at least one CNS HB in our clinic from January 2008 to December 2019. Data collection included the presence of VHL, age, gender, morphology (solid/cystic), location, complications, and outcome at discharge (Glasgow outcome scale). We compared solid with cystic HBs as well as sporadic HBs with HBs associated with VHL. Statistical analysis was performed using Fisher"s exact test (significance level two-sided p-value ≤ .05).

Results

From 2008 to 2019, 29 patients underwent surgery for 30 HBs. Four patients were positive for VHL. The resected HB appeared cystic in 13 patients and predominantly solid in 15 patients. A cystic and a solid HB were resected during one surgery in one case. The gender distribution was 1:1 in the VHL group, but 2,5:1 male predominance in the sporadic group. Mean age in the sporadic solid group (M=62,36 y; SD=17,8) was higher than in the sporadic cystic group (M= 44,36 y; SD=12.9). VHL-patients were younger (M= 41,5 y; SD= 11,9) than patients with sporadic HBs (M=54,44 y; SD=18). Four patients presented with multiple HBs, all of them were positive for VHL. The cerebellum was the most common location (67%), especially in the cystic group (79%) and less common in the solid group (56%). Eight patients presented with a recurrent HB in the study period; 4 of them were positive for VHL. The complication rate was 40% (n6) in the solid group and 15% (n2) in the cystic one (p = .22). However, only one complication was severe – a severe postoperative bleeding. The good recovery outcome was 69 % (n9) in the cystic group and 53% (n8) in the solid one (p = .46). One VHL-patient had a postoperative complication (p = 1) and 2 VHL-patients had good recovery (p = 1).

Conclusion

This study demonstrates the impact of VHL on HBs in terms of earlier onset of the disease, multiple occurrences of HBs and the recurrence rate. Sporadic solid HBs present at a higher age compared to cystic HBs. Cystic HBs are located mainly in the cerebellum, whereas solid HBs show a higher distribution in CNS locations. Neither the tumour morphology nor the presence of VHL seem to affect the short-term outcome and the complication rate. A limitation of this study is the small number of cases due to the low prevalence of the disease.

Fig. 1

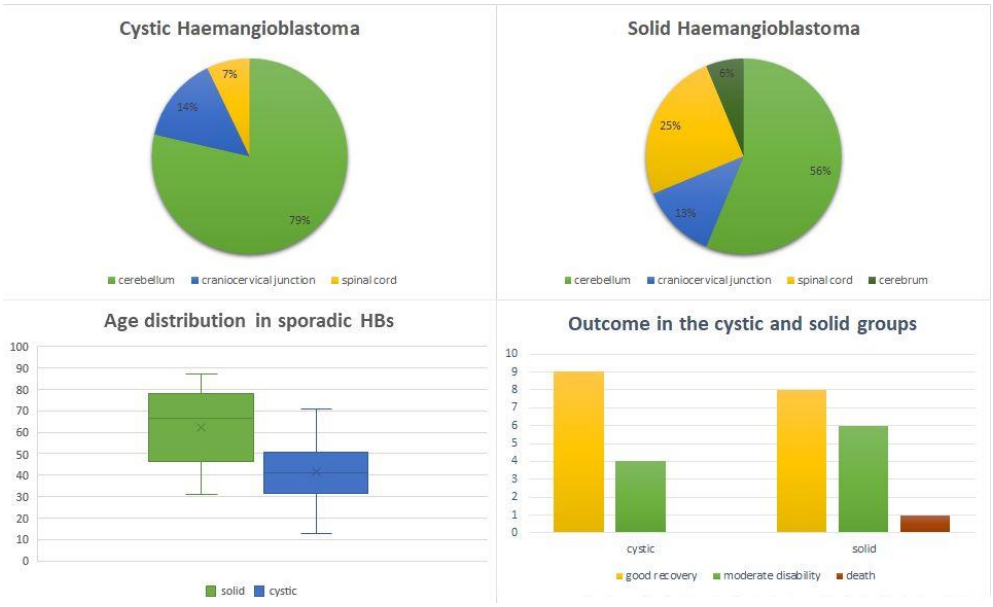
Cystic Haemangioblastoma
7%
14%
79%
cerebellum
craniocervical junction
spinal cord
Solid Haemangioblastoma
6%
25%
56%
13%
cerebellum
craniocervical junction
spinal cord
cerebrum
Age distribution in sporadic HBs
100
90
80
70
60
50
40
30
20
10
0
solid
cystic
Outcome in the cystic and solid groups
10
9
8
7
6
5
4
3
2
1
0
cystic
solid
good recovery
moderate disability
death

Fig. 2

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P019

Thalamotomie mittels Magnetresonanztomographie-geführtem fokussierten Ultraschall bei mit der Spinocerebellären Ataxie 12 assoziiertem Tremor – ein Case Report

Magnetic resonance imaging-guided focused ultrasound thalamotomy in spinocerebellar ataxia 12 associated tremor – a case report

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Objective

Spinocerebellar ataxias (SCAs) are progressive, neurodegenerative disorders generally associated with oculomotor dysfunction, dysarthria and ataxia. The SCA12 is typically associated with action tremor of the upper extremity. The treatment of SCA12 is challenging. Single case series have previously demonstrated the effective use of deep brain stimulation (DBS) for the treatment of tremor in SCAs. Beside DBS, MRI-guided focused ultrasound (MRgFUS) is a promising technique to ablate deep brain targets such as ventrointermedius nucleus (ViM) or cerebello-thalamic tract (CTT) resulting in significant tremor reduction in essential tremor (ET) and Parkinson"s disease (PD). However, to our knowledge no patient with SCA has been treated with MRgFUS so far. Herein, we report on a patient suffering from SCA12 with severe action tremor and his outcome after lesioning of the CTT using MRgFUS.

Methods

a 65-year-old man presented with severe bilateral action tremor of the upper extremity accompanied by a moderate head and voice tremor. Therapeutic strategies, including propranolol, primidone, topiramate and cannabinoids showed either little benefit or had to be stopped due to side effects. In 2014, a genetic analysis confirmed the diagnosis of SCA12. The clinical evaluation regarding the Scale for the Assessment and Rating for Ataxia (SARA) revealed a score of 18,5/40 and on the Fahn-Tolosa-Marin Tremor Scale (TRS) 90/260. The aim was to relieve the severely disabling tremor. Therefore, we performed unilateral lesioning of CTT with MRgFUS using coordinates based on tractography of CTT.

Results

a total of 5 ablative sonications (peak temperature above 56°C) at two different locations (1st target: 1 mm superior to AC-PC line, 14 mm lateral to midline, 25% of the AC-PC line anterior to PC; 2nd target: movement of 0.5mm laterally and 0.5mm anteriorly) were performed. During the treatment a nearly total tremor reduction in the right arm was observed, side effects did not occur. SARA score was 24/40 after 3 days and improved to 17/40 after 3 months. TRS score improved to 51/260 after 3 days and 48/260 after 3 months.

Conclusion

our experience shows that unilateral lesioning of CTT using MRgFUS might also be effective and safe in terms of tremor reduction in patients with SCA. However, the safety and efficacy of MRgFUS in ET and other tremor conditions as well as the clinical value of diffusion tensor imaging for target determination within the thalamus needs to be further investigated.

Seltene Erkrankungen/*Rare diseases*

P020

Behandlung von Sanduhr-Tumoren der Wirbelsäule über einen minimal-invasiven posterolateralen Zugang mit nachfolgender Kohlefaser-verstärkter PEEK-Instrumentation

Management of spinal dumbbell tumours via a minimally-invasive posterolateral approach and carbon fibre reinforced PEEK instrumentation – technical note and surgical case series

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Objective

Stand-alone minimally-invasive approaches for surgical management of spinal dumbbell tumors carry the risk of incomplete resections and impaired hemostasis. In contrast, more extensive approaches require subsequent instrumentation with metal artifacts impairing follow-up imaging. Here, we present a clinical series on percutaneous instrumentation using carbon fiber reinforced polyetheretherketone (CFR-PEEK) hardware combined with a minimally-invasive posterolateral approach for tumor resection.

Methods

We present a case series of six patients with dumbbell tumors in the lumbar and thoracolumbar spine operated on between 2017 and 2020. CFR-PEEK pedicle screws and rods were inserted percutaneously. Afterwards, a dedicated self-standing retractor for posterolateral approaches was connected to the screws. Following a unilateral facetectomy the tumor was resected in a microsurgical fashion. Clinical data are reported with respect to the PROCESS guidelines.

Results

Three patients presented with de-novo tumors. Three patients were treated for residual tumor mass after previous surgeries. Gross-total resection was achieved in all six cases as demonstrated by early postoperative MRI. Histopathology demonstrated four WHO grade I schwannoma, one grade II hemangiopericytoma and one cavernous hemangioma. No postoperative complications were observed. No misplacement or failure of hardware components were observed. CFR-PEEK hardware allowed unambiguous visualization of the resection cavity on follow-up imaging.

Conclusion

Resection of dumbbell tumors via a minimally-invasive posterolateral approach and instrumentation with CFR-PEEK hardware allows maximal and safe resection. Due to lack of major metal artifacts, carbon fiber hardware improves the interpretation of follow-up imaging as well as planning radiation if required for tumor recurrence.

Seltene Erkrankungen/*Rare diseases*

P021

Der posteriolaterale epidurale supra-C2-Nervenwurzel Zugang für Biopsien von Läsionen im und hinter dem Dens axis nach occipitozervikaler Fusion und Dekompression

Posterolateral epidural supra-C2-root approach (PESCA) for biopsy of lesions of the odontoid process and the retro-odontoid region in same sitting after occipitocervical fixation and decompression

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Objective

This study aims to describe the posterolateral epidural supra-C2-root approach (PESCA), which might be a good alternative to the transoral, anterolateral, and other posterolateral approaches for biopsy of unusual lesions of the odontoid process (OP) and retro-odontoid region.

Methods

The preoperative planning of PESCA included computerized tomography (CT), CT-angiography, and three-dimensional reconstruction (if possible, even with three-dimensional-print) to analyze the angle of the trajectory and the anatomy of the vertebral artery (VA). For PESCA, the patient is positioned under general anesthesia in prone position. In case of an osteolytic lesion with fracture of the OP, an x-ray is performed after positioning to verify anatomic alignment. In the first step, in case of instability and compression of the spinal cord, a craniocervical fusion and decompression is performed (laminectomy of the middle part of the C1 arc and removal of the lower part of the lateral C1 arc).

The trajectory is immediately above the C2-root (and under the upper rest of the lateral part of C1 arc). Even if the trajectory is narrowed, it is possible to perform PESCA without relevant traction of the spinal cord. The vertical segment of V3 of the VA at the level of C2 is protected by the vertebral foramen and the horizontal part of V3 is protected by the remnant upper lateral part of the C1 arc (in case of normal variants).

Results

We performed PESCA in two patients with unusual lesions of the odontoid process (patient 1: 72-year-old man) and the retro-odontoid region (patient 2: 70-year-old woman). Both patients recovered well from surgery. The pathological examination of the masses showed in the first case a very unusual spondylodiscitis of the OP (microbiological analysis of the probe revealed Corynebacterium striatum) and in the second case a crowned dens syndrome. The lesions were treated in the first case with vancomycine and in the second case with non-steroidal anti-inflammatory drugs.

Conclusion

In both of our patietns the pathological findings were the key to the successful treatment of two very rare diseases. PESCA might be a good choice for biopsy of selected lesions of the OP in same sitting procedure after craniocervical stabilization and decompression.

Seltene Erkrankungen/*Rare diseases*

P022

Postmortale Organspende bei seltenen Erkrankungen – Kasuistiken und Algorithmus
Postmortal organ donation in rare disorders – casuistics and algorithm

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Objective

Die Mehrzahl der Organspender weisen SHT oder kardiovaskuläre Grunderkrankungen auf. Zuweilen liegt aber auch "seltene Erkrankungen" vor oder sind zumindest Komorbidität. Dieses soll kasuistisch dargestellt werden inkl. der grundsätzlichenAlgorithmen.

Methods

Kasuistik 1: 15 jähriger Junge mit spontaner intrakranieller Hypotension, umfangreich Malignomausschluß bildgebend. Diagnosestellung vor 3 Jahren. Jetzt nach Fistelverschluß schwerstes Hirnödem. Herz, Lungen, Leber, Nieren und Pankreas werden entnommen und erfolgreich transplantiert.

Kasuistik 2: 73-jähriger Patient, lange Glykogenose Typ 5 Mc Ardle bekannt mit Gendefekt auf 11q13 für die Muskel-Myophosphorylase. Nach Apoplex und Lysetherapie hämorrhagisches Geschehen. Leber und Nieren wurden entnommen und transplantiert, an die Transplantationszentren erfolgt der Hinweis, dass bei diesem Krankheitsbild Rhabdomyolysen bei schwerer Anstrengung möglich. Der weitere Verlauf der Organempfänger ist unkompliziert.

Kasuistik 3: 36-jähriger Mann mit einer Histiozytose Typ Erdheim-Chester, Verlauf 4 Monate. Nach Feststellen des irreversiblen Hirnfunktionsausfalls CT von Thorax, Abdomen und Becken mit Tumorausschluß. In der Koronarangiographie 2-Gefäß-KHK (in der Literatur 75% Inzidenz kardialer Manifestationen). Letztlich werden Lungen, Leber und Nieren an Eurotransplant zur Allokation gemeldet, transplantiert werden die Nieren. 2 Jahre später wird eine Nephrektomie beim Empfänger der rechten Niere erforderlich, histologisch ein histiozytäres Sarkom nachgewiesen. Molekulargenetisch lässt sich nachweisen, dass das Tumorgewebe nicht empfängereigenes Gewebe ist. Die Möglichkeit einer Sarkomentwicklung bei der Histiozytose Erdheim-Chester ist auch kasuistisch beschrieben (Mazor et al. 2013).

Results

Insbesondere bei außergewöhnlichen Spendersituationen bedarf es der Einzelfallentscheidung, Orientierung bietet hier die europäische Leitlinie, der "Guide to the quality and safety of organs for transplantation". Eine Recherche der Literatur ist obligat, im Zweifelsfall auch die Expertenkonsultation. Die Ergebnisse dessen werden mit den Transplantationszentren besprochen, die diese bei ihrer Entscheidung zur Organakzeptanz unter Abwägung von Nutzen und Risiko der Transplantation für einen bestimmten Empfänger berücksichtigen können.

Conclusion

Organspenden sind insbesondere bei seltenen Erkrankungen Einzelfallentscheidung.

Seltene Erkrankungen/*Rare diseases*

P023

Pseudotumor cerebri Syndrom bei einem Kind mit Alagille-Syndrom

Pseudotumor cerebri syndrome in a child with Alagille syndrome – intracranial pressure dynamics and treatment outcome after ventriculoperitoneal shunting

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Objective

Alagille syndrome (AS) is a rare multisystem disease of the liver, heart, eyes, face, skeleton, kidneys, and vascular system. Occurrence of pseudotumor cerebri syndrome (PTCS) in AS is exceedingly rare and, thus far, continuous intracranial pressure (ICP) monitoring has never been utilized before in this subgroup. Owning to their rarity and mostly atypical presentation the diagnosis and natural history of such cases remains uncertain.

Methods

Continuous epidural ICP monitoring. Follow-up after shunt surgery

Results

We report on an atypical case of PCTS in a patient with a known history of AS who presented at 4 years of age with bilateral papilledema on a routine ophthalmological examination. Visual findings deteriorated after initial treatment with acetazolamide. Continuous ICP monitoring was then utilized to confirm the elevated ICP. ICP monitoring demonstrated massive dynamic ICP changes over time with markedly increased ICP values most of the time. The decomposition of pressure traces revealed pressure waves with amplitudes reaching values up to 60 mmHg for several minutes. B-waves dominated ICP dynamics superposing the slower ICP fluctuations in time. Additionally, a relatively high number of A-wave pressure transients were scattered in the traces. The majority of ICP values were measured to be within the range of 15 to 70 mmHg (83%). Successful treatment with resolution of papilledema was achieved after ventriculoperitoneal shunting but relapsed due to growth related dislocation of the ventricular catheter.

Conclusion

This report brings new insights into the ICP dynamics and the resulting treatment in this possibly underdiagnosed subgroup of PTCS patients. It also highlights the importance of ICP monitoring for diagnosing PCTS in atypical patients and demonstrates that ventriculoperitoneal shunting can provide long-term improvement of symptoms for more than 10 years. Our findings among with previously reported cases suggest that a genetic predisposition makes AS patients susceptible for developing PCTS, whereas associated medical conditions and exogenous factors can trigger or exacerbate intracranial hypertension.

Seltene Erkrankungen/*Rare diseases*

P024

Spinale epidurale Lipomatose mit akuter und schnell fortschreitender neurologischen Verschlechterung – systematische Literaturübersicht, Metaanalyse und ein Fallbericht

Spinal epidural lipomatosis with acute and rapidly progressive neurological deterioration – systematic literature review, meta-analysis, and case report

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Objective

Spinal epidural lipomatosis (SEL) is a rare condition defined by hypertrophic growth of epidural fat. The incidence of SEL in the Western world is likely to increase due to the current medical and socio-demographic development. Unfortunately, little is known about this disease, and choosing the best therapy is difficult, especially when facing a rare clinical presentation: "Acute onset SEL with severe neurological deterioration." With this study, we aim to widen current knowledge about this SEL subform and improve its clinical/therapeutic management.

Methods

We performed a systematic literature search using PubMed, Scopus, Web of Science, and Cochrane Library to identify all original articles published before November 04th, 2020, reporting on acute/rapidly-progressing, severe SEL (≤72 h from first symptoms to severe disability). Additionally, according to CARE guidelines, we report on the diagnostic workup, decision-making, surgical treatment, and outcome of a 67 years old male suffering from acute functional paraplegia caused by SEL.

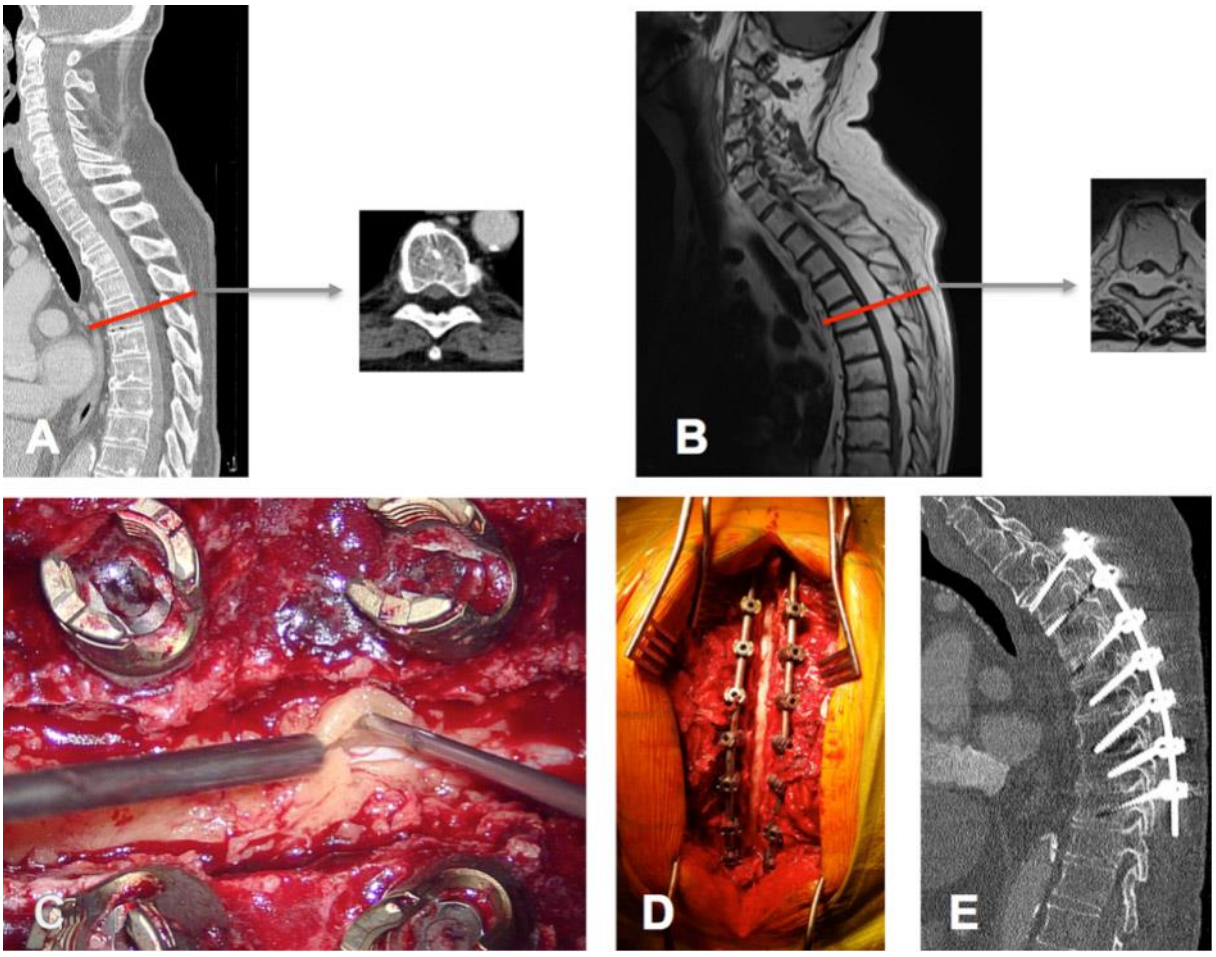
Results

Of 509 identified unique records, the final analysis comprised 11 patients with acute, severe SEL reported in 10 publications (published between 1987 and 2014). The majority of the patients were male (9/11) and multimorbid (9/11; quantified by a median Charlson Comorbidity Index [CCI] score of 2). The SEL mainly affected the thoracic part of the spinal cord (11/11, with one case, also involving the cervical and the lumbar spine, respectively) and extending a median number of 4 spinal levels (range: 4-19). Surgery was the only chosen therapy (10/11) except for a critically-ill patient who died shortly after the diagnosis. Regarding the outcome, only half of the patients regained independence (5/10; = mMcCS ≤ II).

Conclusion

Acute, severe SEL is a rare condition, which seems to affect mainly multimorbid patients. The prognosis is devastating in nearly 50% of the patients, even when they received maximum therapy. Further research is needed to differentiate patients who are better managed conservatively from those requiring surgery.

Fig. 1



Seltene Erkrankungen/*Rare diseases*

P025

Extrem lateraler trans-odontoidaler Zugang zur Resektion von bilateral ausgedehnten Clivus-Chordomen und zur Kranio-zervikalen Stabilisierung über einen chirurgischen Zugangsweg – chirurgische Technik und klinisches Fallbeispiel (Video)

The extreme lateral trans-odontoid (ELTO) approach for bilaterally extending clivus chordomas and occipito-cervical stabilisation in a single approach – surgical technique and illustrative clinical case (video)

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Objective

Bilaterally extending clivus chordomas with brain stem compression and instability of the cranio-cervical junction (CCJ) require radical tumor removal and stabilization. Often multiple approaches are necessary. Resection is typically performed by a trans-nasal / -clival/ -oral/ -petrous or -condylar route. Occipito-cervical stabilization (OCS) is only possible by a posterior approach. The extreme lateral trans-odontoid approach (ELTO) was recently described. It allows resection of bilaterally extending tumors at the anterior CCJ and posterior OCS in a single stage.

Methods

Detailed description and illustration of the surgical technique of ELTO. Illustrative presentation of a clinical case (video) and critical discussion of advantages and limitations of the ELTO.

Results

ELTO is performed in a lateral position and via a hockey-stick incision. One main feature is extra-dural access to the anterior CCJ from a very lateral angle. The angle is perpendicular to the trans-nasal or –oral route and therefore well-suited for very laterally extending tumors. The ipsilateral C0C1 articular complex, the anterior arch of atlas, the odontoid process, the lower clivus up to the contralateral C0C1 articular complex are in the line of sight. Anteriorly, the retropharyngeal space and posteriorly, the dura covering the clivus are reachable for tumor resection. At the end a screw-rod construct (C0C4) may be routinely performed via the same approach.

A 15-y.o. girl with a giant clivus chordoma extending bilaterally was operated via ELTO. OCS was performed in the same session. A contralateral tumor remnant extending very posteriorly had to be resected in a second stage by a far lateral approach from the opposite side. At last follow-up (1y), the patient was asymptomatic and tumor free.

ELTO had several advantages over trans-nasal or -oral routes: 1.) uncontaminated corridor, 2.) no muco-septal flap, 3.) single-stage procedure including extensive tumor resection and OCS. In the present case, tumor control of the opposite side seemed not completely safe (blind spot) so that a second approach was decided to resect a small remnant.

Conclusion

ELTO seems very useful for extradural tumors of the anterior CCJ. The angle of attack is perpendicular to classical routes allowing bilateral control. Major advantages are an uncontaminated corridor and the possibility of OCS in a single-stage. Careful pre-operative evaluation of imaging is necessary to judge the possibility to safely reach the opposite side.

Seltene Erkrankungen/*Rare diseases*

P026

Management und Outcome von operierten NF-2 assoziierten spinalen Ependymomen
Management and outcome of operated NF2 associated spinal ependymomas

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Objective

To evaluate the clinical effects of surgery for symptomatic and/or progressive Neurofibromatosis Type 2 (NF2) associated spinal ependymomas.

Methods

We retrospectively reviewed clinical reports and T1- and T2-weighted magnetic resonance images in 180 patients with NF2. 109/180 patients (61%) did not bear spinal ependymomas, 7 operated cases were excluded due to insufficient data.

Neurological function before and after surgery was classified using an established scoring system including the 5 categories sensibility (incorporating pain), motor, bladder/bowel and gait function. Preservation of neurological function was determined as maintenance of preoperative scoring class.

Results

13/64 patients with spinal ependymomas (20%) required surgery either due to rapid growth (2/13, 15%), worsening of neurological function (8/13, 62%) or combination of both (3/13, 23%).

The most common symptoms leading to surgery were gait disturbances (7/13, 54%), followed by sensory and motor deficits and pain (4/13, 31%) and bladder and bowl impairments (3/13, 23%). 10/13 patients exhibit two or more symptoms before surgery.

Within the first 24-months of follow-up after surgery, the clinical status was stable in 6/13 (46%), improved in 3/13 (23%) and worsened in 4/13 (31%).

Conclusion

40% of NF2 patients harbour spinal ependymomas and the majority of those is asymptomatic and does neither require treatment nor biopsy for securing the diagnosis, as these tumours totally behave different compared to sporadic forms. In cases with developing neurological symptoms mostly combined with rapid tumour progression, surgical intervention appears to be a promising and low-risk approach in experienced hands to maintain or improve the neurological function in about 70% of cases.

Seltene Erkrankungen/*Rare diseases*

P027

Chirurgisches Management von peripheren Nervenscheidentumoren in Patienten aller Altersgruppen mit Neurofibromatose

Surgical management of peripheral nerve sheath tumours in all age-groups with neurofibromatosis

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Objective

Peripheral nerve sheath tumours are a heterogenous group, consisting mostly of benign tumours as well as malignant neoplasms. Especially in the setting of neurofibromatosis, diagnostics and indication for therapy pose relevant challenges for neurosurgeons.

Methods

We retrospectively reviewed all cases treated at our department between 2006 and 2017 for peripheral nerve sheath tumours. We analysed clinical signs, symptoms, histology, and sensory / motor function in the cohort with phacomatosis

Results

Of 414 identified patients, the majority had sporadic tumours (n=169, 40.8%). 151 patients (36.5%) had NF1, 54 NF2 (13.0%), and 33 schwannomatosis (8.0%). 7 patients had other syndromes (1.7%) which? A total of 772 surgical interventions were performed and 1132 tumours removed. In 238 patients with phacomatosis, 584 surgeries were performed for.

Indication for surgery was in most instances pain (50.9%), followed by significant tumour growth (22.8%). New deficits led to surgery in 21.9% of interventions, malignancy was suspected in 4.5%. Histopathology revealed mostly schwannomas (48.4%), followed by neurofibromas (46.9%). This group could be divided into cutaneous neurofibromas (6.5%), infiltrating plexiform neurofibromas (8.5%) and peripheral nerve born neurofibromas (31.9%). 2.5% of tumors were MPNST, we found 3 ganglioneuromas, 8 hybrid-neurofibromas and 1 perineurinoma. Leading symptoms, such as pain, motor and sensory deficits improved after 641/772 interventions (83.0%), remained unchanged following 96 interventions (12.4%) and worsened in 35 occasions (4.5%).

Conclusion

Surgical outcome is in general favourable. Surgery is safe and effective for (phacomatosis associated) peripheral nerve sheath tumours, however management needs a multidisciplinary setting. We propose early surgical resection in patients with peripheral nerve sheath tumours with significant growth, or pain, or motor deficit, or suspected malignancy.

Fig. 1

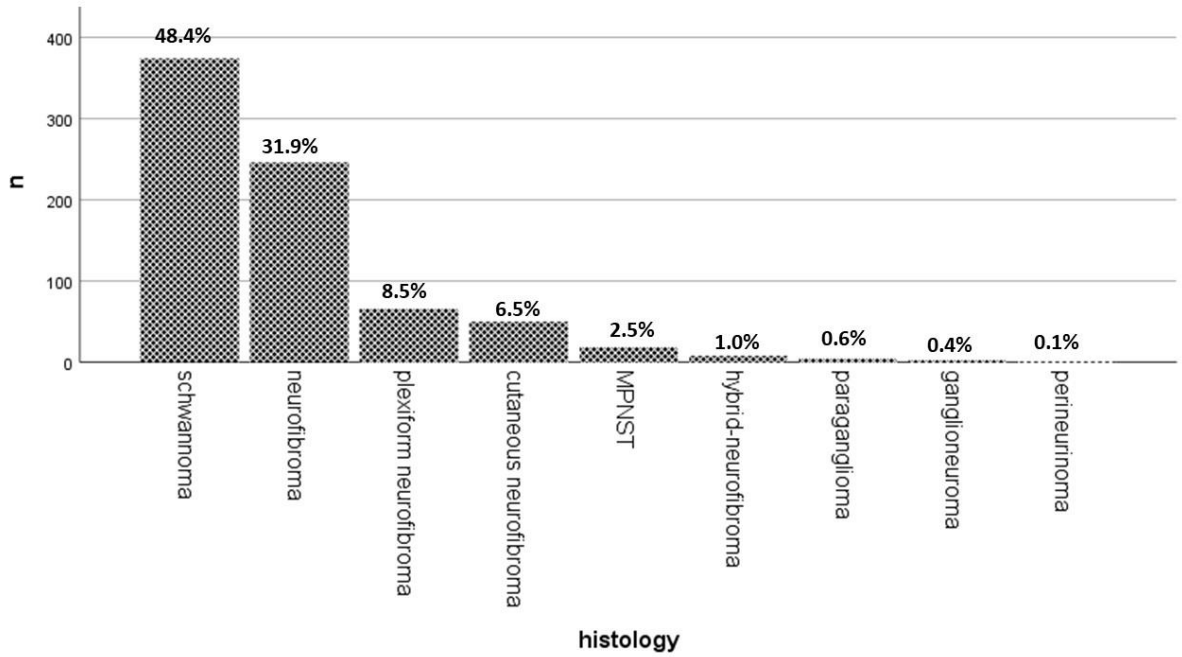
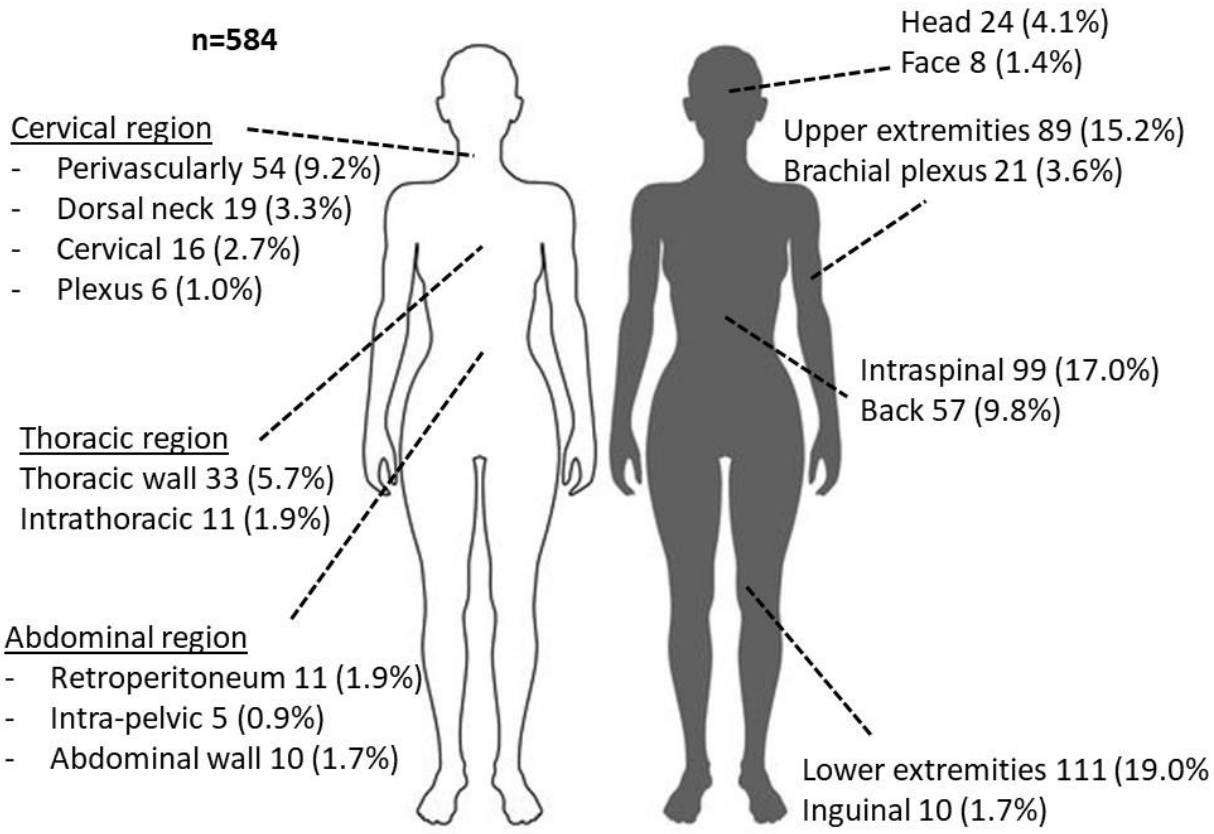

48.4%
31.9%
8.5%
6.5%
2.5%
1.0%
0.6%
0.4%
0.1%
n
400
300
200
100
0
schwannoma
neurofibroma
plexiform neurofibroma
cutaneous neurofibroma
MPNST
hybrid-neurofibroma
paraganglioma
ganglioneuroma
perineurinoma
histology

Fig. 2


n=584
Head 24 (4.1%)
Face 8 (1.4%)
Cervical region
- Perivascularly 54 (9.2%)
- Dorsal neck 19 (3.3%)
- Cervical 16 (2.7%)
- Plexus 6 (1.0%)
Upper extremities 89 (15.2%)
Brachial plexus 21 (3.6%)
Intraspinal 99 (17.0%)
Back 57 (9.8%)
Thoracic region
Thoracic wall 33 (5.7%)
Intrathoracic 11 (1.9%)
Abdominal region
- Retroperitoneum 11 (1.9%)
- Intra-pelvic 5 (0.9%)
- Abdominal wall 10 (1.7%)
Lower extremities 111 (19.0%
Inguinal 10 (1.7%)

Neuroonkologie I/*Neurooncology I*

P028

5-ALA induziertes Porphyringehalt in unterschiedlichen Hirntumoren – Implikationen für Visualisierungsintrumente und deren Validierung

5-ALA-induced porphyrin contents in various brain tumours – implications regarding imaging device design and their validation

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Objective

Fluorescence-guidance with 5-Aminolevulinic Acid (5-ALA) has been approved for malignant glioma surgery by the European Medicine Agencies (EMA) in Europe and the Food and Drug Administration (FDA) in the USA. Multiple systems have since been developed for visualizing fluorescing Protoporphyrin IX (PPIX). Employing such systems for fluorescence-guided resections implicitly assumes that qualitative fluorescence detection is equivalent to the established standard tested in a randomized setting and approved by EMA and FDA. This assumption needs to be critically assessed. Goal of this study was to define a threshold of fluorescent tissue discrimination under the BLUE400 filter-system (Carl Zeiss Meditec, Oberkochen, Germany), based on the expressed concentration of PPIX (cPPIX) in tumor tissue.

Methods

Utilizing a hyperspectral imaging system, tumor samples from patients harboring different tumor tissues were analyzed. Absolute values of cPPIX were calculated after calibrating the system with fluorescence phantoms with known cPPIX.

Results

524 samples from 162 patients harboring different tumor types were analyzed. Visual fluorescence under the BLUE400 filter was documented by the attending neurosurgeon. A 0.9 µg/ml threshold of cPPIX could be defined as the minimal concentration required to detect and discriminate visual fluorescence.

Conclusion

The current generation of fluorescence microscopes enables fluorescence discrimination in tumor tissue with a threshold of cPPIX of 0.9 µg/ml, thus defining specificity and sensitivity of this technology as initially tested in a randomized trial. Novel technologies should show similar characteristics in order to be used safely and effectively. If more sensitive, such technologies require further assessments of tumor selectivity.

Neuroonkologie I/*Neurooncology I*

P029

Azaindol Derivate verursachen eine Umprogrammierung des Tumorzellmetabolismus und haben eine ausgeprägte anti-neoplastische Aktivität im Glioblastom *in vitro*

Azaindole derivatives cause a metabolic reprogramming and have a strong anti-cancer activity in glioblastoma cells in vitro

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Objective

In this study, we screened nine synthetic azaindole derivatives for anti-neoplastic activity in glioblastoma cells in an *in vitro* setting.

Methods

Cell viability analyses were performed to assess effects on various glioblastoma cells following treatment with nine azaindole derivatives. A selection of the two most promising candidates underwent further testing. Cell count analyses and staining with propidium iodide followed by flow cytometry were performed to characterize effects on the cellular viability. Scratch-induced migration assays and time-lapse analyses were used to examine a potential influence on non-directed movement. Western blot analyses were done to determine specific protein expression of members of the Bcl-2 family of proteins and complexes of the respiratory chain. Extracellular flux analyses were performed to determine effects on oxidative phosphorylation (OCR) and the glycolytic rate (ECAR). Phospho tyrosine kinase arrays were used to detect effects on cell signaling patterns on the phospho protein level.

Results

All azaindoles tested, displayed a significant anti-proliferative activity among U251 and U87MG established glioblastoma cell lines as well as ULM-GBM-PC38 glioblastoma primary cultures. The two most potent derivatives had IC50-values ranging between 0.94 µM and 4.44 µM and were selected for further analyses. Both derivatives led to a significant inhibition of non-directed migration in U251 and ULM-GBM-PC38 glioblastoma cells. Metabolic analyses revealed a diverse response towards the two compounds tested. While compound 1 led to a downregulation of the oxidative consumption rate and an upregulation of the glycolytic rate, compound 2 caused mostly a decreased glycolytic rate. Similar, a diverse response was found with respect to the phospho tyrosine kinase activation pattern among the two derivatives. While compound 1 caused a reduced activation of ERK and RAS, compound 2 led to reduced activation of AKT and increased phosphorylation of p53.

Conclusion

We identified two promising drug candidates with potent anti-proliferative and anti-migratory activity among multiple *in vitro* models of glioblastoma. The mechanisms that underly the differential metabolic reprogramming warrant further investigation.

Neuroonkologie I/*Neurooncology I*

P030

Gehirnmetastasen des malignen Melanoms exprimieren potentielle Angriffspunkte für eine Therapie mit Checkpoint Inhibitoren

Cerebral metastases of melanoma express potential targets for immunotherapy with checkpoint inhibitors

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Objective

Checkpoint inhibitors such as Ipilimumab and Nivolumab have significantly improved survival in patients with inoperable or metastatic melanoma. Many cancers produce proteins that suppress the immunological response, specifically cytotoxic T-cells. Checkpoint inhibitors aim to block the inhibitory pathway these proteins stimulate in T-cells, thereby reactivating the cells ability to fight the tumour. Cytotoxic T-lymphocyte-associated antigen 4 (CTLA4), programmed cell death protein 1 (PD1) and programmed death-ligand 1 (PDL1) are current targets used in the treatment of melanoma and thus may present potential targets for the precise treatment of cerebral metastases. The objective is to identify and quantify the listed targets in brain metastases.

Methods

The tumours were acquired via operation and immediately frozen using liquid nitrogen. A total of 16 matched tumour samples, 8 metastatic melanoma tumours and 8 recurrent brain tumours, were selected and the proteins were extracted and separated using SDS-PAGE and transferred to a nitrocellulose membrane for incubation with anti-PD1, -PDL1 and -CTLA4 primary antibodies. Secondary antibodies linked to a peroxidase were used for band detection.

Results

PDL-1 was shown to be expressed in metastases (0,747+/-0,1921) and the recurrent tumour (0,7868+/-0,2038). CTLA4 and PD1 are significantly over-expressed in metastases (0,4499+/-0,1877 and 0,4792+/-0,2584 respectively) and the recurrent tumour (0,4757+/-0,4449 and 0,4599+/-0,2289) versus the control group (0,2484+/-0,17 and 0,1049+/-0,0616).

Conclusion

PD1 and CTLA4 are both over-expressed in malignant melanoma and also in its cerebral metastasis. Furthermore, they may also present a target for immunotherapy in the treatment in metastatic melanoma.

Neuroonkologie I/*Neurooncology I*

P031

Ergebnisse nach der iMRT-assistierten Resektion der STH-produzierenden Hypophysenadenome
Clinical features and outcome after iMRI assisted resection of GH producing pituitary adenomas

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Objective

Growth hormone (GH) producing adenomas are still challenging. Long term sequelae of high GH levels are severe and surgical resection is the primary treatment option. The use of intraoperative MRI increases extent of resection and it seems to be beneficial for transsphenoidal pituitary surgery. We have evaluated the clinical outcome of patients with acromegaly treated with iMRI assisted transsphenoidal pituitary surgery.

Methods

We conducted a retrospective analysis of patients treated by iMRI assisted transsphenoidal surgery at our department between 2012 and 2020. A total number of 52 patients (54 surgeries) with acromegaly was selected for the further analysis. Detailed volumetric tumor measurement before surgery, intraoperatively and three months after surgery was performed (Brainlab, Elements). Pituitary adenomas were graded according to Knosp classification. Additionally, demographic data, clinical symptoms as well as complications and endocrine outcome were evaluated.

Results

Out of 54 pts, 68.5% (N=37) were graded as Knosp 0-2. Mean age was 45 years and mostly male patients were treated (59.3%, N=32). Median tumor volume was 1.47 cm3 (ratio 0.06-39.1 cm3). Endoscopic surgery was performed in 48.1% (N=26). Recurrent adenoma was treated in 14.8% (N=8). Biochemical remission was achieved in 62.9% (N=22/35) and it was significantly associated with lower Knosp grade (p=0.009). We found no significant association between remission and surgical technique (p=0.122). Additional tumor resection after iMRI was performed in 26.4% (N=14/53) and was significantly associated with more infiltrative growth pattern (p=0.019). We found no significant difference between additional resection and surgical technique (p=0.866). Revision due to cerebrospinal fluid fistula was performed in 7.4% (N=4). New permanent diabetes insipidus was found in 3.7% (N=2).

Conclusion

Intraoperative MRI might be a helpful tool in the treatment of acromegaly in order to achieve gross total resection and biochemical remission of the disease independently on surgical technique. Adenomas infiltrating cavernous sinus seem to profit from iMRI, however it might help to achieve this goal even in adenomas without invasive growth pattern treated by endoscopic technique.

P032

Risikostratifizierung des motorischen Outcomes in der Hirntumorchirurgie – ein Vergleich zweier Modelle
Comparison of two different risk stratification models to predict the postoperative motor outcome in brain tumour surgery

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Objective

Brain tumor surgery near the motor cortex or the corticospinal tract bears the risk of a new postoperative paresis. Two motor outcome prediction models have been recently published. One model is based on a sum score of clinical and MR-morphological features while the other one relies on navigated transcranial magnetic stimulation (nTMS). The aim of this study was to compare two risk stratification models with respect to their prognostic value for the postoperative motor outcome.

Methods

We retrospectively analyzed a consecutive cohort of patients who underwent resection for motor eloquent glioma between 2008 and 2020, and received a preoperative nTMS examination with TMS-based DTI fiber tracking. The sum score (Spena et al. 2018) ranges from 1-8 (with lower scores indicating an increased risk) and bases on : tumor margins, volume, presence of cysts, contrast agent enhancement, MRI index (defined gradation of subcortical white matter infiltration levels), preoperative seizures, preoperative sensor-/ motor deficit. For the nTMS, the following items were assessed: infiltration of motor cortex, tumor-tract-distance, resting motor threshold. Associations to the motor outcome were evaluated postoperatively and after 3 months according to the British Medical Research Council (MRC) grading.

Results

204 patients (75 female) with a median age of 50 years (20-81) were analyzed. 34 out of 188 patients (18%) suffered from a new permanent motor deficit, all of whom were classified as high-risk patients in the TMS stratification (sensitivity 100%), whereas only 35% of the patients with a new deficit had a low sum score (8mm: 0%; $p < 0.001$). The individual RMT values for each hemisphere were correlated (sick hemisphere: $p = 0.009$, Pearson"s $r = 0.19$; healthy hemisphere: $p = 0.003$, Pearson"s $r = 0.22$).

Conclusion

The functional-derived parameters of the nTMS stratification had a higher sensitivity and a higher NPV for prognostication of postoperative motor outcome compared to the clinical and MR-morphological variables of the sum score.

Neuroonkologie I/*Neurooncology I*

P033

Korrelation von Olig2 mit der Tumoranhaftung an Gliomstammzellzonen bei Patienten mit neu diagnostiziertem Glioblastom

Correlation of Olig2 with tumour attachment to glioma stem cell zones in newly diagnosed glioblastoma patients

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Objective

Glioma stem cells (GSC) are deemed to play a crucial role during the tumor invasion in glioblastoma (GBM) patients. The oligodendrocyte lineage transcription factor 2 (Olig2) is a highly specific GSC marker, which is increasingly gaining attention for the biomolecular GBM characterization among other well-established molecular markers such as MGMT (methylguanine methyltransferase)-methylation and IDH (isocitrate dehydrogenase)-mutation. However, its prognostic role is still not clear, and the literature reports are controversial. The aim of the study was to evaluate a possible correlation of Olig2 with GBM localization in relation to GSC zones

Methods

A retrospective analysis of patients with newly diagnosed GBM and treated at our department from 2016 to 2019 was performed. Information about different molecular markers such as IDH-mutation, MGMT-methylation, p53, Ki67 and Olig2 was gathered from the neuropathological reports. The localization of the tumor on the first magnetic resonance imaging (MRI) and relation to several GSC zones such as the subventricular (SVZ) and the subgranular zone (SGZ) was evaluated by reviewing the MRI scans.

Results

Of the 109 cases analyzed, 91 (83.49%) stained at least partially positive for Olig2 -our primary marker of interest. Only 6 (5.50%) showed an IDH-1 mutation. We further analysed MGMT status, tumor volume and relation to GSC zones. 44 GBMs (40.37%) demonstrated MGMT-methylation. Mean tumor volume on MRI scans was 31cm3. We found 62 (56.88%) had contact with a GSC zone. We performed correlation analysis and found a statistically significant positive correlation between tumor volume and contact to GCS zones (r=0.29; p=0.006). However, we could not demonstrate a positive correlation between Olig2 and contact to GSC zone.

Conclusion

Olig2 expression is a frequently found neuropathological parameter in newly diagnosed GBM, which showed no statistically significant correlation with tumor attachment to the GSC zones in this retrospective study. This might be due to the lack of further sub-differentiation of the Olig2-positive tumor cells regarding their phosphorylation. Consideration of the Olig2-phosphorylation-status may further shed light on the prognostic role of Olig2 in GBM patients by providing insight about different tumor invasion/proliferation pathways which we aim to further evaluate in a prospective study.

P034

Expression von ALDH1 Isoformen in Glioblastomen und Glioblastom Stammzellen
Expression of ALDH1 isoforms in glioblastoma and glioblastoma stem cells

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Objective

Aldehyde dehydrogenase 1 (ALDH1) is a detoxifying enzyme involved in the oxidation of intracellular aldehydes. In glioblastomas (GB), isoforms A1 and A3 have been implicated in the regulation of tumor growth and resistance to cytotoxic therapy. Recent evidence suggests that A1 or A3 may have non-redundant functions in newly diagnosed and recurrent GB (ndGB and recGB, respectively). Up to date, investigations on ALDH1 isoforms have been confined to analyses of GB tissues or long-term cell lines lacking the properties of cancer stem cells. This study aims to characterize ALDH1 isoforms A1 and A3 in glioblastoma stem cells (GSC) representing a therapeutically relevant target in GB.

Methods

ALDH1 expression in FFPE tissue or cultured GSC was analyzed. FFPE tissue and GSC were obtained from freshly resected ndGB oder recGB. GSC were isolated using the Neural Tissue Dissociation Kit (Miltenyi Biotec) and maintained in NeuroBasal medium supplemented with B27 component and self-renewal factors bFGF and EGF . GSCs differentiation was induced by bFGF/EGF withdrawal. ALDH1 expression was analyzed by immunostaining using antibodies recognizing A1 or A3 isoforms. Antibody epitope mapping was performed by western blot using a panel of antibodies, binding to different regions of the ALDH1(A3) protein.

Results

Immunohistochemistry showed a high degree of inter- and intra-tumoral heterogeneity of A1 expression in either ndGBs (n=62) or recGBs (n=62). A1 expression was found to be primarily associated with tumor-infiltrating macrophages (CD68 co-staining). In contrast, GSC cultures showed a consistent pattern characterized by homogeneous expression of A3 and a lack of A1 expression. A3 expression in tumor cells could be confirmed in selected cases (n=6) in FFPE material. GSC-associated A3 was found to have an abnormal localization in the nuclear matrix. Biochemical analyses revealed the expression of a 33 kDa protein that is recognizable by different ALDH1(A3) antibodies and abundantly expressed in a panel of 8 ndGB- and 4 recGB-derived GSCs. Antibody epitope mapping suggests the A3 identity of a 33 kDa peptide lacking the A3 catalytic domain.

Conclusion

Our results indicate that ALDH1(A3) but not ALDH1(A1) is a marker associated with GSCs. Our findings urge to unequivocally determine the identity and functions of a putative A3 peptide expressed in GSCs and establish the role of the nuclear A3. Given the diagnostic merits of ALDH1, clarification of these aspects has considerable clinical importance.

Neuroonkologie I/*Neurooncology I*

P035

Günstige Verträglichkeit von CUSP9v3 in Phase I-Studie (NCT02770378) beim Glioblastomrezidiv
Favourable tolerability in phase 1 study of CUSP9v3 (NCT02770378) in recurrent glioblastoma

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Objective

In an attempt to address the variety and ever-shifting array of growth-promoting pathways glioblastomas (GB) use to thrive and circumvent our treatment efforts, we developed a nine repurposed drug regimen, CUSP9v3, designed to be given with temozolomide at 40 mg/m^2/d. When conceptualizing this study, we judged that the advantages of continuous low-dose temozolomide - low side effect burden and rarity of severe adverse events - would outweigh any advantages of higher doses. The nine repurposed drugs all have robust preclinical databases of inhibiting experimental glioma growth. *In vitro* work by our laboratory, independently confirmed by others, showed that the combination of these nine repurposed non-oncological drugs was quite effective in inhibiting growth of GB cells.

Methods

Prospective clinical proof-of-concept trial NCT02770378, 10 patients, one arm. All patients with recurrent GB had previous first-line treatment with neurologically safe maximal tumour resection followed by irradiation and concomitant plus adjuvant temozolomide. Diagnoses were histologically proven on initial resection. Tumour recurrence was determined by contrast-enhanced magnetic resonance imaging.

Results

Three patients have currently achieved progression-free survival (PFS) of 38, 38, and 50 months, ongoing as of this writing, which clearly exceeds previous PFS on first-line treatment in these cases. Molecular status for ^{6}-methylguanine-DNA methyltransferase promoter hypermethylation/isocitrate dehydrogenase was positive/mutant, positive/wild-type and negative/wild-type, respectively. Among the other patients, five died in the first few months after starting CUSP9v3, and two patients remained progression-free beyond 12 months of study treatment but died from delayed tumour progression thereafter. No deaths were deemed treatment-related. The most common side effects were nausea, fatigue and headache. Drug doses were reduced as required on individual bases. There was little evidence of bone marrow toxicity, and nausea was usually

evanescent. In the three long-term survivors, the median neutrophil-to-lymphocyte ratio decreased from 2.5 to 1.5 during CUSP9v3 treatment while in the group of the three shortest-term survivors, that ratio increased from 4.7 to 14.3.

Conclusion

CUSP9v3 was well-tolerated and gave signal of potential benefit requiring confirmation in a phase 2 clinical trial which is currently being prepared.

P036

Punkt-basierte vs. automatische iCT basierte Registrierung – Auswirkungen auf die Registriergenauigkeit
Fiducial vs. automatic iCT-based registration – impact on registration accuracy

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Objective

Mapping image space and physical space in neuronavigation is most commonly performed using fiducial based imaging approaches based on MR or CT images, whereas CT images show superior registration accuracy due to image distortion within the MR images. Fiducial based registration for navigation has an overall clinical application accuracy of 3-4 mm. The aim of this study was to compare fiducial based and automatic registration using the AIRO iCT scanner (Brainlab, Munich) regarding registration accuracy analyzing a wide range of CT protocols.

Methods

To investigate registration accuracy with different scan protocols, a plexiglas phantom was used consisting of a base plate and 24 randomly distributed notched rods on varying length. To perform both registration approaches, also 7 additional adhesive fiducial markers were attached diffusely scattered. A reference data set (helical, full dose scan) was acquired, to allow for defining the target points of each notched rod in the image space. Fiducial based registration was performed for axial and helical CT data (160 mA, 120 kV). Automatic registration was performed using scan protocols with varying amperage (160 mA, 80 mA, 40 mA, 20 mA, 10 mA, 5 mA) and voltage (120 kV, 100 kV, 80 kV) and all notched rods were localized and acquired with the tool tip of a pointer. For each notched rod the Euclidean distance between reference point and acquired point was calculated as target registration error (TRE).

Results

Standard fiducial based registration showed an overall TRE of 1.15 ± 0.43 mm. Automated axial iCT based registration revealed an overall TRE of 1.08 ± 0.18 mm ranging from 0.86 mm to 1.24 mm, showing comparable ($p > 0.05$) or significantly improved mean TRE results ($p < 0.05$) depending on the scan protocol. Automated helical iCT based registration revealed an overall mean TRE of 0.47 ± 0.23 mm, ranging from 0.34 mm to 0.70 mm, showing a significantly improved ($p < 0.05$) mean TRE for all scan protocols compared to fiducial based registration.

Conclusion

ICT-based automatic registration delivers even in this optimal set-up for fiducial based registration (e.g. no soft tissue shift during data acquisition and registration) in case of axial scans at least comparable or even significantly better registration accuracy, in case of helical acquisition, significantly better registration accuracy is achieved across all scan protocols and is therefore a useful tool for user-independent and fast, highly accurate registration in neurosurgery.

Neuroonkologie I/*Neurooncology I*

P038

Steigerung des therapeutischen Potentials neuartiger anti-Hirntumorstammzell-gerichteter Pharmakotherapie mittels Gold-Nanopartikel

Increasing the therapeutic potential of novel anti-brain cancer stem cell pharmacotherapy with gold nanotechnology

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Objective

Stem cells in glioblastoma (GBM) are considered to be a main contributor for the high levels of therapy resistance of the disease. The identification of metabolic dependencies of those GBM stem cells (GSCs), such as glutaminase 1 activity, opens a new area for future management of neuro oncology patients. We sought to optimise therapeutic potential of GLS1 inhibitor CB839, previously shown to possess promising anti-GSC activity, by improving its target delivery using gold nanoparticles (Au NPs)

Methods

Au NPs were synthesized using a bottom-up approach and covered with various polymers, which allowed the attachment of the inhibitor via physical adsorption. Synthesis and quality control assays include transmission electron microscopy, energy-dispersive X-ray spectroscopy, Fourier transform infrared spectroscopy, ultraviolet–visible spectroscopy, high performance liquid chromatography amongst othersThe efficacy of the CB839 inhibitor with and without the Au carriers was assessed in a collection of GBM neurospheres known to recapitulate core pathophysiological properties of the disease. Mode of action and functional validation assays of our drug development project include colony formation, Western Blot- based protein analysis as well as fluorecence stainings.

Results

Au NPs proved to be an efficient carrier for CB839 with a drug loading efficiency of up to 12%, a values proofing solid non-covalence atomic binding. Optical verification proofed efficient penetration of NP into the GSCs. A delivery with NPs resulted in an increased therapeutic effect of the drug of up to 45% increase, compared to the drug alone, as assessed by colony formation assay. However, NP-assisted treatment did not alter total GLS1 protein of the cells as compared to control counterparts.

Conclusion

Au NPs are potential carriers to deliver anti-metabolic inhibitor CB839 into therapy resistant GSCs more efficiently leading to enhanced efficacy of this promising pharmacotherapy. However, mechanistic explanation of the observed effect on molecular level, such as GLS1 enzymatic activity assessment or quantification of intracellular drug release kinetics are ongoing to comprehensively characterize the mode of action of our NP-drug conjugate. Given the amendable nature of our NP synthesis and functionalization procedures, we hypothesize that our results can be the basis for additional nanomedicine approaches in neuro oncology and beyond.

Neuroonkologie I/*Neurooncology I*

P039

Infiltration von Vestibularisschwannomen mit inflammatorischen Zellen ist mit einem größeren Tumorvolumen aber nicht mit einem volumetrischen Wachstum assoziiert

Infiltration of vestibular schwannomas with inflammatory cells is associated with increased tumour size but not with volumetric growth

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Objective

The impact of inflammatory processes in vestibular schwannoma growth has been suggested by prior studies. A clear impact of inflammatory cell infiltration and tumor size growth has not yet been shown in a detailed volumetric analysis.

Methods

We performed immunohistochemical analyses of inflammatory cell markers (CD3, CD8, CD68 and CD163) in 923 newly diagnosed sporadic vestibular schwannomas. We constructed an inflammatory score based on the immunohistochemical marker scores of each tumor. Volumetric measurement of preopertaive images was done. The immunohistochemical results were compared with preoperative radiographic tumor volume and volumetric growth.

Results

A higher tumor volume prior to resection was seen in vestibular schwannomas with an increased infiltration with CD3, CD8, CD68, CD163 positive cells. There was no difference in volumetric tumor growth when regarded for each marker separately. But when the immunohistochemical results were taken together as an inflammatory score, a slower growth rate with higher inflammatory score was observed.

Conclusion

Infiltration of vestibular schwannomas with inflammatory cells is associated with increased tumor volume but slower growth.

P040

Klinische Einblicke – Märchenfiguren mit Hypophysenadenomen aus den Erzählungen der Brüder Grimm
Clinical insights to pituitary adenomas among fairytale characters by Brothers Grimm

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Objective

Grimm's fairytales are known worldwide and everyone has encountered them at some point in time. Most of the characters are famous and known to be physically abnormal with e.g. giantism or prominent facial features. In fact, we wonder if these characters were inspired by people with pituitary diseases among the general population in the age of Brothers Grimm.

Methods

We systematically studied a collection of fairytales by the Brothers Grimm (edition 1937 by Karl Hobrecker). We defined typical neurological and endocrinological signs and symptoms possibly related to pituitary adenomas as followed: Neurological deficit: Chiasmal syndrome. Endocrinological signs: gigantism, dental malocclusion, prominent lips, nose, enlarged hands and feet (acromegaly), moon face, buffalo hump, mood swings, redistribution of fat, hirsutism (Cushing's Disease), galactorrhea, gynecomastea (prolactinoma), polydipsia (diabetes insipitus). We reviewed all fairytales from a medical perspective and matched the listed symptoms with the description of the characters. We then compared the description of specific individuals with illustrations by Ruth Koser-Michaels.

Results

We studied 106 fairytales in total and detected 7 fairytale individuals being described with clinical signs of acromegaly (4), Cushing's Disease (1), Diabetes insipidus (1) and chiasmal syndrome (1). All characters have been surprisingly illustrated with the classic signs of their 'pituitary disease'.

Conclusion

We offer a potential insight to pituitary adenomas among fairytale characters. Some individuals were described with signs of neurological and endocrinological disorders possibly reflecting the prevalence of pituitary disease in the age of Brothers Grimm. Hormone-secreting adenomas such as Cushing's Disease or acromegaly are rare. People affected by these conditions in the early 18th century were possibly recognized by the population as monsters, trolls and outcasts as portrayed in Grimm's fairytales. With this study we want to raise awareness for patients with long duration of mal- or undiagnosed active disease in secreting pituitary adenomas.

P037

Das Gen PBRM1 ist häufig mit papillärem Meningeomen vergesellschaftet

Frequent inactivating mutations of the PBAF complex gene PBRM1 in meningioma with papillary features

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Objective

Papillary meningioma (PM) is a World Health Organization (WHO) grade III tumor that has been associated with brain invasion and aggressive clinical behavior. The genetic alterations associated with PM remain unclear.

Methods

We mined data collected as part of our clinical comprehensive genomic profiling (CGP) initiative which has to date analyzed 8 PM (>50% papillary morphology) and 22 meningiomas with focal papillary features (10–50%) amongst 562 meningiomas of other subtypes. CGP was performed on hybridization-captured, adaptor ligation-based libraries to a mean coverage depth of > 650 × for 236 or 315 genes plus the introns from 19 or 28 genes frequently involved in cancer.

Results

In our cohort of eight PMs, we identified three cases with inactivation of *PBRM1*. Of the 22 meningiomas with only focal papillary features, 8 cases were *PBRM1*-mutant. Thus, 11 of 30 cases with at least focal papillary morphology had inactivation of *PBRM1*. In the entire cohort of 562 meningiomas that represents a general population of all WHO grades, we identified five additional cases with inactivating alterations in *PBRM1* that did not display overt papillary morphology. Thus, 11 of 16 *PBRM1*-mutant cases (69%) occurred in meningioma with papillary histologic features, supporting a significant association between papillary features and *PBRM1* mutation ($p<0.0001$). Among the 16 PBRM1-mutant cases (2.8% of cohort), the detected *PBRM1* alterations included six intragenic deletions, four frame-shifting insertions, four frame-shifting deletions, and two truncating mutations. All showed biallelic inactivation by SNP array analysis and mutant allele read count data analysis. The majority of *PBRM1*-mutant meningiomas occurred in female patients (n=10/16, 62.5%), and median age was 51 years. Most cases were located supratentorially (n=10).

Conclusion

We identify the tumor suppressor gene *PBRM1* as a recurrently altered gene in meningiomas with papillary histomorphology. Further investigational studies are needed to determine whether *PBRM1* mutations are an independent negative prognostic biomarker.

Neuroonkologie I/*Neurooncology I*

Neuroonkologie II/*Neurooncology II*

P041

inovivo – ein spezielles *in vivo* System zur Verabreichung von Tumor Treating Fields (TTFields) bei Mäusen
inovivo – a dedicated in vivo system for Tumor Treating Fields (TTFields) delivery to mice

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Objective

Tumor Treating Fields (TTFields) therapy is an CE certified anti-cancer treatment, delivered to patients continuously by 2 pairs of transducer arrays attached to the skin. In vivo TTFields studies were so far limited due to the lack of a dedicated animal delivery system. Two main challenges in this respect relate to ensuring: 1) adequate contact between arrays and the animal"s skin throughout the entire treatment; and 2) minimization of animal stress, due to motility limitations imposed by wires and individual housing needs (ie, to prevent wire entanglement from different mice). This work aimed to develop an in vivo system for continuous and effective TTFields delivery to mice.

Methods

To develop a viable system, several designs were tested: 1) various electrode layouts; 2) a variety of adhesive materials; 3) devices that prevent wire coiling; and 4) housing methods to reduce stress. Simulations were performed to ensure electric fields were generated at the desired locations.

Results

The final transducer array design for TTFields included 2 layers, an inner layer to improve adherence, and an outer layer to secure electrodes to the depilated skin. The conductors were compacted into a single printed circuit cable that connects to a novel electric swivel machine, which rotates in accordance to the animal"s movement to prevent cable coiling. Indeed, fewer cable entanglements occurred and fewer array replacements were needed, thus allowing for decreased need for animal handling and increased TTFields treatment compliance (continuity). A new cage was developed to allow pairs of mice to maintain dyadic social interactions during the experiment, while being housed separately. Indeed, animals treated with the inovivoTM system for 1 week displayed lower weight loss than animals treated with the previous non-dedicated system, indicative of reduced stress. In this initial tested torso orthotopic model, TTFields treatment was shown to generate above threshold intensities (>1 V/cm) in the lung, liver, pancreas, and other major organs, suggesting tumors in these torso organs may be treated effectively using the inovivo system.

Conclusion

The novel TTFields inovivo system provides means for continuous TTFields delivery to torsos of mice (while minimizing stress) to facilitate in vivo studies. The development of mouse head arrays to allow further research of TTFields for use in glioblastoma treatment (application of widespread interest) is currently underway.

Neuroonkologie II/*Neurooncology II*

P042

Lokalisierungsgenauigkeit bei rahmengestützten stereotaktischen Prozeduren
Localisation accuracy in frame-based stereotactic procedures

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Objective

To perform deep brain stimulation, an accurate localization of anatomical target structures as well as the precise placement of the electrodes within the target structures is required. To map preoperative data to the patient"s anatomy, stereotactic frame-based techniques are applied. As optimal frame positioning in relation to the scanner's coordinate system might be difficult to achieve in some cases, localization accuracy might also be affected. In this study localization accuracy was evaluated with respect to deviations of the frame from optimal positioning corresponding to rotation, flexion and lateral bending of the head.

Methods

To analyze the accuracy of frame localization related to different frame positions, a stereotactic frame (Zamorano-Duchovny) including a CT localizer box was attached to a head phantom. Deviations from optimal frame positioning were revealed by adjusting the frame according to rotation, flexion or lateral bending or a combination of those (0°, 9° or 18° each). The localizer box was positioned in the iso-center of the AIRO® iCT scanner (Brainlab, Munich, Germany). For localization a full-dose and super-low-dose protocol was used covering the whole localizer box. Frame localization was performed using the Stereotaxy Element (Brainlab, Munich, Germany). The localization accuracy was calculated as deviation of slice-by-slice detected points along each rod.

Results

In case of the full-dose protocol, reference localization accuracy was 0.17 ± 0.09 mm (rotation – flexion – lateral bending: 0-0-0). Successful localization was revealed in eight other cases with localization accuracies of 0.18 ± 0.09 mm (9-0-0), 0.18 ± 0.10 mm (18-0-0), 0.18 ± 0.09 mm (0-9-0), 0.21 ± 0.16 mm (0-0-9), 0.19 ± 0.09 mm (9-9-0), 0.18 ± 0.09 mm (9-0-9), 0.18 ± 0.09 mm (18-0-9) and 0.17 ± 0.09 mm (18-9-0), not significantly differing from the reference. In case of the super-low-dose protocol, reference localization accuracy was 0.14 ± 0.07 mm (0-0-0). Successful localization could be performed in eight cases with localization accuracies of 0.15 ± 0.08 mm (9-0-0), 0.16 ± 0.08 mm (18-0-0), 0.17 ± 0.08 mm (0-9-0), 0.17 ± 0.09 mm (0-0-9), 0.15 ± 0.08 mm (9-9-0), 0.14 ± 0.07 mm (9-0-9), 0.15 ± 0.07 mm (18-0-9) and 0.16 ± 0.09 mm (18-9-0), not significantly differing from the reference. However, the remaining scans could not be used for localization.

Conclusion

For frame-based stereotactic procedures, moderate deviations in all spatial planes are tolerated without loss of localization accuracy.

P043

Der MIB-1-Index von Meningeomen korreliert mit einer klinischen Verbesserung nach Resektion
MIB-1 index in meningioma correlates to clinical improvement after surgical resection

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Objective

High MIB-1-scores correlates with new cranial nerve deficits after resection of skull base meningioma. However, the role of MIB-1 as an indicator of systemic inflammation on functional impairment at presentation and at follow-up is unclear.

Methods

445 patients with meningioma were analyzed. Indicators of systemic inflammation, i.e. serum C-reactive protein (CRP), and white blood cell (WBC) count were assessed. Karnofsky performance status (KPS) score was assessed prior surgery, at 3 months, and at 12 months after treatment. Patients were divided into two groups, low (≤4%), and high (>4%) MIB-1-score. Univariate and multivariate analyses were performed.

Results

KPS score did not differ pre-operatively. CRP levels did not differ between the groups. WBC counts were significantly higher in the high Mib-1-score group (10.3 versus 8.9; p= 0.01). The rate of presurgical administration of corticosteroids did not differ between the groups.

In the multivariate analysis, patients with high Mib-1-score (>4%) were more likely to have a clinical improvement after surgical treatment, compared to patients with low MIB-1 score (p=0.01, OR 2.2, 95% CI 1.2 - 4). KPS score after 12 months did not differ between the groups.

Conclusion

While the underlying mechanism is not clear, patients with high MIB-1 score seem to have a higher rate of clinical improvement after surgery at 3 months, compared to patients with low MIB-1 score.

Neuroonkologie II/*Neurooncology II*

P044

Mikrostrukturelle Analyse der endo- und perineuralen Zellen in humanen Neuromen
Microstructural analysis of endo- and perineurial cells in human neuroma

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Objective

Neuromas are pathologic nerve distensions caused by a nerve"s response to trauma. Following traumatic peripheral nerve injury (PNI), sprouting axons attempt to cross the injury site as long as scar tissue, a gap or lacking axonal guidance do not counteract sprouting. If target-oriented sprouting is prevented, a neuroma will form. Following PNI, endoneurial cells provide axonal guidance for successful regeneration, while perineurial cells form a diffusion-barrier via tight-junctions to provide a physiologically restricted intra-fascicular space. The cellular communication between those perineurial cells as well as the exchange of small molecules is mediated via connexins (Cx26 and Cx43). However, the cellular and molecular changes following PNI have not yet been resolved for human nerve.

Methods

The endo- and perineurial cells were detected by immunohistochemistry and immuno-electron microscopy using antibodies directed against CD34 (endoneurial fibroblast like cells, EFLCs) and the Glucose-Transporter 1 (Glut1, perineurial cells). Furthermore, the formation of tight-junctions and the expression of connexins in endo- and perineurial cells was analyzed using antibodies directed against the tight junctional marker protein Claudin1 as well as Cx26 and Cx43 in six human traumatic neuromas.

Results

Following PNI, axons as well as the endo- and perineurial structures were disrupted and mini-fascicles of regenerating axons were detectable in the neuromatous tissue. In the proximal neuroma, mini-fascicles were ensheathed by a single layer of CD34 expressing EFLCs and surrounded by a reduced number of Glut1 positive perineurial cells, compared to fascicles of an intact nerve. Those perineurial cells were expressing a highly reduced amount of Claudin1, Cx26 and Cx43 protein. In the distal neuroma segment as well as in the degenerated end, located distal to the injury site, endo- and perineurial ensheathment of the regenerating axons was absent. The immunhistological labeling revealed scattered endo- and perineural cells in the distal and degenerated neuroma segments. However, no tight-junction formation and a highly decreased connexin expression was observed in those cells.

Conclusion

Unsuccessful axonal regeneration might be related to the lack of endoneurial as well as perineurial structures in the distal neuroma and the degenerated end, which results in the disruption of the perineurial nerve barrier and the axonal guidance to the target organ.

Neuroonkologie II/*Neurooncology II*

P045

MRT-Veränderungen nach Protonentherapie in Kombination mit Tumor Treating Fields bei Glioblastompatienten
MRI changes after proton therapy for glioblastoma with and without tumor treating fields therapy

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Objective

Tumor treating fields (TTFields) are an approved treatment modality for glioblastoma (GBM) with significant improvement of progression free survival and overall survival. Growing evidence suggest, that proton therapy increase early magnetic resonance imaging (MRI) changes. The aim of this study was to evaluate the morphologic changes in serial MRI after combination treatment of TTFields and proton therapy.

Methods

Twenty-four patients with GBM were included in this prospective analysis. All patients received initial tumor resection followed by combined chemo- and radiation therapy and temozolomide maintenance. Radiation therapy was performed with 50.0 Gy photons and a proton boost with 10 Gy equivalent (Gy(RBE)). In 12 patients additionally a therapy with with TTFields during temozolomide maintenance was performed.

Results

An increase of contrast enhancement and a progress in the T2 FLAIR hyperintensity were found in 50.0% (N=12) at 3 months and in 29.2% (N=7) at 6 months. No differences were observed between patients with and without TTFields therapy at 3 months [58.3% (N=7) vs. 41.6% (N=5); P=0.414] and at 6 months 57.1 (N=4) vs. 42.9% (N=3); P=0.673).

By the RANO criteria, a progressive disease (PD) was observed in seven patients (29.2%) at 3 months and in eight patients (33.3%) at 6 months. Pseudoprogression (PP) was observed in in 33.3% (N=8) at 3 months and in 25.0% (N=6) at 6 months. Neither for PD at 3 months [57.1% (N=4) vs. 42.9% (N=3); P=0.653] or at 6 months [62,5% (N=5) vs. 37.5% (N=3); P=0.386), nor for PP at 3 months [62.5% (N=5) vs. 37.5% (N=3); P=0.386] or at 6 months [33.3% (N=2) vs. 66.6% (N=4); P=0.346] differences for patients with and without TTFields therapy were found.

Conclusion

An increase of contrast enhancement and/or T2 FLAIR MRI hyperintensity after proton boost therapy is common. The rates of new contrast enhancement, PD, and PP after photon therapy are in range with the results of patients with additional TTFields therapy.

P046

Behandlungsergebnisse nach Operation cerebellärer Metastasen
Outcomes after surgical treatment of cerebellar metastases

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Objective

To critically review our institutional experience with surgical treatment of cerebellar metastases (CM).

Methods

Pertinent data of 80 consecutive patients who underwent surgery for removal of CM 2015-2020 were analysed retrospectively. Standard statistical methods (SSPS 25, IBM) were employed.

Results

The cohort was 58.8% female. Median age was 61 years. The most frequent primary tumours were lung (48.8%) and breast cancer (26.3%). 38 patients (48.5%) had multiple (2-3: 19, >3: 19) metastases. Neuroimaging revealed obstructive hydrocephalus in 36.3% with clinical signs and symptoms in 20.0%. Four cases required external ventricular drains, and 2 patients a permanent VP shunt.

Median overall survival (medOS) was 9.2 months (GPA 0–1.0, 1.5–2.5, 3.0, 3.5–4.0: 5.1, 9.2, 23.9, 23.3 months; p=0.048). Prominent prognostic factors included single vs. multiple metastases (medOS 14.2 vs. 7.4 months; p=0.028), the preoperative KPI<70 vs. 70-100 (medOS 6.5 vs. 14.2 months; p=0.005) and clinical (but not radiological) hydrocephalus (medOS 6.6 vs. 14.0 months; p=0.009). Age and presence of extracerebral metastases did not significantly influence survival. Prognosis also varied significantly with the degree of resection (resection of all cerebellar and supratentorial disease vs. unresected supratentorial tumour, resection of all cerebellar disease vs. residual cerebellar tumour: 14.2, 7.9, 2.6 months; p=0.011).

The median postoperative KPI was 80 (25-75% IQF: 60-90). Postoperative KPI worsening vs. improvement ≥20 was observed in 9 (11.3%) vs. 7 (8.8%) cases, respectively. 30 days mortality was 5%. Serious (CTCAE grade 3–5) neurological adverse event persisting at discharge were seen in 5/76 cases (6.6%). There were 14 surgical and 7 medical CTCAE grade 3-5 complications.

Conclusion

Survival in this series compares favourably with the literature. Survival after resection of all metastases was comparable to survival after surgery for a single metastasis. Resection of CM only was still associated with reasonable survival. A significant negative prognostic impact was seen for clinical but not radiological hydrocephalus, which favours timely surgery. The presence of extracerebral disease had no prognostic influence suggesting that postponing staging after the metastasectomy is acceptable. Surgery for CM carries a substantial complication rate, however, functional outcomes are not as bad as often thought.

P047

Primäres cerebrales B-Cell-Lymphom im Cavum Meckeli als seltene Ursache einer Trigeminusneuralgie – Fallbericht

Primary cerebral B-cell-lymphoma in Meckel's cave as a rare cause of trigeminal neuralgia – case report

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Objective

Primary central nervous system lymphomas (PCNSL) are a rare occurence in general population with incidince of 0,5 per 100.000. 2-4% of all primary tumors of the brain are PCNSLs. Manifestations are often supratenorial-periventricular. Clinical symptoms could be unspecific and depend on localisation of the lesion. We describe an extra-axial localisation in the right Meckel"s cave including consecutive trigeminal neuralgia, which was initially diagnosed as giant cell arteriitis (GCA).

Methods

Primarily, a 63 year old female suffered from neuropathic pain in the lower right facial quadrant. At time of consultation, symptoms persisted for 9 months. 3 months after onset, she was prescribed pregabalin and carbamazepine for an assumed trigeminal neuralgia without success. She developed hypesthesia in the lower-right quadrant of her face, diplopia and temporal pain while chewing. MRI showed an inflammation of the right temporal artery. Biopsy was negative for GCA. The symptoms improved under steroid therapy and pain and diplopia returned after its ending. Further MRI revealed a contrast enhanced lesion in right Meckel"s cave with compression of the right trigeminal nerve.

Results

Exploration, biopsy and mass reduction of the lesion was performed by right subtemporal approach under functional intraoperative neuromonitoring. Hypesthesia, pain and diplopia subsided completely because of steroid therapy. Tissue sample showed large B-cell lymphoma. Staging detected no other lesions extracranial. Finally, the patient recieved immunochemotherapy consisting of rituximab, methotrexate, cytarabine and thiotepa in our departement of oncology.

Conclusion

If there is suspected GCA without positive biopsy, which is about 10% of cases, further investigations including repeated cranial MRI with and without contrast should be performed to rule out a possible trigeminal neuralgia. In rare cases as we reported in our case, lesions in Meckel"s cave are the cause for the symptoms and even more rare are lymphomas in that region. Tissue sampling and exploration is required to plan further treatment regime. Debulking can be performed to reduce symptoms.

Fig. 1

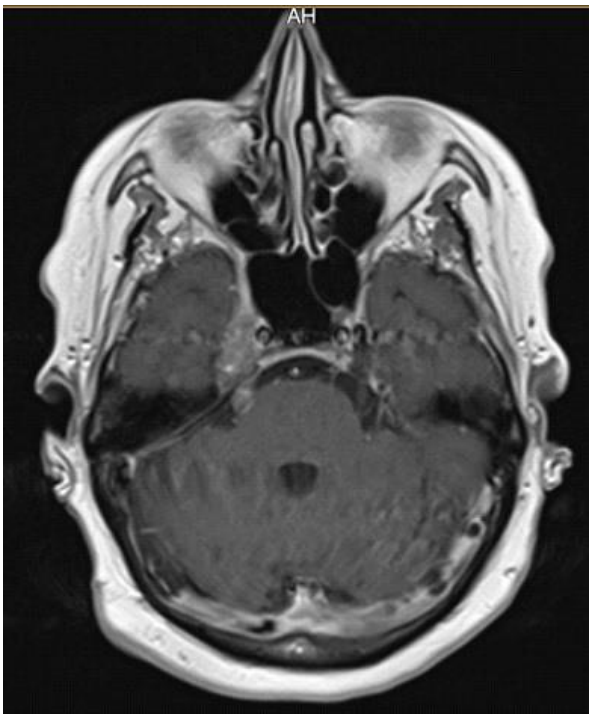
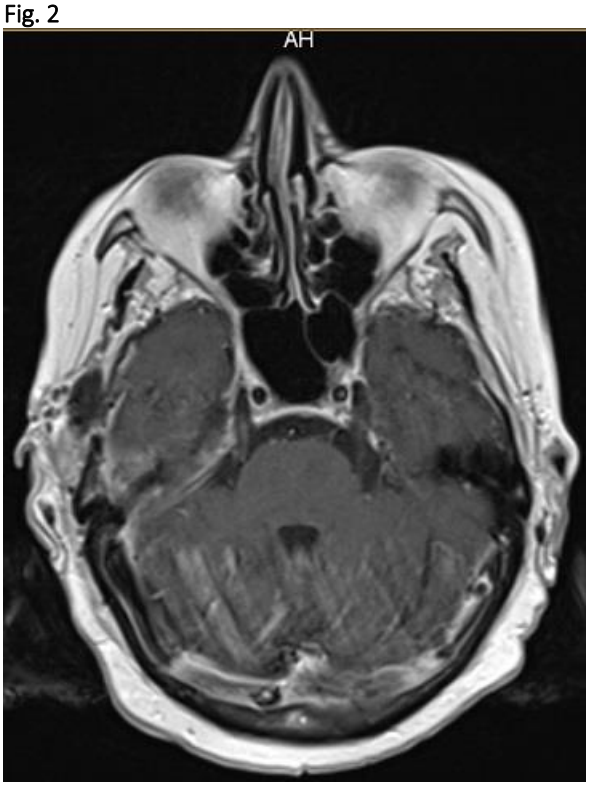


Fig. 2



P048

Protokoll zur Kartierung des supplementär motorischen Areals mittels repetitiver navigierter transkranieller Magnetstimulation (rnTMS)

Protocol for mapping of the supplementary motor area using repetitive navigated transcranial magnetic stimulation (rnTMS)

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Objective

The supplementary motor area (SMA) has been suggested to mediate movement planning, execution and coordination. Navigated transcranial magnetic stimulation (nTMS) offers the possibility to induce transient lesions of the SMA to study the specific role on this region in performance of motor tasks. Further, detailed mapping of functionally relevant areas within the SMA could potentially aid preoperative diagnostics in patients. The aim of this study was the development of a repetitive nTMS protocol for non-invasive functional mapping of the SMA.

Methods

The SMA was mapped in the dominant hemisphere of nine healthy subjects (28.3 ± 8.1 years, 5 females) using repetitive nTMS at 20 Hz (120% RMT), while subjects performed a finger tapping task. The location of induced errors was marked in each subject"s individual MRI. Additionally, a SMA hotspot was defined as the point consistently eliciting the largest disruptions of task performance upon stimulation. To exclude effects due to indirect stimulation of M1, effects of SMA stimulation were directly compared to effects of M1 stimulation in four different tasks (finger tapping, writing, line tracing, pointing at small circles with a pencil). M1 was targeted with the intensity of the residual electric field reaching the motor hotspot during SMA stimulation.

Results

Mapping of the SMA was possible in 7 of 9 subjects. Stimulation of the SMA led to a significant reduction of finger taps compared to baseline (BL: 45.8 taps, SMA: 35.2 taps; $p = 0.017$), as well as a non-significant reduction compared to M1 stimulation (M1: 40.0 taps; $p = 0.104$). Line tracing, writing and targeting of circles was less accurate during SMA stimulation. Further, effects of SMA disruption increased with stimulation time, while effects of M1 stimulation were present from the beginning on. Noteworthy, a significant variation of effect size was observed between subjects.

Conclusion

Mapping of the SMA using repetitive nTMS is feasible in the majority of subjects. While errors induced in the SMA are not entirely independent of M1 due to the proximity of both regions, disruption of the SMA seems to induce functionally distinct errors. Thus, error maps of the SMA assessed with nTMS can give valuable insights into the functional organization of this region, potentially aiding preoperative diagnostics in patients with SMA related brain lesions.

P049

Reduktion des Risikos für chirurgisch induzierte motorische Defizite durch intensive niedrig-frequente repetitive navigierte transkranielle Magnetstimulation (rnTMS) – eine Machbarkeitsstudie

Reducing the risk of surgically inflicted motor deficits by accelerated low-frequency repetitive navigated transcranial magnetic stimulation (rnTMS) – a feasibility study

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Objective

Low frequency repetitive transcranial magnetic stimulation (rTMS) can induce changes in the functional organization of underlying brain areas, thus being a promising tool to reduce the risk of surgically inflicted motor deficits preoperatively. However, current rTMS protocols are often time-consuming and hence difficult to implement in clinical settings where patients are only seen for limited times. The aim of the present study was to show the feasibility and safety of an accelerated low-frequency rTMS protocol applying multiple sessions daily, thus offering a new treatment approach for patients.

Methods

Nine healthy subjects (age: mean 25.4 years, range = 22-31 years; 1 female) were recruited for this feasibility study. All subjects received 14 sessions of rTMS (1 Hz, 30 minutes, 110% RMT) to the hand motor hotspot. Subjects were divided to receive stimulation for either 14 days once daily (classical low-frequency rTMS; c-rTMS), 7 days twice-daily (accelerated rTMS; a-rTMS) or sham stimulation for 14 days once-daily (s-rTMS). Daily stimulation sessions in the a-rTMS group were delivered with a 90-minute break in between. Directly after the stimulation, a motor training of 10 minutes targeted to the stimulated hand muscles was performed to support reorganization of motor function via recruitment of other brain areas.

Results

In total, 74% of rTMS sessions in the c-rTMS group, 89% in the a-rTMS group and 98% in the s-rTMS group were free of any side effects. Subjects reported occurrence of brief headaches in 14% of sessions in the c-rTMS group, 2% in the a-rTMS group and 0% in the s-rTMS group. Headaches were always reported to be at maximum mild and of short duration. Dizziness during stimulation was reported in 5% of sessions in the c-rTMS group, 2% in the a-rTMS group and 0% in the s-rTMS. Subjects reported a feeling of fatigue in the stimulated hand muscles in 2% of all sessions in the c-rTMS group, 7% in the a-rTMS group and 0% in the s-rTMS group. This feeling was noticeable specifically during the consecutive motor training and vanished quickly afterwards.

Conclusion

Accelerated low-frequency rTMS of the motor cortex is a safe and feasible method, previously shown to induce a functional reorganisation of the motor system. This offers a promising new treatment approach also for preoperative patients by shortening treatment duration and thus, potentially making rTMS protocols more accessible to a wider range of patients.

P050

Rückkehr in den Beruf nach Gliom-Behandlung unter Berücksichtigung der kognitiven Funktionsfähigkeit
Returning to work after glioma-therapy in regard to cognitive functioning

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Objective

Being employed is of considerable importance for patients with cancer in general. For brain tumour patients, often suffering from various cognitive impairments, returning to work is a challenging task, and has been shown to be associated with age, occupational group, and self-reported fatigue. The aim of the study was to investigate the quality of life, cognitive functioning and the employment situation in patients after surgery and adjuvant treatment of gliomas in eloquent areas.

Methods

Fifty-two patients with gliomas WHO grades I-III, who underwent surgery between 2013 and 2018, were interviewed retrospectively about their attitude to work, their pre- and postsurgical workload, and their physical and mental constitution. Patients" postsurgical employment situation and cognitive functioning were analyzed descriptively.

Results

After completion of therapy (i.e. surgery, radiation and/or chemotherapy), 37 patients (71.2%) had returned to work. Nine patients (24.3%) had reduced their workload from full-time to part-time jobs, and eight patients (21.6%) worked in another position within the same or a new company. Regarding the postsurgical cognitive functioning, 13 patients (35.1%) experiencing persistent attentional deficits, 14 patients (37.8%) reporting difficulties finding words, and 18 patients (48.6%) describing sustained memory impairments.

Conclusion

Given the presumable association between cognitive impairments and changes in patients" situation after completion of glioma-therapy, individualised socio-medical care is of utmost importance. A comprehensive support for these patients is required, in order to facilitate both, their return to work as well as their return into a fulfilled sociocultural life.

P051

Resektion rezidivierender pertoclivaler Meningeome – Berechtigen die Ergebnisse eine wiederholte Operation?
Surgery of recurrent petroclivaler meningiomas – Do the results justify repeated surgeries?

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Objective

Surgery of petroclival meningiomas (PCM) is challenging and is associated with high morbidity and mortality due to tumor localization. The question arises, whether repeated surgery of these difficult tumors is indicated with particular emphasis on postoperative neurological deficits and quality of life for the patients.

Methods

In a retrospective study, we evaluated the outcome of 25 patients with recurrent PCMs who underwent repeated surgery. We compared these results with 123 primarily PCMs, resected in our institution.

Results

24 of 25 patients were available for long-term follow-up. The median age was 60.4 years. The gender distribution m: f was 1:3. Twenty patients underwent one, four two and one patient three surgeries upon tumor recurrence. The cranial approaches were subtemporal/pterional (n=14), suboccipital retrosigmoid (n=10), and combined in one case. The median tumor size amounted to 16.6 ccm. In 22 patients the tumor removal was subtotal, whereas in 5 patients gross total resection was achievable. The histology revealed in 6 cases a malignant transformation of the primarily removed meningioma (4 WHO grade II and 2 WHO grade III). The overall neurological results showed in three patients (12.5%) deterioration of the neurological functions, while 18 patients demonstrated a KPS $\geq$ 70. When comparing these results with the 123 primarily operated patients, it was obvious that the completeness of resection (72/123, p= 0.0007) was significantly more favorable and higher-grade tumors were less common (13/106, p= 0.09) in the group with primarily PCM. However, the functional neurological deterioration with 22.3% was higher in the primary group than in the recurrent group.

Conclusion

Repeated surgery of petroclival meningiomas is indicated. The risk for neurological deficits is not higher than after primary surgeries. Since gross total resection might not be possible in most of the cases, adjuvant radiotherapy should be discussed after maximal tumor volume reduction.

Neuroonkologie II/*Neurooncology II*

P052

Synergistischer Effekt von 5-Aminolävulinsäure und Goldnanopartikeln bei der photodynamischen Therapie von immortalisierten humanen Vestibularisschwannom-Zellen

Synergistic effect of 5-amino-levulinic acid and gold nanoparticles in photodynamic therapy of immortalised human vestibular schwannoma cells

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Objective

Vestibular schwannoma (VS) is a common benign brain tumor. Current management includes wait and scan, surgery or stereotactic irradiation or a combination. Photo-dynamic therapy (PDT) was shown to be effective in a number of tumors. In order to explore novel adjuvant treatment strategies, we sought to investigate PDT in VS. Therefore, we tested PDT based on 5-ALA in the immortalized human VS cell line HEI-193. Furthermore, we analyzed if PDT effectiveness may be enhanced by gold nanoparticles (GNP) as observed previously.

Methods

For PDT treatment, cells were seeded in 96-well plates. Three drug constellations were tested: 5-ALA only, GNP only and a combination of both. After reaching adherence, cells were incubated for 6 h with different concentrations of gold nanoparticles (20 – 50 µg/ml, group I) or 5-ALA (20 – 50 µg/ml, group II), respectively. In group III, cells were first incubated for 6h with GNP and then 6h with 5-ALA at varying doses as in the other groups. Afterwards cells were irradiated by a diode laser for 625 seconds at λ=635 nm with 15.6 J/cm2. Cell viability was assessed by WST-1 assay. Negative controls were also performed.

Results

Both drugs and their combination induced a dose-dependent lethal PDT effect, respectively. The strongest effect was observed for gold nanoparticles plus 5-ALA as compared to 5-ALA or GNP only ($p < 0.01$).

Conclusion

Gold nanoparticles and 5-ALA showed a synergistic effect in PDT of immortalized human vestibular schwannoma cells as compared to the effect of each photosensitizer alone. Based on this preliminary *in vitro* study further testing on primary cell cultures is warranted.

Neuroonkologie III/*Neurooncology III*

P053

Ein Multi-Omics Ansatz zur Identifizierung von Markern für Glioblastom-Rezidive
A multi-omics approach to identify markers for glioblastoma recurrency

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Objective

Knowledge of individual time-to-recurrence (TTR) of GBM patients is critical to enable life-prolonging repeated surgery. MicroRNAs (miRNAs) are non-coding single-stranded RNA molecules of 21 to 25 nucleotides and related to numerous tumor cell functions in GBM. Extracellular vesicles (EVs) are small, stable, membrane-closed particles secreted by tumor cells. EVs encapsulate various tumor-specific molecules such as miRNAs and contribute to GBM progression. We envisage realization of a multi-omics approach integrating miRNAs, EVs and proteomics to enable a combined rational detection of markers associated with GBM recurrence.

Methods

Pre- and postoperative serum samples from newly diagnosed GBM patients and patients with GBM recurrencies were subjected in parallel to proteomic and radiomic analysis in conjunction with RNASeq analysis. EVs were separated from serum samples via differential high-speed centrifugation. Isolation of miRNA was performed using the total exosome RNA and protein isolation kit and miRNA from cells and tissues were isolated using the miRNeasy tissue/cells advanced mini kit. Micro RNAs were detected using qPCR. Osteopontin protein levels were determined by ELISA.

Results

238 different miRNAs were identified in a first setup of 10 patients (GBM WHO°IV, IDH WT) by RNASeq analysis. Interestingly, some particular miRNAs were identified as significantly expressed in overlapping groups comparing serum, EDTA and serum-EV samples (p-value >0.05, FC-2.0). Initially, we identified four candidate miRNAs (miR-19a-3p, miR-29b-3p, miR-130a-3p and miR-181a-5p) with functional relevance in GBM. In particular, miR-181a-5p is correlated to several genes and is linked to improved survival and decreased recurrence in GBM. Its expression levels positively correlate with those of *MMP9* (n=21, p=0.01, r^2= 0.3) and *MMP14* (n=19, p=0.04, r^2= 0.22) in GBM tissue samples. Osteopontin (OPN) protein, a potent inducer of tumor angiogenesis was also correlated with different miRNA expression levels and high levels of OPN in preoperative EDTA samples (ELISA) are linked with poor prognosis (Kaplan-Meier-Curve, n=12).

Conclusion

This study demonstrates, although with a limited number of GBM patients analysed so far, that a combination of serum markers could potentially be used to monitor GBM progress and identify recurrence at an early stage in disease progression. In particular, the combination of miRNA and proteins isolated from serum EVs have a high potential to be considered as specific.

Neuroonkologie III/*Neurooncology III*

P054

Analyse des Einflusses der Kortextemperatur auf die Patientenkognition während Wachoperationen
Analysis of influence of cortex temperature on patient cognition during awake-surgery – a pilot study

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Objective

During skull trepanning, it is possible to observe an intraoperative heat loss at the brain surface due to convection as well as thermal radiation. This effect is intensified involuntarily, when rinsing fluid adapts to room temperature during surgery, or intentionally, when cerebral seizures are stopped by active ice-water rinsing. However, the patient"s active cognitive cooperation is essential, especially during awake phase. The aim of this pilot study is to investigate the influence of cortex temperature on cognition during awake-surgery.

Methods

During an awake-surgery, the complete course of the cortex"s temperature was analysed continuously by an imaging camera. This was performed with 21 patients at a total of 116 measuring points. The body"s core and the cortical temperature changes were determined over time – split into phases where no water, warm flush (36°C) or ice water was used. As a surrogate for the cognitive performance of patients, a reaction time test was performed intraoperatively on the patient.

Results

During the first measurement the cortex"s temperature was 37.2°C (36.0-37.5°C). The cortex"s surface temperature approached room temperature (median: 25.8°C) without proper regular irrigation (mean - 1.2°C in the first 10 min, mean - 2.3°C in the first 15 min).

Average reaction time was 769 milliseconds. At the same time, average reaction time at a cortex temperature < 35°C was 1378 milliseconds, at a cortex temperature 35°C 587 milliseconds ($p < 0.05$). At a cortex temperature < 35°C, reaction time improved again after rinsing with warm liquid.

Conclusion

Our pilot study suggests a continuous drop in the cerebral cortex"s temperature during (awake) phase of surgery. Furthermore, the average reaction time correlated with the temperature of the cortex significantly. The brain"s temperature may have significant impact on the cognitive performance of patients during the awake phase. This possible connection should be investigated in further studies.

Neuroonkologie III/*Neurooncology III*

P055

AT101 als spezifische Therapie gegen stammzell-ähnliche Gliomzellen – Wirkmechanismus innerhalb der Mikroumgebung des Tumors

AT101 – a specific therapy against glioma stem-like cells – mechanism of action in the microenvironment of the tumour

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Objective

Glioblastoma multiforme (GBM) is the most malignant brain tumor in adults. Despite the standard therapy including surgical resection and adjuvant combined radio/chemotherapy, the average survival of GBM patients is still poor and reaches approximately 12-15 months. Thus, there is an urgent need to develop alternative treatment strategies in order to overcome the resistance against the preferred chemotherapeutic drug temozolomide (TMZ). A promising candidate for the treatment of GBMs is AT101, the R(-) enantiomer of gossypol. The present study evaluates the effects of the alternative compound AT101 on two GBM cell lines (U87MG and U251MG) with a focus on the effects on tumor stem-like cells, which are often found to mediate the development of tumor recurrences.

Methods

The analysis comprised cytotoxicity assays and growth analysis, as well as the investigation of changes in signaling pathways and on the gene expression level. Furthermore, the role of the tumor microenvironment was analyzed by stimulating native cells with stem-like cell conditioned medium. The therapeutic response towards AT101 was thereby compared between treatment with TMZ or the combination of both.

Results

AT101 was found to induce strong cytotoxic effects in U251MG and U87MG stem-like cells in comparison to the respective native cells, whereas treatment with TMZ had only moderate effects on both native and stem-like cells. In addition, a higher sensitivity against treatment with AT101 was observed upon incubation of native cells with stem-like cell conditioned medium, indicating the role of the tumor microenvironment, especially the stem cell niche, on the therapeutic response of GBMs. The different responses of native cells and stem-like cells to treatment with TMZ, AT101, or a combination of both were also found to be reflected by a different activation of the Erk signaling pathway. Analysis of the expression level of various cytokine and chemokine receptors revealed that especially CXCR7 was found to be consistently downregulated in both cell lines upon stimulation of native cells.

Conclusion

The obtained results indicate that AT101 represents an alternative drug for future GBM therapy. Since the tumor stem-like cells responded strongly to treatment with AT101, this might represent a promising approach in order to kill the remaining tumor cells after resection more efficiently than the therapy with TMZ and thus, prevent the development of tumor recurrences.

Neuroonkologie III/*Neurooncology III*

P056

Durchbrechen der Blut-Hirn-Schranke (BHS) über TTFields
Breaching the blood-brain Barrier (BBB) via Tumour Treating Fields (TTFields)

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Objective

BBB tightness accounts for the vast challenge in drug delivery to the brain. Although numerous potent compounds can treat central nervous system (CNS) disorders such as glioblastoma (GBM), failure to cross the BBB render them futile. Thus, novel methods for BBB disruption to enable passage of therapeutics into the CNS are necessary. To date, few such methods approved for clinical use exist. In the light of GBM, the use of TTFields as a treatment modality in combination with chemotherapeutics has increased overall patient survival. Recently, we showed their ability to reversibly open the BBB both *in vitro* and *in vivo*. As a follow-up, we herein aimed to further discern the action of TTFields relative to BBB function and disruption.

Methods

TTFields of various intensities at 100 kHz were administered to murine brain endothelial cells (cerebEND) for 24-72h prior to tight junction protein claudin-5 staining. Likewise, mathematical simulations of TTFields delivery and distribution to the rat brain were performed. Median field intensities for the various brain segments were calculated as defined for dynamic contrast-enhanced (DCE) MRI. In addition, tumour-induced rats were treated with TTFields or sham heat, in combination with paclitaxel (PTX). Tumour volume was assessed using MRI. Tumour cell proliferation ratio was quantified using the marker Ki67.

Results

TTFields intensity of 1.62 V/cm RMS disrupted the cerebEND boundaries as shown by claudin-5 delocalisation. No notable physical alteration was displayed at 0.97 and 0.76 V/cm RMS. Furthermore, a significant increase in gadolinium accumulation in the middle and posterior rat brains was observed 72 h post-TTFields. In contrast, no significant accumulation was detected in the anterior brain, which is in accordance with the lower intensities applied to this section based on simulations. Eventually, administration of PTX together with TTFields significantly decreased tumour volume compared to sham or TTFields alone or sham combined with PTX in tumour-induced rats. Moreover, tumour cell proliferation ratio was significantly reduced in TTFields and PTX-treated rats compared to TTFields alone.

Conclusion

Our data point towards the ability of TTFields to open the BBB, suggesting a possible clinical translation. The potential of using TTFields for this purpose would ultimately offer a solution to the current CNS drug delivery problem.

Neuroonkologie III/*Neurooncology III*

P057

Carbonsäureanhydrase XII blockiert Antikörper 6A10 kann ZEB1 und die Motilität von Glioblastom-Stammzellen reduzieren

Carbonic Anhydrase XII blocking Antibody 6A10 can reduce ZEB1 and motility of glioblastoma stem cells

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Objective

Glioblastoma (GBM) is the most aggressive form of brain cancers. Yet, there is still no targeted therapy clinically approved to prolong survival time of the patients.

Carbonic anhydrase XII (CA XII) is highly expressed on glioma cells while being absent from normal brain. Given the strong association between CA XII and brain cancer, better understanding of CA XII inhibitory monoclonal antibody, termed 6A10, might help in developing future therapy.

Methods

We studied the effect of 6A10 on a pathophysiological stem cell disease model platform *in vitro*. Cells were treated up to 4 days with 25µg/ml of testing antibody 6A10 that specifically targets CA XII epitope. Further functional assays were conducted, such as quantification of cell proliferation using Ki67 assay, apoptosis by Annexin V and caspase 3/7 assay as well as PI-based cell cycle analysis as well as appreciation of tumorigenicity using Soft agar assay as well as cell invasion using transwell assay. Effects on the regulation on a series of biomarkers indicating stemness was conducted via RT-qPCR and Western blot. Clinical significance of findings are validated by interrogating patient bioinformatics data from public sources.

Results

Elevated CA XII mRNA levels are negative prognostic value for predicting overall survival of brain cancer patients. No association to CD133, MGMT promoter methylation status is detected. In addition, experimental data reveal the growth-limiting effect of the 6A10 antibody to some extent on GBM *in vitro*. Additionally, it significantly reduces ZEB1, a critical stemness regulator, and significantly impaired the invasive feature of GBM1 cell line. Of note, a trend of CA XII upregulation was observed in all treated cell lines, which might indicate a negative feedback regulation in response to 6A10 treatment.

Conclusion

6A10 antibody might be a promising drug candidate in glioblastoma. However, *in vivo* experiments are needed for further confirmation. Moreover, the characterization of the biological meaning of observed upregulation of target upon treatment is warranted to appreciate risk of emergence of therapy resistance in stem cells of GBM.

Neuroonkologie III/*Neurooncology III*

P058

Charakterisierung der Carbonic Anhydrase 2 (CA-2) als ein Faktor der Resistenzvermittlung in GBM Stammzellen
Characterisation of carbonic anhydrase 2 (CA-2) as a factor conferring temozolomide resistance in GBM stem cells

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Objective

About 95 % of GBM patients show tumor relapse leaving them with limited therapeutic options as recurrent tumors are often resistant to temozolomide (TMZ). GBM-like stem cells (GSCs) are considered as the major obstacle in therapy resistance, so that characterization of their response to TMZ is informative to identify genes associated with TMZ resistance. We have identified Carbonic Anhydrase 2 (CA-2) as a major factor responsible for TMZ resistance of GBM stem cells.

Methods

Four independent patient derived GSC lines and the GBM cell lines U251 and U87 were analysed for expression levels of CA2 by qPCR. CA-2 expression in GBM sections was detected by IHC-staining with established markers (GFAP, Nestin). Stable CA2- expressing U251 and U87 cells were transfected with a CA-2 construct and analyzed for proliferation, cell migration, invasion, and cell viability assays using co treatment of TMZ with CA-2 inhibitors. To assess the energy metabolism of these cells, "Seahorse" experiments were performed to measure metabolic parameters in these cells, such as oxygen consumption and glycolysis.

Results

CA-2 expression is detected in GBM tissue and is accumulated in GSCs of recurrent GBM. Moreover, CA-2 is highly expressed in GSCs, but merely present in U87 and U251 cells. Using acetazolamide as pan-CA inhibitor, we showed that co-treatment of TMZ with100-400 µM Acetazolamide (ACZ) significantly sensitizes GSCs to TMZ ($p<0.01$). Similar effects were observed using a novel specific CA-2 inhibitor brinzolamide (100 µM) in GSCs. Stable CA-2 overexpressing U251 and U87 cells exerted a significantly (at least 2.3-fold, $p<0.001$) higher resistance to TMZ. In addition, CA-2 overexpressing cells show enhanced proliferation, enhanced cell viability and are metabolically more active as revealed by higher oxygen consumption rate and extracellular acidification rate.

Conclusion

We described Carbonic Anhydrase 2 as a potential resistance factor against temozolomide treatment in GSCs and demonstrate here that CA-2 has a high metabolic impact on tumor cells when expressed in amounts that are comparable to that of GSCs. Our results form the basis for a rational combination therapy to enhance the therapeutic efficacy of TMZ.

Neuroonkologie III/*Neurooncology III*

P059

Charakterisierung des heterogenen Antigenexpressionsmusters von Glioblastom-Zelllinien, Primärzellen von Patienten und Tumorgewebe

Characterisation of heterogeneous antigen-expression pattern comparing glioblastoma cell lines, patient-derived cells and patients' glioblastoma tissue

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Objective

Immunotherapeutic treatment of glioblastoma (GBM) is one of the most challenging tasks due to heterogeneous surface expression of target antigens. It has previously been reported that GBM cell lines (GCL), patient-derived cells (PDC) and patients" tumour tissue (PT) differ strongly in their level of antigen expression. Here, we analysed the surface expression of the 8 most frequently therapeutically addressed antigens in vitro by flow cytometry. Subsequently, the expression patterns displayed by GCL, PDC and PT were compared.

Methods

7 GCL (GaMG, U87, U373, U343, U251, U138, DKMG), 7 PDC, as well as PT of 9 patients were stained for GD2, CSPG4, CD133, CD70, HER2, Il13Rα2, EGFRvIII and EphA2, measured by flow cytometry (BD FACSCanto II) and analysed using FlowJo software (TreeStar). Antigen expression was scored (0-1.0: low, 1.1-2.0: medium and 2.1-3.0: high expression) and the mean expression and range were calculated.

Results

GD2 was mildly expressed in GCL ($\bar{x}$=1.3), but showed higher levels in PDC ($\bar{x}$=2.6) and PT ($\bar{x}$=2.4). In contrast, CSPG4 displayed low expression in GCL ($\bar{x}$=0.3) and PT ($\bar{x}$=0.4), but medium expression in PDC ($\bar{x}$=1.9). Interestingly, CD133, a stem cell marker, showed low expression in GCL ($\bar{x}$=0.8) and PDC ($\bar{x}$=0.4), whereas the expression in PT was medium ($\bar{x}$=1.4). CD70 and Il13Rα2 were both weakly expressed in GCL, PDC and PT ($\bar{x}$=0.2, 0.4, 0.0 and 0.5, 0.6, 0.4, respectively). HER2 displayed medium expression in GCL ($\bar{x}$=1.4) and PDC ($\bar{x}$=1.4) and only low expression in PT ($\bar{x}$=0.6). For EGFRvIII, medium expression was detectable in all three entities ($\bar{x}$=1.4, 1.1 and 1.1). EphA2 was mildly expressed in GCL ($\bar{x}$=0.1), medium expressed in PT ($\bar{x}$=2.0) and highly expressed in PDC ($\bar{x}$=2.6). Overall, high variability of antigen surface expression was visible even within the groups (Table 1).

Conclusion

Surface expression cannot be assumed to be similar in GCL, PDC and PT and even within these groups there was high variability. GCL and even PDC do not represent PT features. Rupture of cell-cell-contacts during lysis, duration of cultivation, lack of tumor microenvironment and hypoxic gradients might be reasons for changes in antigen surface patterns. New ex vivo models like organoids or tumour slices might overcome these hurdles.

Fig. 1

	GCL	PDC	PT
GD2	1.3 (0.25-2.25)	2.6 (2.0-3.0)	2.4 (1.0-3.0)
CSPG4	0.3 (0.0-1.25)	1.9 (1.0-3.0)	0.4 (0.0-1.0)
CD133	0.8 (0.0-1.5)	0.4 (0.0-1.0)	1.4 (1.0-2.0)
CD70	0.2 (0.0-1.0)	0.4 (0.0-1.0)	0.0 (0.0-0.0)
Her2	1.4 (0.25-1.25)	1.4 (0.0-2.0)	0.6 (0.0-2.0)
IL13α2	0.5 (0.0-0.75)	0.6 (0.0-2.0)	0.4 (0.0-2.0)
EGFRvIII	1.4 (0.5-2.25)	1.1 (0.0-2.0)	1.1 (0.0-3.0)
EphA2	0.1 (0.00-0.5)	2.6 (2.0-3.0)	2.0 (1.0-3.0)

Neuroonkologie III/*Neurooncology III*

P060

ZNS Invasion in Meningeomen - die intraoperative und histopathologische Detektion und ihre prognostische Wertigkeit

CNS invasion in meningioma – detection by the surgeon and pathologist and its prognostic value

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Objective

CNS invasion in meningiomas has been included in the current WHO classification as a sign of atypia. However, its prognostic value has been challenged and discussed. The histopathological detection is highly dependent from the surgical sampling, which is not always feasible from all areas of interest. Therefore the intraoperative assessment of invasive growth may be of additive prognostic value.

Methods

A comparative analysis of the prognostic impact of the intraoperative and histopathological detection of CNS invasion was done. Clinical data of 1517 cases with follow up data regarding radiographic recurrence was reviewed.

Results

Invasive growth was seen during resection in 23.7%(n=345) while histopathology detected it in 4.8%(n=73). The histopathological and intraoperative assessments were compatible in 63%. The prognostic impact of histopathological and intraoperative assessment was significant in the univariate but not in the multivariate analysis. Both methods of assessment combined reached statistical significance in the multivariate analysis (p=0.0409). A score including all independent prognostic factors divided the cohort into three prognostic subgroups with a risk of recurrence of 33.8%, 64.7% and 88.5% respectively.

Conclusion

The intraoperative detection of infiltrative growth of primary meningiomas into central nervous system tissue can complement the histopathological assessment of CNS invasion. The combined assessment is an independent prognostic factor regarding tumor recurrence and allows a risk-adapted tumor stratification.

Neuroonkologie III/*Neurooncology III*

P061

Personalisierter Therapieansatz in der Translationalen Neuroonkologie – JAK/STAT-Hemmung kehrt die durch myeloide Zellen-induzierte Antitumor-Immunität in T-Zellen um

Personalised treatment option in translational neuro-oncology – JAK/STAT-inhibition reverses myeloid cell-induced anti-tumour-immunity in T cells

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Objective

Recently, we demonstrated that JAK/STAT-inhibition leads to the conversion of the immune environment of glioblastoma from "cold" to "hot". Here, we explored transcriptional programs of tumor-associated T cells and potential targets to reverse the major group of dysfunctional T cells using a human neocortical slice model in addition to computational models.

Methods

We acquired single-cell sequencing of 50k $CD45^+$ cells (8 patients) and inferred transcriptional programs and fate decisions using RNA-velocity. A novel algorithm ("Nearest functionally connected neighbor", NFCN) was used to predict neighboring cells, validated by spatial transcriptomics and immunohistochemistry. A human neocortical glioblastoma slice model with autografted T cells was used to test a JAK/STAT inhibitor, further used in neoadjuvant treatment of a single patient.

Results

We observed that most T cells in the GBM microenvironment showed either increased expression of exhaustion markers or hypoxia related non-functional signatures. Pseudo-time analysis revealed increased Interleukin 10 (IL10) response during the transformation of T cells from the effector to the exhausted state. Using our novel NFCN-algorithm, we identified a subset of myeloid cells marked by increased HMOX1 expression (in STAT/HMOX axis) to be responsible for release of IL10. We validated our computational findings by using human neocortical glioblastoma slice model with autografted T cells, confirming that IL10R-inhibition or myeloid cell depletion rescued T cells from exhaustion. In order to target the STAT/HMOX axis, we used a JAK/STAT inhibitor in our GBM model, which showed a significant reduction of IL10 release and consecutive activation of T cells. In a clinical setting, a single patient treated with a JAK/STAT-inhibitor showed clear activation of T cells, validated by means of scRNA sequencing and immunostainings.

Conclusion

Our findings suggest that targeting the myeloid cell environment of GBM provides an opportunity to convert a "cold" into "hot" immune environment which might be helpful to improve all T cell-based therapies in the future.

Neuroonkologie III/*Neurooncology III*

P062

Quantifizierung der PpIX-Fluoreszenz zerebraler Brustkrebs-Metastasen
Quantification of PpIX-fluorescence of cerebral breast cancer metastases

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Objective

Introduction of the 5-ALA technique is one major advance in neuro-oncological surgery. Protoporphyrin IX (PpIX)-fluorescence was observed in about half of cerebral metastases. For now, no study found a correlation between the dichotomized PpIX-fluorescence of breast cancer metastases and neither the receptor status nor the histological subtype of breast cancer metastases. Aim of the present pilot study was to quantify PpIX-induced fluorescence of breast cancer metastases and correlate this with the hormone receptor status.

Methods

5-ALA induced fluorescence intensity was quantified in 26 patients suffering from cerebral breast cancer metastases. A systematic spectrometric evaluation of tumor specimen and the resultant PpIX-induced fluorescence was performed using a spectrometer connected by optic fiber to a handheld probe. The difference between maximum PpIX-fluorescence at 635 nm and baseline fluorescence was considered as PpIX fluorescence intensity of the metastasis. In addition, results were correlated with receptor status (PD-L1, estrogen receptor, progesteron receptor, HER-2/neu) and histopathological examinations.

Results

All 26 patients had breast cancer with cerebral metastases. The mean age was 49 year (32 – 81 years). All patients were female. All 26 cerebral breast cancer metastases were considered as ALA fluorescent by the surgeon. A PpIX fluorescence over $1.1x10^6$ AU was observed as "ALA-positive" by the surgeon. The mean PpIX fluorescence of analyzed cerebral breast cancer metastases was $3.4x10^6$ AU ($2.1x10^6$ – $6.5x10^6$ AU). After quantification we observed no significant difference in the levels of 5- ALA fluorescence in cerebral breast cancer metastases with different hormone receptor status.

Conclusion

Firstly, PpIX fluorescence over $1.1x10^6$ AU was observed as "ALA-positive" by the surgeon. Secondly, all cerebral breast cancer metastases were tested as "ALA-positive" by the spectrometer. Thirdly, quantification of 5-ALA fluorescence showed no significant difference between cerebral breast cancer metastases with different hormone receptor status in our cohort.

Neuroonkologie III/*Neurooncology III*

P063

Rapalink-1 zielt auf Glioblastom-Stammzellen ab und wirkt synergistisch mit Tumortherapiefelder, um die Resistenz gegen Temozolomid zu verringern
Rapalink-1 Targets Glioblastoma Stem Cells and Acts Synergistically with Tumor Treating Fields to Reduce

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Objective

Glioblastoma (GBM) is a lethal disease with limited clinical treatment options available. Recently, a new inhibitor targeting the prominent cancer signaling pathway mTOR was discovered (Rapalink-1), but its therapeutic potential on stem cell populations of GBM is unknown.

Methods

We applied a collection of physiological relevant organoid-like stem cell models of GBM and studied the e ect of RL1 exposure on various cellular features as well as on the expression of mTOR signaling targets and stem cell molecules. We also undertook combination treatments with this agent and clinical GBM treatments tumor treating fields (TTFields) and the standard-of-care drug temozolomide, TMZ. Low nanomolar (nM) RL1 treatment significantly reduced cell growth, proliferation, migration, and clonogenic potential of our stem cell models. It acted synergistically to reduce cell growth when applied in combination with TMZ and TTFields. We performed an in silico analysis from the molecular data of diverse patient samples to probe for a relationship between the expression of mTOR genes, and mesenchymal markers in di erent GBM cohorts. We supported the in silico results with correlative protein data retrieved from tumor specimens.

Results

RL1 treatment significantly reduced cell growth, proliferation, migration and clonogenic potential of our stem cell models in the low nM range. It acted synergistically to reduce cell growth when applied in combination with TMZ and TTFields.

Conclusion

Our study further validates mTOR signaling as a druggable target in GBM and supports RL1, representing a promising therapeutic target in brain oncology.

P064

Neuordnung der GBM-Landschaft zur gezielten Bekämpfung chemoresistenter Tumore
Reshaping the GBM landscape to enable targeting of chemo-resistant tumours

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Objective

Novel insights into the developmental trajectory exhibited by glioblastoma (GBM) has shown that it has the capability to respond to its microenvironment by clonal selection of specific phenotypes. Similarly, malignant GBM develop intrinsic mechanisms to resist chemotherapeutic treatments during the course of the disease. Paracrine and autocrine glutamate signaling via ionotropic and metabotropic receptors have been reported to sustain malignant hallmarks. However, the extent to which glutamatergic signaling modulates the GBM landscape and facilitates chemoresistance remains unknown. In this study we aimed to prove the manifold concept of glutamate signaling in GBM as the basis to further discover the modulatory role and interactions of specific receptors within the GBM microenvironment.

Methods

Human neo cortical slices were inoculated with primary Glioblastoma cell lines and Glutamate release using an enzyme based colorimetric assay. Transcriptomic analysis highlighted the importance of mGlur3 receptor in GBM network maintenance and axonogenesis, which was validated by the usage of LY341495, a specific inhibitor of mGlur3. Glioblastoma innoculated sections were treated with TMZ and with TMZ+LY341495 for the period of 10 days. The sections were imaged on a daily basis to analyze the effect of the treatments on tumor growth and proliferation

Results

We present evidence that the inhibition of mGluR3 through a minimally toxic synthetic antagonist, LY341495, is sufficient to drive the transcriptional profile of chemoresistant GBM to a mesenchymal state that allowed cytotoxic targeting by temozolomide. Ultimately, GBM growth and proliferation were dramatically reduced ($p<0.001$, $n=3$) when GRM3 inhibition was combined with temozolomide application. These results were validated in both cell culture and in a human neocortical section based GBM model.

Conclusion

Through the integration of diversified molecular-biological analyses and novel sequencing data analysis we present a new concept, where we not only illustrate mechanisms of resistance, but rather a new picture of how glutamate signaling via mGluR3 interacts with the phenotypical GBM landscape formation in the light of recently published GBM cell-state discoveries.

Neuroonkologie III/*Neurooncology III*

P065

Erhebung der Notwendigkeit einer interdisziplinären virtuellen Tumorkonferenz für neuroonkologische Patienten – vorläufige Ergebnisse einer Zuweiserumfrage

Evaluating the need for a regional virtual neurooncological tumour board – a survey study

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Objective

The ongoing improvements in oncology and the demographic development in western countries have led to an over proportional increase in cancer patients. Cancer care is best facilitated through tumor board (TB) conferences, as these are associated with overall improvement of outcome. Because of limited resources and limited access to TB conferences, multidisciplinary care is not available at every institution. This has further deteriorated due to the COVID-19 pandemic. Aim of this survey was to evaluate the acceptance for a regional virtual TB for neurooncological patients.

Methods

A survey comprising of 7 questions was send to 9 secondary care hospitals and 33 outpatient practise centers specialized in oncology within the catchment area of 2 million inhabitants of the University Hospital Augsburg, Bavaria.

Results

The questionnaire response rate was 43% (18/42). Most of the participating institutions (89%) care for <50 patients/year with primary or secondary central nervous system tumors of the neurocranium or spine. There was a high satisfaction rate of neurooncological treatment of 89%. All of the participating centers consider an interdisciplinary tumor board recommendation as "important" or "very important" for further patient treatment. For more than half of the participants (56%), it was difficult to access a TB conference. The willingness to participate in a virtual TB conference was high (89%) without financial compensation (61%).

Conclusion

The need for a virtual interdisciplinary neurooncological tumor conference within secondary care hospitals and oncological outpatient centers is high.

P066

Kognitives Defizit bei Hirntumorpatienten – Füllen der diagnostischen Lücke? Montreal Cognitive Assessment (MoCA) Test als kurzes Screening Instrument für kognitive Defizite

Cognitive deficits in patients with brain tumours – Bridging the diagnostic gap? Montreal Cognitive Assessment (MoCA) test as a brief screening tool for cognitive deficits

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Objective

Neurocognitive deficits are common symptoms in patients with primary brain tumors. They may affect patients" daily routine similar to neurological deficits, however these symptoms might be missed or underestimated in routine clinical assessment. The aim of our study was to screen patients' for latent neurocognitive deficits by Montreal Cognitive Assessment (MoCA) test additional to clinical routine assessment.

Methods

Adult patients harboring supratentorial glioma were preoperatively (0-2 days) and postoperatively (3-7 days) assessed by using MoCA test. The data was collected in the time between 2016 and 2020. MoCA results <26 indicate neurocognitive deficits. Retrospectively, clinical and sociodemographic data was collected such as gender, age, neurological symptoms and Karnofsky performance score (KPS), any subjective and objective description of potential neurocognitive symptoms in patients records were screened. We compared rate of significant neurocognitive deficits using Pearson chi-square test. Pearson correlation was used to compare MoCA test result and KPS at the day of admission, to compare pre- and postoperative results signed rank test was used.

Results

We assessed results of 55 MoCA tests in 35 patients. The median age of the patients was 55. 23 patients had high-grade glioma and 12 patients had low-grade glioma. In only 13 patients objective cognitive deficits were documented, while 29 patients had a significant deficit according to MoCA test result (p=0.01). Comparing subjective deficits, 31 patients claimed to have no subjective deficit while actually 10 had a test result <26 (p=0.01). Using signed rank test, there was no significant difference between the MoCA test result pre- and postoperative. Patients older than 55 years showed postoperative significantly more cognitive deficits (MoCA<26 points) than patients younger than 55 years (p<0.05). Pearson correlation showed a positive relation between the preoperative MoCA test result and the KPS.

Conclusion

The preliminary data indicates that subtle neurocognitive deficits may be missed in clinical routine without routine neurocognitive screening procedures. The MoCA test could be a helpful tool in the clinical neurosurgical routine.

Neuroonkologie IV/*Neurooncology IV*

P067

Übereinstimmung unterschiedlicher Berechnungsstrategien bei der *in vitro* Bestimmung der Chemotherapieresistenz von Hirntumoren

Different calculation strategies are congruent in determining chemotherapy resistance of brain tumours in vitro

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Objective

In pharmacology, a drug candidate's therapeutic potential is typically expressed as its ability to suppress cell growth. Different methods in assessing the cell phenotype and calculating the drug effect have been established. However, terminology is not standardised and inconsistencies in drug response outcome have been reported. It is still unclear whether and to what extent the choice of data post-processing methods is responsible for that.

Methods

We exposed a collection of nine *in vitro* models of glioblastoma to a library of 231 clinical drugs. Cell viability was modelled by a four-parameter Hill equation. The therapeutic potential of the drugs was determined using three established criteria: 1) the drug concentration needed for 50% growth inhibition (GI50), 2) the drug concentration for which the drug starts to show an effect, also known as point-of-departure (PoD), and 3) area under the curve (AUC). The curves were fitted to experimental data using least-squares on non-linearly transformed data, which allowed for reliable computation of confidence intervals (CIs). PoD was defined as the drug concentration at which the CI of the effect ceases to overlap with the CI when no drug was present.

Results

An effect was detected on 36% of drugs when relying on GI50 and on 27% when using PoD. For the area under the curve (AUC) a threshold of 9.5 or 10, depending on whether GI50 or PoD was used as the "ground truth", could be set to discriminate between the drugs with and without an effect. GI50, PoD, and AUC were highly correlated ($R^2 > 0.94$, $p < 10^{-30}$ for all three). The exact ranking of substances by different criteria varied somewhat, but the group of the top 20 substances according to one criterion always included 17-19 top candidates according to another.

Conclusion

The three methods were largely in accord, at least for the top 20 ranked substances. The differences arise when a substance shows an effect at low concentrations, but plateaus afterwards, so that GI50 is never reached, or when the variance in the effect is so large at the beginning, so that PoD is never reached, despite achieving GI50. Regarding reported inconsistencies we hypothesise that unclear/inconsistent terminology plays a role. PoD can be defined in different ways and IC50, which describes the point half-way between the curve"s upper and lower plateaus, is occasionally used instead of GI50. It remains to be seen whether the observed effects can translate into clinical practice.

Fig. 1

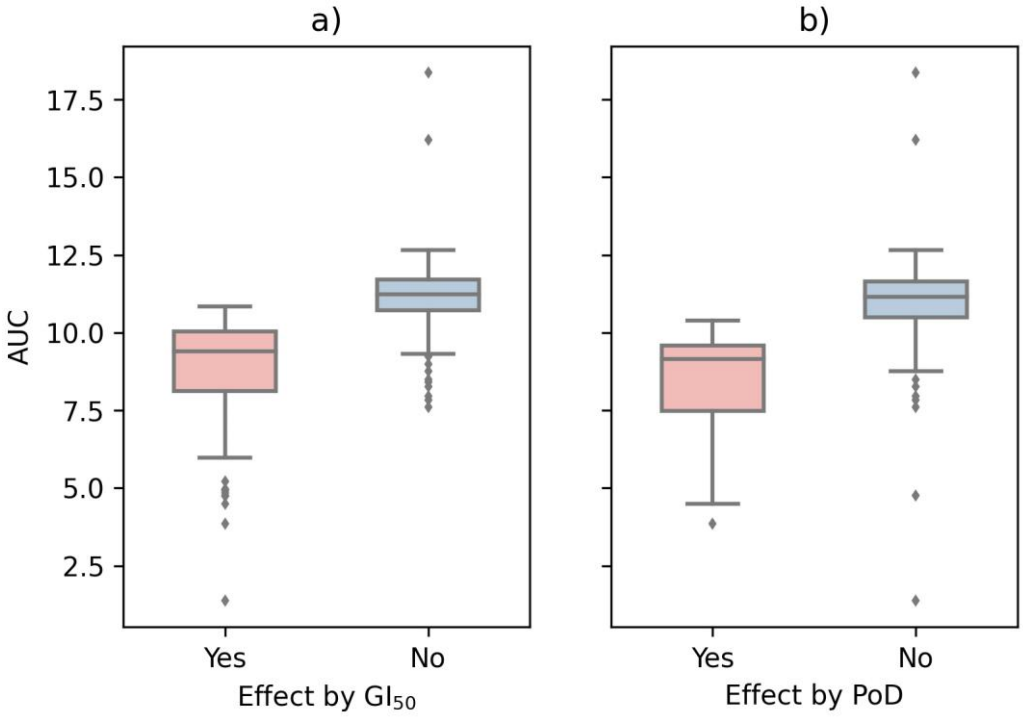
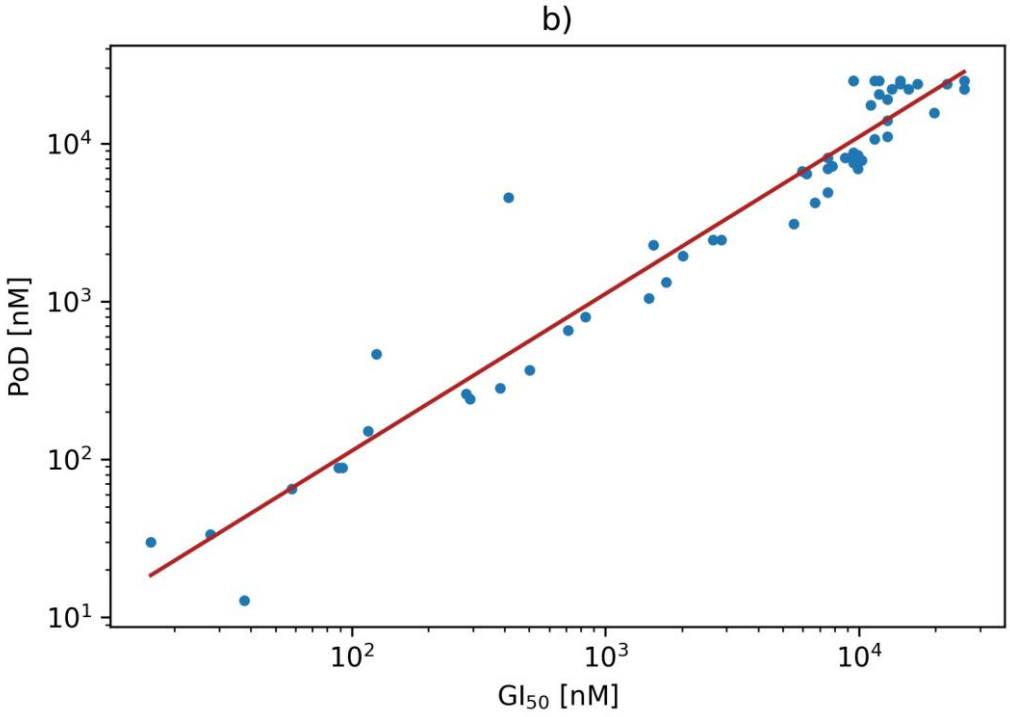

a)
b)
AUC
17.5
15.0
12.5
10.0
7.5
5.0
2.5
Yes
No
Effect by GI50
Yes
No
Effect by PoD

Fig. 2


b)
PoD [nM]
10^4
10^3
10^2
10^1
10^2
10^3
10^4
GI50 [nM]

P068

Ein diffuses Wachstumsmuster in der MRT-Bildgebung ist mit einer schlechten Prognose bei IDH-Wildtyp Gliomen WHO Grad 2 und 3, jedoch nicht bei IDH-mutierten Gliomen, assoziiert

Diffuse MRI-based tumour growth pattern is associated with worse outcome only in IDH wildtype but not in IDH mutant gliomas WHO II and III

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Objective

Magnetic resonance imaging (MRI) based characterization has previously shown heterogeneity in tumor appearance according to IDH mutation status. We have recently investigated the relevance of contrast enhancement to be dependent on IDH mutation status in glioma WHO II and III. Here, we aimed at further characterizing tumor growth patterns and their prognostic value in these tumors.

Methods

MRI and clinical data of patients with newly diagnosed glioma WHO II and III from two different centers were retrospectively reviewed. Radiological data such as localization, presence of contrast enhancement, T2-volume as well as tumor growth pattern ("diffuse" vs. "circumscript") were obtained. Progression-free (PFS) and overall survival (OS) were determined and correlated with clinical, radiological and molecular characteristics using univariate and multivariate regression analyses.

Results

390 patients were included, 69% thereof having an IDH mutation. The median T2- volume was 46.0 ml, IDH mutant tumors being larger (50.7 ml) than IDH wildtype tumors (36.0 ml), $p = 0.01$. A total of 172 tumors were classified as "circumscript" and 218 as "diffuse"; the majority of IDH wildtype tumors (71%) were well delineated compared to 51% in the IDH mutant group ($p< 0.0001$). Apart from clinical parameters such as younger age, lower KPS, complete resection and delayed treatment, "circumscript" tumor growth pattern was associated with improved survival in the entire group ($p = 0.016$). When analyzed according to IDH mutation status, "circumscript" tumor growth pattern was significantly associated with OS and PFS ($p = 0.006$ and $p = 0.002$) in the IDH wildtype, but not in the IDH mutant group ($p = 0.34$ and $p = 0.81$).

Conclusion

IDH wildtype tumors present more often with a "circumscript" growth pattern on initial T2 MRI. However, this "circumscript" growth pattern was associated with improved survival only in the IDH wiltdtype but not in IDH the mutant group

Neuroonkologie IV/*Neurooncology IV*

P069

DKG Zertifizierung zum Neuroonkologischen Zentrum – Veränderungen und Konstanten – Erfahrungen eines Zentrums nach 5 Jahren

DKG certification for neuro-oncological centres in Germany – change and continuity – experiences and lessons of a single centre after 5 years

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Objective

Certifications of specialized oncological centres play an increasing role in quality management and quality assurance. There are currently 42 neuro-oncological modules certified by the German Cancer Society (DKG). The objective of this study is to assess the impact of the certification process on the quality of care and to further identify challenges within the certification process based on a single centre's experience.

Methods

Quantitative and qualitative data were collected from documents submitted for DKG certifications for each observed year (2014-2019). To identify trends in performance indices, statistical analysis was performed using a Mann-Kendall trend test, with a p-value of < 0.05 considered significant.

Results

The initial implementation of the certification process increased the number of preoperative case presentations in tumor conferences (TCs) and of patients included into clinical trials (case presentation TC quota from 37% in 2014 to 94% in 2015, clinical trial inclusion from 0% in 2014 to 33% in 2017). However, after primary certification, there were no further significant changes in any of the categories required by the DKG (e.g., primary neuro-oncological cases, TC presentation quotas, psycho-oncological counseling, and postoperative complications). Auditor recommendations during the certification process catalyzed structural and organizational quality improvements such as additional staffing dedicated to care of tumour patients, the implementation of a fully digitalized drug prescription system, and improved documentation of operative procedures. The preparation for yearly certification processes decreased from approximately 3 months to 3 weeks. Meeting the > 95% preoperative TC quota was considered as the main challenge in order to obtain certification.

Conclusion

Primary certification of a neuro-oncological centre can increase multidisciplinary-based decision making and scientific commitment. Further improvements in tumour patient care may arise from suggestions below the level of formal certification criteria. The amount of work per certification process decreases significantly with growing experience. The certification procedure provides opportunities to critically evaluate and optimize interdisciplinary neuro-oncological care – thereby serving as a catalyst rather than a generator of clinical quality and performance. Regular recertifications warrant a once achieved standard of care.

Neuroonkologie IV/*Neurooncology IV*

P070

Doppelte Dosis von 5-ALA und deren Auswirkung auf die PPIX-Expression in niedriggradigen Gliomen
Double dose of 5-ALA and its effect on PPIX expression in low-grade glioma

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Objective

5-ALA-induced fluorescence does not regularly delineate low-grade glioma (LGG) tumor margins. It is possible that an intact or minimally disrupted blood-brain barrier is the reason for these difficulties. However, the clinical value and efficacy of fluorescence-guidance are still under current investigation. In this study, we aimed to analyze the effects of increasing 5-ALA administration dose in LGG glioma surgery on inducing visible fluorescence.

Methods

Patients undergoing surgery for lesions suspicious of malignant glioma, which were later diagnosed as LGG, were included in this study. 5-ALA (Gliolan®) was administered at a dose of 20 mg/kg b.w. four hours prior to induction of anesthesia. Several patients received a higher dose of 40 mg/kg b.w. at the same time point prior to surgery. Fluorescence was evaluated during surgery and by hyperspectral measurements in extracted biopsies. Estimated tumor Protoporphyrin-IX concentration (cPPIX) was assessed by evaluating fluorescence phantoms with known cPPIX.

Results

A total of 23 patients were enrolled in this study. Thirteen (n=13) patients received 20 mg/kg b.w., as a single dose, whereas 10 patients received 40 mg/kg b.w. as a double dose of 5-ALA. In the single-dose group, 30.8% (n=4) of patients harbored visible fluorescence, whereas in the double-dose group this occurred in 60% of cases (n=6). This demonstrates an increase of 95%. In both groups, the majority of evaluated pixels was found to be in concentrations below 2µg/ml. Below this threshold, mean cPPIX was 0.26 µg/ml in the single-dose and 0.35 µg/ml in the double-dose group, indicating an increase of 35%.

Conclusion

It appears that a double dose of 5-ALA on average doubles fluorescence in LGG. This might suggest a linear relationship between dosage and fluorescence, however, it does not seem to affect tumors that would otherwise have had an extremely high cPPIX. It appears to increase the frequency of "medium to high" concentrations in the 0.5-12µg/ml range. However, due to the small sample size of this cohort, further studies are still required to analyze optimal dosage for patients harboring this type of tumors.

Neuroonkologie IV/*Neurooncology IV*

P071

Früh-postoperative Depressionen bei Patienten mit Glioblastom
Early postoperative depression in patients with newly diagnosed glioblastoma

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Objective

Depressive disorders are common in patients with cancer, frequently influencing the disease course. Although the overall survival (OS) of glioblastoma (GBM) has improved under multimodal therapies, the prognosis remains generally poor. This study aimed to assess the occurrence, risk factors and clinical impact of early depression in patients with GBM.

Methods

Medical records of patients with newly diagnosed GBM between 2008 and 2018 were analyzed regarding demographic, clinical, molecular characteristics and outcome (overall survival [OS]) was assessed. Patients with perioperative depressive disorders that needed medical treatment were considered as patients with early postoperative depression (EPD). Univariate and multivariate analysis were carried out. Patients with pre-existent history of depression (n=7) and pediatric cases (n=5) were excluded from further analysis.

Results

Of 710 patients in the final analysis, 118 patients (16.6%) were diagnosed with EPD. In univariate analysis, sex, body mass index, arterial hypertension, diabetes, midline tumor location, allocation to the stereotactic biopsy and postoperative KPS were associated with EPD. Multivariate analysis confirmed an independent association of the female sex (aOR=1.82 p=0.005), age (aOR=0.98 per-year-increase, p=0.044), arterial hypertension (aOR=1.84, p=0.018) and midline tumor location (aOR=2.07, p=0.033) with the occurrence of EPD. Cox regression analysis showed that EPD was associated with a shorter OS (aHR=1.23, p=0.05) independently of common survival predictors of GBM (age, preoperative KPS, extent of resection, IDH1 mutation, and MGMT methylation status).

Conclusion

EPD is a frequent event in GBM and is associated with demographic characteristics (female sex and younger age), comorbidity (arterial hypertension) and tumor location (affecting midline structures). Since EPD is independently associated with poor OS, there is a crucial need to screen GBM patients for depressive symptoms to offer adequate psycho-oncological care during postoperative treatment.

P072

Effektive Therapie oder treibende Kraft für aggressives Tumorwachstum? Auswirkungen der Langzeitbehandlung mit Temozolomid auf GBM Stammzellen unterschiedlicher molekularer Charakteristika

Effective therapy or driver of tumour aggression? Effects of long-term temozolomide treatment on stem-like GBM cells with different molecular profiles

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Objective

Glioblastoma multiforme (GBM) is one of the most aggressive cancers, with an overall survival of less than 2 years in over 60% of patients. Chemotherapy with temozolomide (TMZ) is the most commonly applied standard treatment. However, the effect of TMZ is counteracted by the cellular repair enzyme O6-methylguanine-DNA methyltransferase (MGMT). Its expression is regulated by the methylation of its promoter, making it a valuable prognostic and therapeutic biomarker. Previously, it has been shown that MGMT promoter methylation can change between primary tumour and recurrence and that TMZ might play a significant role in this phenomenon. However, these changes are not acknowledged by clinical guidelines yet, and their therapeutic implications are unclear.

Methods

We treated 3 patient-derived stem-like GBM cell lines with different molecular profiles with TMZ in an on/off scheme or continuously, reflecting the current therapeutic standard. We collected 144 samples to examine the MGMT promoter methylation of these cells by high resolution melting PCR, migration and proliferation by xCELLigence and TMZ-response by MTT assays 0, 4 and 8 weeks after treatment.

Results

We observed persistent and strong effects of TMZ treatment on MGMT promoter-methylated cells even after end of treatment. TMZ led to a decrease of MGMT promoter hypermethylation from 100% to 5-25% and a migratory rather than a proliferative phenotype. Cells without MGMT promoter methylation grew more aggressively after 6 weeks of long-term TMZ treatment (median doubling time with DMSO: 217h vs. TMZ: 63h, $p<0.05$). Isocitrate dehydrogenase mutated GBM cells and cells with initially low MGMT methylation showed varied response. There was a difference of 0.05 delta cell index/h in their migration rate in case the cells were treated with an on/off scheme (95% CI: 0.03-0.07, $p<0.001$), whereas cells did not change migration when treated with a continuous scheme ($p>0.05$).

Conclusion

Our results indicate that it might be useful to re-evaluate the current concept of TMZ chemotherapy and instead implement a therapeutic scheme based on molecular characteristics. Also, it may be interesting to determine additional pathogenic mutations that might occur during relapse due to TMZ treatment. Our observations are a starting point for further investigations, especially on co-interaction of TMZ and MGMT promoter methylation during recurrence development, based on molecular features of the primary tumour.

P073

Patienten im fortgeschrittenen Alter mit Glioblastoma multiforme – Wann ist best supportive care die beste Therapiemöglichkeit?

Elderly patients with glioblastoma multiforme – When is best supportive care the best option?

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Objective

Frailty is an emerging concept often used in geriatric medicine to denote a syndrome of physiological decline, characterized by marked vulnerability to adverse health outcomes. Studies have shown that frailty can predict outcome in elderly patients undergoing craniotomies for primary central nervous system tumors. In this study, we aim to determine whether frailty can identify elderly patients suffering from glioblastoma multiforme (GBM) at increased risk for adverse outcomes.

Methods

We conducted a retrospective study of elderly patients, aged 65 years or older, diagnosed with GBM at our institution from January 2010 to September 2020. We evaluated patient"s frailty with the clinical frailty scale (CFS), and dichotomized them in "frail" for CFS ≥5, and "not frail" for CFS <5. Extent of resection (EoR), molecular markers (MGMT methylation status, IDH-1 mutation status, and ATRX status), and adjuvant therapies were recorded. These established predictive variables were compared among both groups by means of Chi Square test. Primary endpoint was overall survival (OS), assessed with a log-rank test.

Results

A total of 82 patients were included in the study, of which 19 were lost to follow-up. Of the remaining 63 patients, 13 (22%) were categorized as "frail". No statistically significant difference was observed among both groups regarding EoR or molecular pathological profile. However, frail patients were not considered suitable candidates for adjuvant concomitant radiochemotherapy in 9/13 cases, a statistically significant difference to non-frail patients, who underwent Stupp protocol in 42/50 cases (p<.001). Frail individuals had a statistically significant lower mean OS of 3.3 months, when compared to "non-frail" patients, whose mean OS was 9.8 months (p=.002).

Conclusion

Frailty screening in neuro-oncologic patients could aid in risk stratification and clinical decision-making, identifying individuals who might be better suited for best supportive care instead of maximal neuro-oncologic therapy.

Neuroonkologie IV/*Neurooncology IV*

P074

Elektrolyt- und Nierenfunktionsstörung bei Patienten mit Glioblastom
Electrolyte and renal disorders in patients with newly diagnosed glioblastoma

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Objective

Electrolyte disturbances and altered renal function have been linked to the prognosis of critically ill patients and recently also of cancer patients. Little is known about the prevalence and prognostic impact of electrolyte and renal disorders in patients with glioblastoma (GBM), the most frequent malignant primary brain tumor. This study aimed to assess electrolyte and renal disorders in GBM patients and evaluate their effect on patients" outcome.

Methods

Patients treated for newly diagnosed GBM between 2005 and 2018 were included. Electrolytes and renal function parameters were assessed preoperatively. Medical records of patients were retrospectively reviewed for demographic and clinical parameters, as well as patients" survival.

Results

Electrolyte and renal disorders at admission were present in 275 (30.6%) and 544 (60.4%) of 900 GBM patients respectively and were more common in patients with higher age, previous comorbidities and poor initial clinical performance status. In univariate analysis and Kaplan-Meier survival plots, presence of hyponatremia, hypochloremia, hypocalcemia, hyperuricemia and low glomerular filtration rate were associated with poorer survival. Multivariate analysis revealed hypochloremia as an independent prognostic factor for overall (p=0.004) and 1-year (p=0.021) survival.

Conclusion

Preoperative electrolyte and renal disorders are common in GBM patients. Of them, only hypochloremia showed a strong association with GBM prognosis, independently of age, sex, extent of resection, clinical performance status, postoperative therapy, and molecular status. Further studies are needed to evaluate the impact of hypochloremia on GBM survival.

P075

Evaluation der Morphologie und des Verhaltens der Mikrogliazellen aus humanen Gliomen
Evaluation of morphology and behaviour of microglia obtained from human glioma

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Objective

Microglia, mono-nuclear cells distributed throughout the CNS, are key immune effector cells of the brain. The complex interactions between microglia and the other cell types in glioma play a crucial role in the development of novel treatments, presumably via the regulation of tumor progression and anti-tumor immune responses. This study was aimed to evaluate the morphology and behavior of microglia isolated from human glioma and compare these characteristics with microglia obtained from epileptic brain tissues.

Methods

The morphology, expression of the microglia-specific binding protein, migration ability, phagocytosis, apoptosis, and the expression of excitatory as well as inhibitory receptors were assessed.

Results

Our preliminary findings have shown a wide range of various morphologies of both activated- and non-activated microglia associated with strong spatiotemporal alterations in morphology over 4 weeks of cell culture. Furthermore, different forms of microglia exhibited different patterns of migration ability. Various patterns of the microglia-specific binding protein, as well as glutamate and GABA receptor expression, were identified in microglia with different morphologies. Microglia with different morphologies exerted different phagocytic properties. The behavior and morphology of microglia obtained from glioblastoma tissues were markedly different from those from epileptic brain tissues.

Conclusion

Our findings provide comprehensive information on the behavior of microglia in glioma, setting the basis for a more detailed classification and new insights for the designation of novel glioma treatment via targeting microglia.

Neuroonkologie IV/*Neurooncology IV*

P076

Ausmaß und prognostische Relevanz der MGMT Promotor Methylierung unterscheidet sich nicht zwischen Glioblastomen und IDH-Wildtyp TERT mutierten Astrozytomen

Extent and prognostic relevance of MGMT promotor methylation does not differ between glioblastoma and IDH-wildtype TERT-mutated astrocytoma

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Objective

The cIMPACT-NOW update 6 introduced glioblastoma diagnosis based on the combination of IDH-wildtype status and TERT promotor mutation. MGMT promotor methylation is associated with outcome in glioblastoma as defined by histopathology according to the WHO 2016 classification. However, it is yet unclear whether this is also valid in molecularly defined glioblastoma.

Methods

We searched the institutional database for patients with: 1.) glioblastoma defined by histopathology; and 2.) IDH-wildtype astrocytoma with TERT promotor mutation. MGMT promotor methylation was analysed using methylation-specific PCR and Sanger sequencing of CpG sites within the MGMT promotor region.

Results

We identified 224 patients with glioblastoma diagnosed based on histopathology, and 71 patients with IDH-wildtype, TERT-mutated astrocytoma including 32 WHO°II and 39 WHO°III astrocytomas. There was no difference in the number of MGMT methylated tumors between the two groups as determined per PCR, and also neither the number nor the pattern of methylated CpG sites differed as determined per Sanger sequencing. Progression-free (PFS) and overall survival (OS) was similar between the two groups (glioblastoma vs IDH-wildtype, TERT-mutated astrocytoma; PFS 9 vs 8 months, p=0.191; OS 18 vs 22 months, p=0.655). In both glioblastoma and IDH-wildtype TERT-mutated astrocytoma higher numbers of methylated CpG sites were associated with prolonged radiographic progression free survival.

Conclusion

Extent of MGMT promotor methylation and its clinical impact is similar in both histopathological glioblastoma and IDH-wildtype, TERT-mutated astrocytoma. Our data appear to support the role of MGMT promotor methylation also in molecularly defined glioblastoma according to the cIMPACT-NOW update 6.

Fig. 1

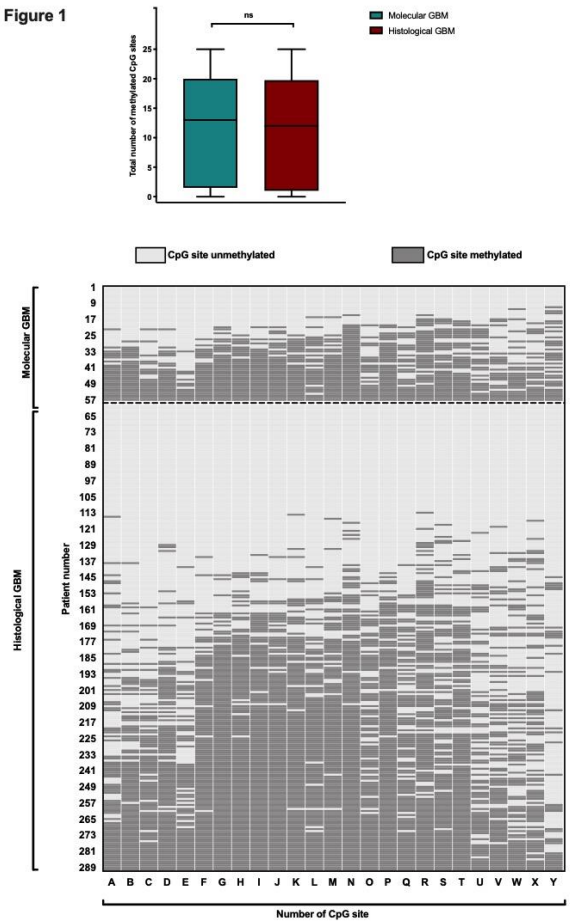
Figure 1
ns
Molecular GBM
Histological GBM
Total number of methylated CpG sites
CpG site unmethylated
CpG site methylated
Molecular GBM
Histological GBM
Patient number
Number of CpG site

Fig. 2

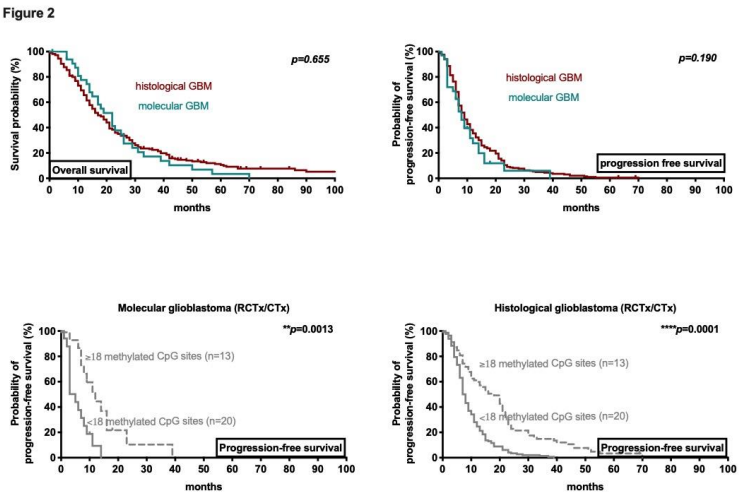
Figure 2
p=0.655
histological GBM
molecular GBM
Overall survival
Survival probability (%)
months
p=0.190
progression free survival
Probability of progression-free survival (%)
Molecular glioblastoma (RCTx/CTx)
**p=0.0013
≥18 methylated CpG sites (n=13)
<18 methylated CpG sites (n=20)
Progression-free survival
Histological glioblastoma (RCTx/CTx)
****p=0.0001

P077

Auswertung der perioperativen und postoperativen Verläufe chirurgischer Eingriffe bei pinealen Germinomen der SIOP CNS GCT 96 Studie

Evaluation of the perioperative and postoperative course of surgery of pineal germinoma according to the SIOP CNS GCT 96 trial

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Objective

CNS germinoma, being marker-negative, are diagnosed by surgical biopsy. Here we evaluate the perioperative status and postoperative complications of patients with pineal germinoma who underwent a primary biopsy or resection, treated according to SIOP CNS GCT 96.

Methods

235 patients with histologically confirmed germinoma were registered, of which 113 were pineal: 55 were biopsied and 58 underwent primary resection. Initial symptoms, tumour size, complications and neurological status were assessed. 111 patients were evaluable.

Results

Pure germinoma was present in 101 patients; 10 had additional teratoma components. The main clinical symptoms at diagnosis were headache (n=98), hydrocephalus (n=93), double vision (n=62), Parinaud syndrome (n=57) and papilloedema (n=44). Tumour size was documented in 81 patients (<2cm, n=14; 2-3cm, n=35; ≥3cm, n=32). 17 patients underwent primary total resection, 14 subtotal resection >50%, 26 subtotal resection <50%, 39 stereotactic biopsy, 11 endoscopic biopsy, 2 open biopsy and 2 not documented. The postoperative neurological status after resection was improved in 23 patients, unchanged in 27, deteriorated in 6 and not documented in one. Clinical status after biopsy improved in 26 patients, was unchanged in 15, deteriorated in 2 and not documented in 11. Postoperatively, 16/57 patients after resection and 5/54 after biopsy developed complications (Parinaud syndrome, double vision and hydrocephalus).

Conclusion

Although surgical techniques have improved within recent decades, these results support the practice of biopsy over resection for histological confirmation of germinoma arising at the pineal site.

Digitale und KI-basierte Anwendungen, Perspektiven/*Digital and AI-based implementations, perspectives*

P078

3D MRT Segmentierung von Glioma – Forschungs-Datensätze vs. Daten aus dem klinischen Alltag
3D MRI segmentation of glioma – research datasets vs. routine clinical data

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Objective

Automated segmentation of brain tumors in 3D MR images has seen significant advances in recent years. State-of-the-art algorithms rely on 3D MRI sequences to achieve best results: pre-contrast T1- weighted (T1), post-contrast T1-weighted (T1CE), T2-weighted (T2), and T2 Fluid Attenuated Inversion Recovery (FLAIR). In clinical routine, T2 and FLAIR sequences are typically only acquired in 2D, not suitable as input for current algorithms. We aim to quantify the loss of information when using only the two 3D T1 sequences instead of all four 3D sequences.

Methods

3D MR images and ground-truth segmentations of n = 369 patients (293 subjects are HGG, while 76 are LGG cases, mean age 61(minimum=18 and maximum=86)) were obtained from the Brain Tumor Segmentation (BraTS) Challenge 2020. A set containing ST1±CE := (T1, T1CE), omitting T2 and FLAIR, and SFULL := (T1, T1CE, T2, FLAIR), containing all sequences were defined. An encoder-decoder based CNN architecture with an asymmetrically larger encoder (VAE-RES-NET) was adapted for tumor segmentation using a batch size of four, a cropsize of 160*192*128, trained for 300 epochs with an early stopping of 100. The net architecture is shown in figure 2. We trained two VAE-RES-NET one for each sequence set shown in figure 1. The algorithm was trained (80% of the dataset) to automatically segment the following three labels: the contrast-enhancing tumor (ET), the peritumoral edema (ED) and the necrotic and non-enhancing tumor core (NCR/NET). The accuracy was evaluated using the Dice coefficient averaged over the validation set (20% of the dataset).

Results

The average Dice score for the label NCR/NET was 0.674 for set ST1±CE and 0.685 for set SFULL. For label ET, the Dice coefficient was 0.760 and 0.764, respectively. A marked difference was found for the label ED, with 0.652 for set ST1±CE and 0.800 for set SFULL, a difference of 0.147.

Conclusion

Using incomplete information, i.e. omitting T2 and FLAIR, NCR/NET and ET were segmented with an accuracy comparable to the full set of sequences, while ED segmentation accuracy declined. Even though epitumoral edema is mainly encoded in T2 and FLAIR imaging, reasonable accuracy was obtained using incomplete information. Nevertheless, since in clinical routine T2 and FLAIR sequences are often only acquired in 2D, further work should focus on including these in the modelling to boost ED segmentation accuracy.

Fig. 1

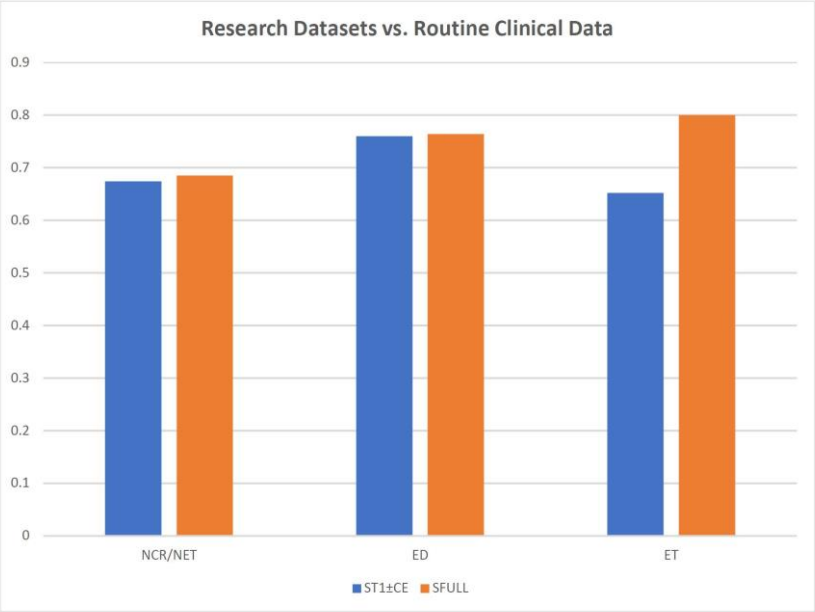
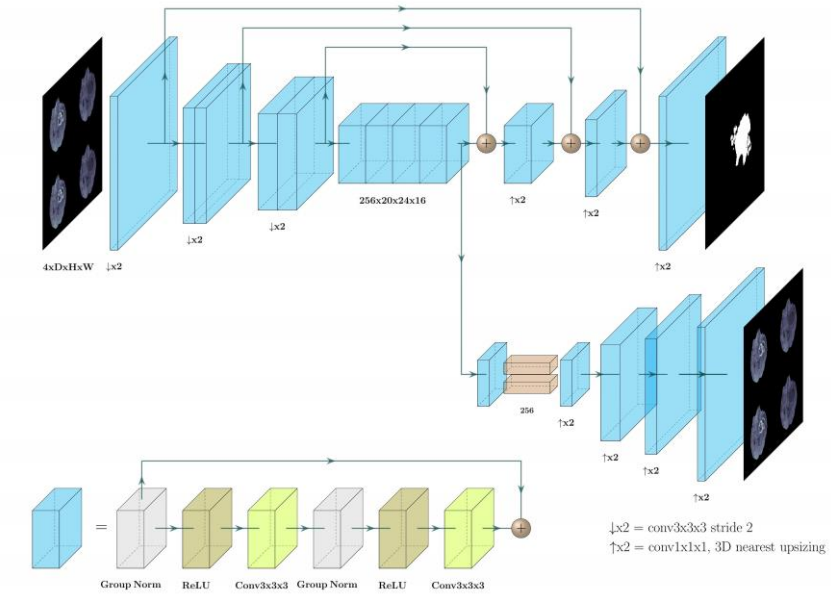

Research Datasets vs. Routine Clinical Data
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
NCR/NET
ED
ET
ST1±CE
SFULL

Fig. 2


4xDxHxW
↓x2
↓x2
↓x2
256x20x24x16
↑x2
↑x2
↑x2
256
↑x2
↑x2
↑x2
=
Group Norm
ReLU
Conv3x3x3
Group Norm
ReLU
Conv3x3x3
↓x2 = conv3x3x3 stride 2
↑x2 = conv1x1x1, 3D nearest upsizing

Digitale und KI-basierte Anwendungen, Perspektiven/*Digital and AI-based implementations, perspectives*

P079

Moderne Echtzeitbildgebung der Medulla oblongata – Ein innovativer bildgebender Biomarker bei der essentiellen arteriellen Hypertonie?

Advanced real-time imaging of the medulla oblongata – A novel imaging biomarker in essential arterial hypertension?

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Objective

Neurovascular compression (NVC) is described as an impressive pathological conflict between cranial nerves and vasculature at the surface of the brainstem. With the application of high resolution MRI the individual neurovascular anatomy can be delineated in a three-dimensional fashion. The primary goal of this contribution was to realize the technical innovation of in-vivo ultra-fast real-time MRI in the visualization of pulsational characteristics of NVC at the medulla oblongata.

Methods

Real-time MRI of the neurovascular dynamics of the medulla oblongata was performed in a young hypertensive proband for the first-time. A 3 Tesla MRI scanner (Prisma, Siemens Healthineers) with an equipped multi-GPU system for real-time MRI was applied. Serial image reconstruction was achieved by calibration-less parallel imaging using nonlinear inversion. The reconstruction time per frame was lower than the acqusition time, so that image reconstruction was based on a convolution of the image with the point-spread function that can be implemented using a fast Fourier transform algorithm.

Results

We firstly performed a real-time MRI of the posterior fossa with the focus on neurovascular morphology and pulsational characteristics of the vertebral arteries. We were able to visualize the in-vivo pulsation of the vertebral arteries towards the ventrolateral medulla oblongata during diastole and systole. The pulsational pattern during heartbeat could be delineated with a narrow intravascular diameter during the diastolic phase and an enlarged intravascular diameter during the systolic phase. In the scanned proband a distinct cerebrospinal fluid layer between the adventitia of the vertebral artery and the pial surface of the lower brainstem could be differentiated.

Conclusion

An etiologic association of pulsatile neurovascular compression at the medulla oblongata with arterial hypertension is widely discussed and there are missing clear translational criteria in detailed patient selection for neurosurgical treatment. Our technique deals with the perspective application of real-time MRI for the in-vivo visualization of pathological neurovascular dynamics at the brainstem. We aim to establish novel imaging biomarkers based on state-of-the-art MRI methods.

Digitale und KI-basierte Anwendungen, Perspektiven/*Digital and AI-based implementations, perspectives*

P080

Die Frequenz von Autoregulationsstörung und reduzierter intrakranielle Compliance ist Diagnose-spezifisch
Frequency of impaired cerebral autoregulation and intracranial compliance reduction is diagnosis specific

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Objective

In neurocritical care, impairment of cerebral autoregulation and reduced intracranial compliance due to brain swelling are frequent events. Recently, we have developed a biophysical approach to reliably detect these pathological conditions. Our method consists of a mathematical tool set, which detects slow homoeostatic correlation patterns between intracranial pressure (ICP) and arterial blood pressure (ABP). A negative correlation (scn) indicates reduced compliance and functioning autoregulation and a positive correlation (scp) implies additional disturbance of the cerebral autoregulation. In this study, we assessed, whether the frequency of the two conditions is different in patients with subarachnoid hemorrhage (SAH) compared or traumatic brain injury (TBI).

Methods

We have included 27 patients, with a median age of 44 years, treated for SAH (n = 18) or TBI (9) on our neurosurgical ICU. The median initial GCS was 7, the median GOS at last follow up was 3. Decompressive craniectomy was performed in 8 patients (29.6%). The baseline characteristics were balanced between the diagnosis groups, except for a male predominance and a higher frequency of craniectomy in the TBI group. To identify positive or negative correlations between isochronic segments of ABP and ICP, we utilized power spectra calculations. From this spectral information an index called selected correlation (sc) is deduced, which reflects the strength correlation. The mean Hilbert phase difference (mhpd) of the segments is calculated to reflect the phasing. If mhpd of ≥ 110 degree a correlation is defined as negative (scn). Conversely if mhpd ≤ 70 degree, the correlation is defined as positive (scp).

Results

We found a significantly higher proportion of scn in TBI patients compared to the SAH group ($p = 0.035$). In contrast, SAH patients showed a significantly higher fraction of scp indicating a higher frequency of impaired cerebral autoregulation. Neither scp, nor scp was different in patients with or without decompressive craniectomy ($p = 0.104$ and 0.827, respectively). Clinical outcome was not different between the diagnosis groups ($p = 0.168$). However, we found a significant correlation between scp and outcome ($p = 0.002$), which was not the case for scn ($p = 0.276$).

Conclusion

Our data demonstrate that the distribution of compliance reduction and autoregulation disturbance is different between TBI and SAH, highlighting the specific pathophysiology of the diseases.

Digitale und KI-basierte Anwendungen, Perspektiven/*Digital and AI-based implementations, perspectives*

P081

Vollautomatische Detektion und Segmentation von Meningiomen durch "deep learning" an multiparametrischen MRTs

Fully automated detection and segmentation of meningiomas using deep learning on routine multiparametric MRI

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Objective

Magnetic resonance imaging (MRI) is the method of choice for imaging meningiomas. Volumetric assessment of meningiomas is highly relevant for therapy planning and monitoring. We used a multiparametric deep-learning model (DLM) on routine MRI data including images from diverse referring institutions to investigate DLM performance in automated detection and segmentation of meningiomas in comparison to manual segmentations.

Methods

We included 56 of 136 consecutive preoperative MRI datasets [T1/T2-weighted, T1-weighted contrast-enhanced (T1CE), FLAIR] of meningiomas that were treated surgically and graded histologically as tumour grade I (n = 38) or grade II (n = 18). The DLM was trained on an independent dataset of 249 glioma cases and segmented different tumour classes as defined in the brain tumour image segmentation benchmark (BRATS benchmark). The DLM was based on the DeepMedic architecture. Results were compared to manual segmentations by two radiologists in a consensus reading in FLAIR and T1CE.

Results

The DLM detected meningiomas in 55 of 56 cases. Further, automated segmentations correlated strongly with manual segmentations: average Dice coefficients were 0.81 ± 0.10 (range, 0.46-0.93) for the total tumour volume (union of tumour volume in FLAIR and T1CE) and 0.78 ± 0.19 (range, 0.27-0.95) for contrast-enhancing tumour volume in T1CE.

Conclusion

The DLM yielded accurate automated detection and segmentation of meningioma tissue despite diverse scanner data and thereby may improve and facilitate therapy planning as well as monitoring of this highly frequent tumour entity.

Digitale und KI-basierte Anwendungen, Perspektiven/*Digital and AI-based implementations, perspectives*

P082

MRT Radiomics zur nicht-invasiven Vorhersage des BRAF-Mutationsstatus in Patienten mit zerebralen Melanommetastasen

Non-invasive prediction of the BRAF mutation status in patients with melanoma brain metastases using MRI radiomics

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[2]University Hospital Cologne, University of Cologne, Department of Stereotactic and Functional Neurosurgery, Köln, Germany
[3]Research Centre Jülich, Institute of Neuroscience and Medicine, Jülich, Germany
[4]University Hospital Cologne, University of Cologne, Department of Neurology, Köln, Germany
[5]Universities of Aachen, Bonn, Cologne and Duesseldorf, Center for Integrated Oncology (CIO), Köln, Germany
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Objective

Malignant melanomas frequently develop brain metastases. Targeted therapies such as BRAF inhibitors have shown relevant intracranial response rates in initial trials. The most frequent BRAF V600E mutation occurs in up to 60% of melanomas. However, recent studies reported a significant discrepancy with respect to the mutational status of the extracranial melanoma and melanoma brain metastases. We evaluated the potential of MR-radiomics for the non-invasive diagnosis of BRAF status in brain metastases.

Methods

Forty-four patients with 48 brain metastases secondary to malignant melanoma underwent brain tumor surgery with subsequent molecular tissue analysis of the BRAF mutational status. All patients received a preoperative MRI including contrast-enhanced (CE) T1- and T2-weighted sequences. Brain metastases were manually segmented based on CE T1-weigthed MRI. After image preprocessing 2632 radiomics features were extracted using pyradiomics. Patients were randomly assigned to a training and a test dataset in a ratio of 50/50. To test predictive performance multiple algorithms were trained based on 5-fold cross validation. Finally, the best performing model was applied to the test dataset to evaluate model generalizability.

Results

Twenty-one patients (48%) showed a BRAF V600E mutation. In the test dataset, the radiomics model using a support vector machine classifier yielded an area under the receiver operating characteristic curve (AUC) of 0.8 (accuracy, 77%; sensitivity, 70%; specificity, 83%) for prediction of the BRAF mutation status.

Conclusion

MRI radiomics allows a non-invasive prediction of the BRAF V600E mutation status in patients with melanoma brain metastases. Further evaluation of the developed model is ongoing.

Fig. 1

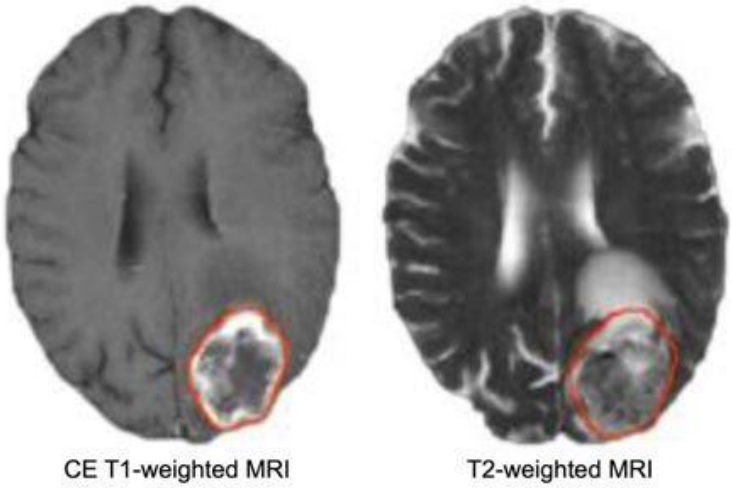

Figure 1. Features were extracted from contrast-enhanced (CE) T1- and T2-weighted MRI. Brain metastases were manually segmented (red contour) based on CE T1-weighted MRI.

Fig. 2

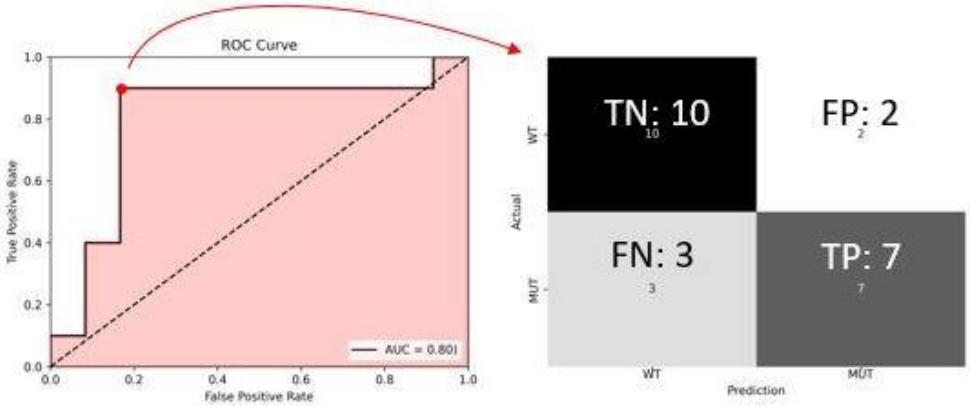

Figure 2. The support vector machines classifier achieved an area under the receiver operating characteristic curve of 0.8 (accuracy, 77%; sensitivity, 70%; specificity, 83%) in the test dataset for the prediction of the BRAF V600E mutation status. The right side shows the corresponding confusion matrix.

Digitale und KI-basierte Anwendungen, Perspektiven/*Digital and AI-based implementations, perspectives*

P083

Optimales Zeitfenster für kortikales Mapping bei der Wachkraniotomie – eine zweizentrige Studie – aktualisierte Datenlage

Optimal time window for cortical mapping in awake craniotomy – a two-centre study – updated database

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Objective

In our previous study we have demonstrated that the optimal time window for cortical mapping in a Sleep-Awake-Awake (S-A-A) craniotomy might begin 20 minutes after extubation of the patient. The assessment of time window beyond 40 minutes after extubation was not possible due to the lack of data. During the last year we have accumulated additional data in order to assess a longer intraoperative time window. In cooperation with Tata Memorial Hospital, we have acquired the data about intraoperative reaction speed during Awake-Awake-Awake (A-A-A) craniotomy.

Methods

Reaction speed was assessed in 102 Patients in S-A-A and 18 Patients in A-A-A group. The registration was done with an application *Reaction Time Sampler* in both groups. Statistical analysis with SPSS v24.0 (IBM, New York, U.S.).

Results

The preoperative (preOP) reaction times (RT) of S-A-A patient cohort (665 ± 333ms) were significantly shorter than those measured during surgery (intraOP) (815 ± 379ms; p<0,001).

In the S-A-A cohort, a one-factorial ANOVA (within) showed a significant increase during surgery (p <0.001). There was a significant difference between the average preOP RT and the reaction speed during the timeframes 0-10min and 10-20min after extubation.

In the A-A-A cohort, the difference between the preOP and intraOP reaction time was insignificant.

Conclusion

Patients in the S-A-A cohort react significantly slower during surgery than preoperatively.

The intraOP reaction times were not significantly longer than preOP in A-A-A cohort. Furthermore, the reaction time in S-A-A cohort was significantly longer during the timeframes 0-10min and 10-20min after extubation. Hence, according to our data the optimal time window for cortical mapping in S-A-A craniotomy possibly starts 20 minutes after the extubation.

Fig. 1

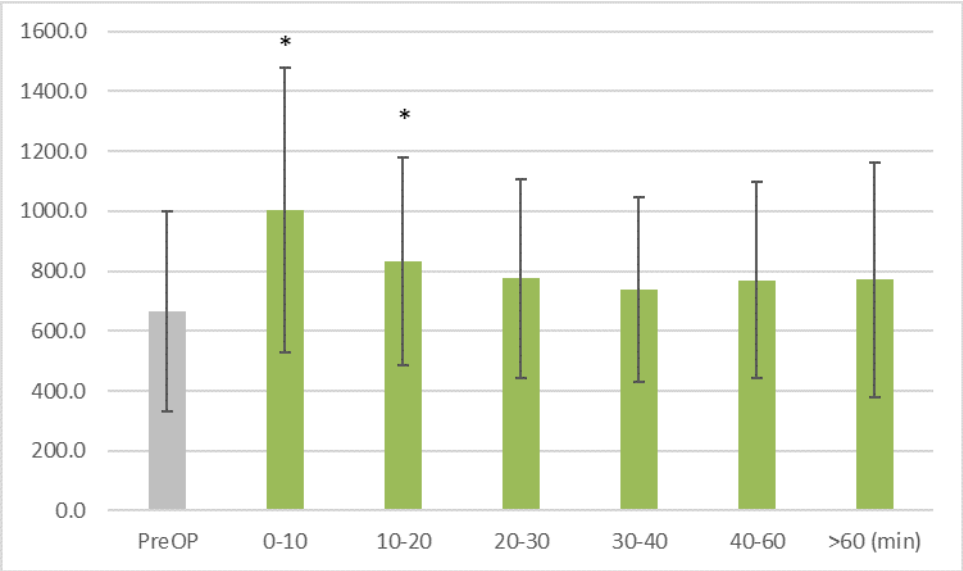
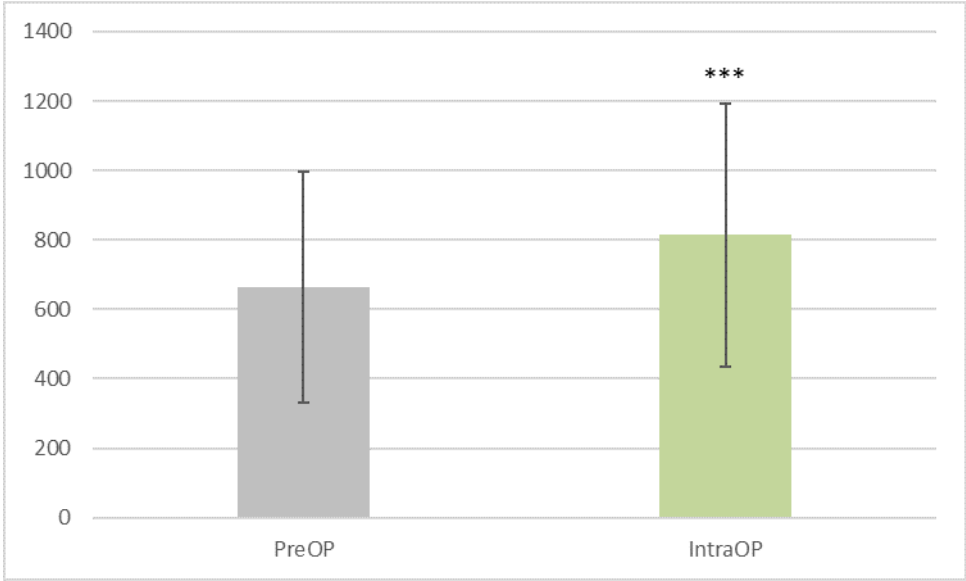

1600.0
1400.0
1200.0
1000.0
800.0
600.0
400.0
200.0
0.0
*
*
PreOP
0-10
10-20
20-30
30-40
40-60
>60 (min)

Fig. 2


1400
1200
1000
800
600
400
200
0
***
PreOP
IntraOP

Digitale und KI-basierte Anwendungen, Perspektiven/*Digital and AI-based implementations, perspectives*

P084

Augmented Reality (AR) geführte Ventriculostomie an einem Kopfmodell
Augmented reality (AR) guided ventriculostomy in a head model

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Objective

Augmented reality (AR) headsets allow to superimpose 3D holograms derived from imaging onto body parts, e.g. the cranial anatomy onto a head. External ventricular drainages (EVDs) are usually placed under guidance of anatomical landmarks, resulting in unfavourable positions in 30-40% of cases. The presented project provides an approach on improving this rate through holographic visualisation of the cranial anatomy, entry point and target area for the EVD placement. Commercially available AR glasses were used as the sole active component in this setting. The goal was minimal disruption to the workflow of this standard procedure.

Methods

A modular head model and segmentation algorithm were developed. Precision of the setup was confirmed. Routine computed tomography (CT) scans of the models were used. Entry point and target for EVD placement are computed automatically. A passive marker system was attached to the head model to be tracked by the headset. Eleven surgeons conducted two ventriculostomies per head to place a total of 110 EVDs. Four of the participants did two additional series to derive a possible learning curve. Abnormalities such as midline shifts or deformities were included in the individually shaped ventricles. EVD catheters were left in place for CT-scans to check for placement accuracy.

Results

The setup worked reliably and showed stable performance. The overall rate of successful ventriculostomies was 68.8%. The mean offset of the EVDs from the displayed reference trajectory was 5.2±2.6mm (mean ± standard deviation). Overall feedback was positive. For the majority it was the first encounter with AR headset technology. General concerns were raised about reliability of the AR hardware in regard to surgical procedures. The subgroup with repeated puncture series showed a significant improvement in precision and successrate.

Conclusion

AR guided EVD placement in head models with varying ventricular anatomy was shown to be feasible. Precision of AR guided EVDs was satisfactory. To our knowledge, this is the first report on AR guided ventriculostomy based on a marker system. The results achieved in this project are promising. Good acceptance of this compact navigation tool could be expected in a presumed clinical application. The learning curve with the proposed setup seems to be steep. Before a translation into clinical application and use in humans is safe, further development on the marker system and visuo spatial uncertainties have to be addressed.

Digitale und KI-basierte Anwendungen, Perspektiven/*Digital and AI-based implementations, perspectives*

P085

Rekonstruktion von 3D Models aus endoskopischen Bildern mit Fotogrammmetrie
Reconstruction of real 3D models from endoscopic images using photogrammetry

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Objective

The comprehensive visuospatial understanding of neuroanatomy is crucial for neurosurgeons. Cadavers represent the gold standard of learning; however, they are very expensive, and their accessibility is also limited. To overcome the limitations associated with cadavers, different computer-assisted methods were developed in the last years to facilitate neurosurgical education. One of them is based on photogrammetry, which means the reconstruction of three-dimensional volumetric models from two-dimensional images. The aim of our study was to evaluate the feasibility of creating freely explorable 3D models from endoscopic images and short videos using photogrammetric approach.

Methods

10 in formalin-fixed human cadaveric heads were involved in this study. The cadavers were donated with educational and research purposes. The opening of the skull and the dura mater was performed according to the classical supraorbital and retrosigmoid approaches. The anatomical structures of the suprasellar region as well as of the cerebellopontine angle were exposed and recorded (in 8 cases) or photographed (in 5 cases) from different angles and distances with a 0-degree rigid endoscope (Aesculap GmbH, Tuttlingen, Germany) mounted on a Canon EOS 5D Mark II body (Canon Inc, Tokio, Japan). To eliminate the optical distortion caused by the endoscope lens, a chessboard pattern was photographed with the same setup. The distortion parameters were estimated using the OpenCV open source software. The images were extracted from the videos before the photogrammetric processing. The three-dimensional volumetric models were reconstructed using the Agisoft Metashape software (Standard Edition, v. 1.6.1)

Results

We have successfully created freely explorable three dimensional models from the endoscopic images and videos in all cases. In 2 cases we were able to reconstruct multiplanar models which allowed the exploration of the deeper structures between the superficial ones. Comparing the two different inputs, the extracted images were also suitable for photogrammetric processing despite their significantly lower resolution.

Conclusion

Photogrammetry is a suitable method to creating volumetric three-dimensional models from endoscopic images for educational purposes. The snapshots extracted from videos are not inferior compared to high quality photographs. The intraoperative application of this technique should be also considered.

Digitale und KI-basierte Anwendungen, Perspektiven/*Digital and AI-based implementations, perspectives*

P086

Virtual-Reality – Evaluation des mikrovaskulären Konflikts bei Patienten mit Trigeminusneuralgie
Virtual reality evaluation of microvascular conflict in patients with trigeminal neuralgia

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Objective

Trigeminal neuralgia (TN) is a lightning bolt of violent, electrifying, and stinging pain, often secondary to the neurovascular conflict (NVC). The vessels involved in NVC are mostly arteries and rarely veins. Evaluation of NVC in the deep infratentorial region is inseparably connected with cranial imaging. We retrospectively analyzed the potential influence of three-dimensional (3D) virtual reality (VR) reconstructions compared to two-dimensional (2D) magnetic resonance imaging (MRI) scans on the evaluation of NVC for the surgical planning of microvascular decompression in patients with TN.

Methods

Medical files were retrospectively analyzed regarding patient- and disease-related data. Preoperative MRI scans were retrospectively visualized via VR software to detect the characteristics of NVC. A questionnaire evaluated the influence of VR visualization technique on identification of anatomical structures involved in NVC and on surgical strategy.

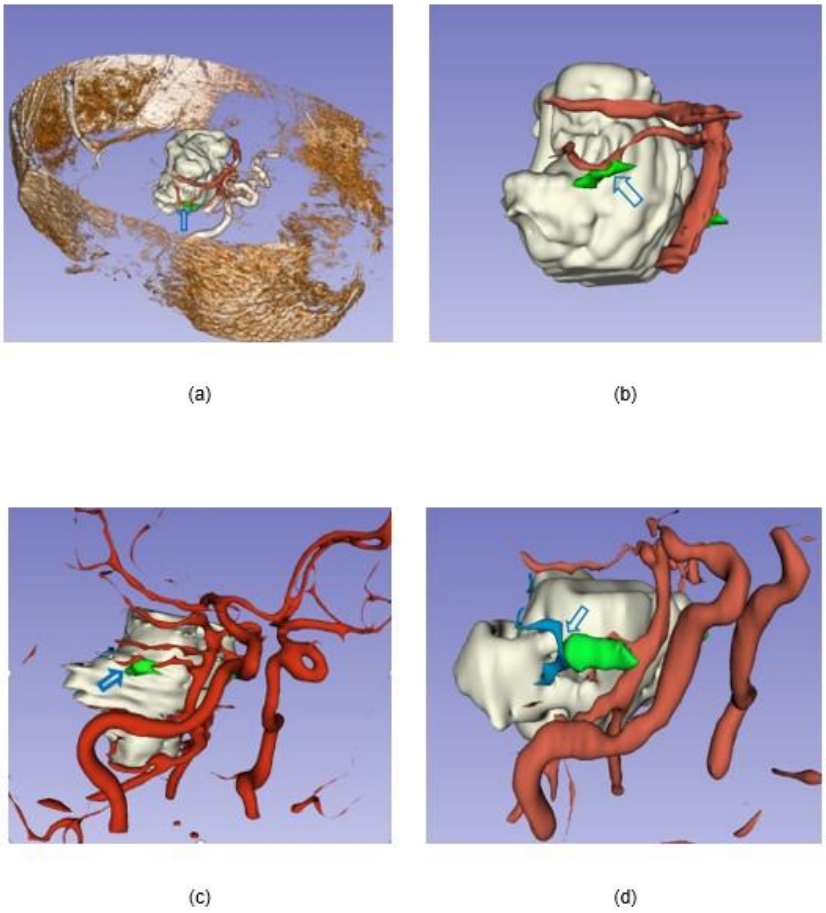
Results

Twenty-four patients were included. Image presentation using 3D-VR modality significantly influenced the identification of the affected trigeminal nerve (p=0.004), the vascular structure involved in the NVC (p=0.0002), and the affected side of the trigeminal nerve (p=0.005).

Conclusion

In patients with TN caused by NVC, the reconstruction of conventional preoperative 2D-MRI scans into 3D images and the spatial and anatomical presentation in VR models offers the possibility of increased understanding of the anatomy and pathology, and thus influences operation planning and strategy.

Fig. 1



(a) (b)

(c) (d)

Digitale und KI-basierte Anwendungen, Perspektiven/*Digital and AI-based implementations, perspectives*

P087

Virtuelle neuronavigierte Ventrikelkatheterplatzierung – eine Trainingsmethode für angehende Neurochirurgen
Virtual ventricular catheter placement using neuronavigation – a training tool for neurosurgeons-in-training

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Objective

The aim of this prospective study is to evaluate practices, pitfalls and traceability in a realistic but virtual set-up for simulating ventricular drainage (VD) placement as a practicable training model. The influence of the level of neurosurgical knowledge and training level were of overall interest, especially in narrow ventricles.

Methods

In this ongoing study, we evaluate the accuracy to hit the target by repeated virtual freehand VD placement using anatomical landmarks by neurosurgeons-in-training and non-neurosurgical staff. The target was to place the VD into the anterior horn of the right lateral ventricle, assuming CSF drainage. Catheter placement was simulated using the pointer of the navigation system with variable tip extension simulating catheter length. The chosen target point was frozen and documented. Until then, the participant has no visual feedback via the navigation system. The results were directly evaluated on-screen, saved to the navigation system and thereafter evaluated in detail using iPlan Net (Brainlab) on the computer. Placement was assessed for the possibility of CSF-flow, injury of eloquent structures, catheter tip length, number of attempts and level of neurosurgical training.

Results

At present, 28 virtual freehand VD were placed into a proband with a narrow ventricular system by 17 participants. These were grouped into a high-knowledge group of 11 participants (neurosurgical training >1 year) and a low-knowledge group of 6 participants (no neurosurgical training or < 1 year). In total, 16 correct VD were performed. The high expertise group fared better with 14 successfully placed VD in 17 attempts than the low-expertise group with 2 successful VD in 11 attempts. Accurate VD placement correlated with neurosurgical experience. The overall low success rate was partially attributed to the narrow ventricles as well as to the fact that catheter length was pre-determined and not modified once CSF-flow is obtained as in reality.

Conclusion

The results emphasize the need for noninvasive training for catheter placement, especially in narrow ventricles and is correlated to the anatomical knowledge and the level of neurosurgical training. Navigation-guided virtual ventricular catheter placement is a perfect and unbloody training model and should be integrated as a simple, non-invasive, inexpensive training of neurosurgeons to improve placement trajectories and techniques in real-life scenarios.

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P088

Clusterakquisition zur Verbesserung klinischer Sprachkartierung und der Bestimmung der Hemisphärendominanz mittels fMRT

Clustered acquisition to optimise clinical fMRI language mapping and hemispheric dominance detection

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[2]Universitätsklinikum Köln, Institut für Diagnostische und Interventionelle Radiologie, Köln, Germany

Objective

Non-invasive assessment of hemispheric language dominance by functional MRI (fMRI) is of great clinical interest e.g. for planning of epilepsy or brain tumour surgery in potentially language-eloquent localization, but still remains challenging. Clustered sparse acquisition can improve language mapping by avoiding acoustic contamination by scanner noise as well as by minimizing task-related head movement artifacts, offering however a relatively short scanning time compared to conventional (i.e., single volume) sparse acquisition. We, here, set out to compare the potential of clustered versus standard sparse fMRI acquisition to detect hemispheric language dominance using different regions of interest (ROI).

Methods

18 healthy, right-handed native speakers of German (m=4) underwent fMRI (Philips Ingenia 3T) during a picture naming task. Sparse acquisition acquired one full volume of the brain every 12s resulting in a silent period of 9.2s (TE: 30ms, FA: 90°, 36 slices, voxel size: 3mm isotropic, 14 min per session). Clustered acquisition acquired three volumes each 12s (TR: 1.2s, 8.4s silence, 7min per session). Here, two slices were acquired simultaneously using the "Simultaneous Multislice Imaging" function of the scanner. Data were analysed using SPM12/Matlab. JuBrain Anatomy Toolbox was used to define the ROIs taken into concern, i.e., inferior frontal gyrus (STG), superior temporal gyrus (STG) and angular gyrus (ANG). AveLI was used to compute laterality indices.

Results

Both protocols revealed activation in the IFG, the ANG and the STG. The extent of activation was comparable between sparse and clustered acquisition. Spatial agreement as indicated by dice similarity was 54.6%. Highest AveLIs were found for clustered sparse acquisition when using the IFG or the IFG+ANG as ROIs (61% of subjects left-lateralized; median AveLI IFG = 0.27 / IFG+ANG = 0.17).

Conclusion

Clustered acquisition offers the advantages of sparse acquisition with halved examination time and shows substantial agreement regarding the task-related activations. Moreover, clustered acquisition seems to be comparatively well suited to detect hemispheric language dominance, especially when considering the IFG or a combination of the IFG and the ANG as ROIs.

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P089

Kombinierte Hochfrequenz-Stimulation als Rettungstherapie bei Patienten mit chronischen Lumboischialgien nach refraktären Schmerzen unter konventioneller SCS

Combined high-frequency stimulation as a rescue therapy in patients with chronic low back and leg pain refractory to chronic SCS

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Objective

We aimed to investigate the efficacy of new stimulation paradigms in patients who initially benefited from conventional spinal cord stimulation (SCS) and lost the effect after months/years of stimulation.

Methods

Patients presenting with refractory low back and leg pain after chronic failure of SCS therapy were included in this study. In the context of a rescue-therapy, patients underwent an externalization of the implanted SCS leads in order to be tested with tonic and either contour or burst stimulation paradigms, and were eventually implanted with new generators. Pain intensity was analyzed using the numeric rating scale (NRS), and data were collected prior to externalization and at variable follow-ups after reimplantation.

Results

Thirty-seven patients (18 females and 19 males) with refractory pain after receiving chronic conventional SCS stimulation for at least one year underwent externalization of intraspinal leads. Mean preoperative NRS score was 8.1/10 points (SD±0.9) for the ON stimulation period. Patients received a combination of high-frequency stimulation at 1.2kHz, burst, tonic or dorsal horn high-frequency stimulation, or a combination of these algorithms. Postoperatively, a mean significant reduction of 48.0% was observed with the new paradigms ($p<0.001$). Mean postoperative NRS score was 3.8/10 points (SD±2.5). After this, 29 patients were reimplanted with new generators and in 8 cases the complete system was removed. No major complications were documented during the follow-up.

Conclusion

Rescue therapy SCS with combined high-frequency, burst and tonic wave forms can be associated with a successful pain reduction in patients with failed conventional chronic SCS. This approach can be considered as a safe and alternative method before considering explantation of the SCS system.

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P090

DBS-Zielpunkte Konnektivitätsmuster bei Patienten mit Tourette Syndrom
Connectivity patterns of different targets for DBS in Tourette syndrome

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Objective

Deep brain stimulation (DBS) is an effective therapy option for patients with treatment refractory Tourette syndrome (TS). Since the first TS case treated with DBS in 1999, several targets have been explored reporting similar success rates. Currently, imaging techniques like probabilistic tractography and normative human connectome data (HCP) have contributed to identify connectivity profiles associated with better outcome for individual targets. The objective of this study is to analyze the connectivity profiles of different DBS targets for TS in order to assist preoperative planning. Further, we compare these connectivity patterns based on HCP and probabilistic tractography using datasets of TS patients.

Methods

We generated volumes of tissue activated (VTA) at standard target coordinates for the centromedial nucleus/nucleus ventrooralis internus (CM/Voi), the CM/parafascicular (CM/Pf), the anteromedial globus pallidus internus (amGPi), the posteroventral GPi (pvGPi), the ventral anterior/ventrolateral thalamus (VA/VL), and the nucleus accumbens/anterior limb of the internal capsule (Nacc/ALIC) based on literature. Probabilistic tractography was performed from the targets to different limbic and motor areas based on diffusion tensor imaging of TS patients. The same connections were analyzed using HCP and connectomic atlases of TS patients using LEAD connectome.

Results

Our analysis showed significant differences among the connectivity profiles of standard DBS targets ($p<0.01$). The thalamic targets VA/VL showed the strongest connection to the motor cortex and the supplementary motor areas, while CM/Voi had higher connectivity to the prefrontal cortex. Out of the pallidal targets the connectivity profile of pvGPi was more associated with the motor cortex, but also showed high connectivity to the amygdala, while amGPi had stronger connection to the prefrontal cortex. Nacc/ALIC had the weakest connection to the motor cortex.

Conclusion

This analysis shows that the connectivity profiles of different DBS targets to main motor and limbic areas differ significantly. This should be considered when planning DBS for TS patients, probably based on the clinical profile of the patient.

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P091

Handhabung, Benutzerfreundlichkeit und Komplikationen von wiederaufladbaren extrakorporalen Neurostimulatoren für die drahtlose Stimulation des Rückenmarks – eine Fragebogen-basierte patientenorientierte Studie

Convenience, usability and complications of rechargeable extracorporeal pulse generators for wireless spinal cord stimulation – a questionnaire-based, patient-centric study

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Objective

Spinal cord stimulation (SCS) has been utilized for more than 50 years to treat refractory neuropathic pain. Currently, SCS systems with fully implantable pulse generators represent the standard. New wireless extracorporeal SCS (wSCS) devices promise higher levels of comfort and convenience for patients. However, to date there are no studies on how charging and using this wSCS system affects patients and their therapy. This study is the first questionnaire-based survey on this topic focusing on patient experience.

Methods

Standardized questionnaires were sent to all patients with a wSCS device in use at the time of trial. The primary endpoint was the convenience of the charging and wearing process scored on an ordinal scale from "very hard" (1) to "very easy" (5). Secondary endpoints included time needed for charging, the amount of time stimulation was used during the day and complication rates.

Results

Questionnaires of 6 patients were returned and included in the analysis. The average age of the patients was 61.3 ± 6.7 (± SD) years. The length of therapy was 20.3 ± 15.9 months (mean ± SD). The duration of stimulation was 17 ± 5.9 hours (mean ± SD) each day. N=5/6 patients rated the overall convenience as "easy" (4) and evaluated the effort of the charging and wearing of wSCS device process as "low" (4). N=5/6 patients considered the wearing and charging process as an active participation in therapy. None of the patients were concerned about forgetting to charge the device. N=5/6 patients would decide in favor of an extracorporeal device as opposed to the conventional SCS systems again. Early or late surgical complication did not occur.

Conclusion

Overall, patients felt confident using extracorporeal wireless SCS devices without any complications. Effort to maintain therapy with this system was rated as low. The results of this pilot study need to be verified with a larger cohort and a longer follow-up.

Funktionelle Neurochirurgie und Schmerz I, Freie Themen/*Functional neurosurgery & pain I, free topics*

P092

Beeinflusst die kabelgebundene Stimulation und Aufzeichnung der neuronalen Aktivität das Wohlbefinden der Ratte?

Does cable-bound stimulation and recording of neuronal activity affect rat's wellbeing?

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Objective

Chronic stimulation and recording of neuronal activity in different rodent models for movement disorders and neuropsychiatric disturbances is carried out via a cable with a swivel that allows relative free movement of the rat without twisting of the cable. Nevertheless, it is still semi-restraining and may therefore impose stress and confound to the animal.

We here subcutaneously implanted transmitters for contactless recording of heart rate and activity of rats during cable-bound stimulation and recording of neuronal activity, which was compared to the perioperative period of intracranial electrode implantation.

Methods

Male Sprague Dawley rats (n=8, 180 g) were implanted with electrodes in the subthalamic nucleus (STN) under general anesthesia with local anesthesia and perioperative pain management with non-steroidal anti-inflammatory drugs. Two weeks after electrode implantation the threshold for stimulation-induced side effects was determined in each rat. Thereafter, a five-day sham-stimulation period started with only the cable connected to the rat"s electrode head stage but no current applied. Finally, the cables were disconnected and rats were allowed to move freely in their cages for another two days. In addition to continuous monitoring of heart rate and activity via a subcutaneously implanted transmitter, the rats" well-being and general health condition were monitored by daily body weight measures and clinical scoring.

Results

Clinical scoring and weight measures during the course of the study did not show any substantial alterations. Right after electrode implantation, heart rate was elevated, however, without reaching the level of significance. Only the first two days of cable-bound sham-stimulation resulted in decreased locomotor activity ($p<0.05$) as compared to pre- and post-stimulation values, whereas heart rate measures were not affected.

Conclusion

Electrode implantation and semi-restraint caused by tethered electrodes had only a transient and mild effect on rat`s activity. Since so far even advanced and fully implantable devices do not allow flexible switching between recording and electric stimulation with different settings, as e.g., needed for adaptive "closed loop" stimulation, our stimulation/recording setup may be valid and ethically justifiable in neuroscience rat models.

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P093

Experimentelle Genauigkeitsanalyse – Robotik vs Stereotaxie – eine Phantomstudie
Experimental comparison of robotic and stereotactic accuracy – a phantom study

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[2]Universitätsklinikum Köln, Stereotaktische Neurochirurgie, Köln, Germany
[3]Goethe Universität Frankfurt am Main, Biostatistik, Frankfurt am Main, Germany

Objective

The development of robotic systems has brought an alternative to frame-based stereotactic procedures. In this experimental setting we aim to reduce procedural errors to a minimum when comparing the ROSA robot and the Leksell stereotactic system regarding mechanical accuracy.

Methods

In order to precisely compare mechanical accuracy, the stereotactic system was chosen as means of referencing for both methods. We performed a 0,67 mm slice thin layer CT Scan with an acrylic phantom fixed to the frame and a Localizer enabling the software to recognize the coordinate system. For each of the 5 phantom targets, 2 different trajectories were planned, resulting in 10 trajectories. We performed a series of 5 cycles, each time based on a new CT scan. We therefore analysed 50 trajectories for each method. X-rays of the final canula position were fused with the planning data. The coordinates of the target point and the endpoint of the robotic or stereotactic probe were visually determined using the robotic software. The target point error (TPE) was calculated applying the Euclidian distance. We separately calculated the depth deviation along the trajectory and the lateral deviation.

Results

In this experimental setting, robotics was significantly more accurate, with an arithmetic TPE mean of 0.53 mm (95% CI 0.41 – 0.55 mm) compared to 0.72 mm (95% CI 0.63 – 0.8 mm) in stereotaxy ($p < 0.05$). Direct comparison showed a mean difference in TPE of 0.19 mm. In robotics, the mean depth deviation along the trajectory was -0.22 mm (95% CI -0.25 – -0.14 mm). The mean lateral deviation with 0.43 mm (95% CI 0.32 – 0.49 mm). In stereotaxy, the mean depth deviation amounted to -0.20 mm (95% CI -0.26 – -0.14 mm), the mean lateral deviation to 0.65 mm (95% CI 0.55 – 0.74 mm).

Conclusion

Both robotic and stereotactic approaches proved accurate. In this experimental phantom study, the robotic procedure showed significantly higher accuracy. For both methods, procedural factors occurring during surgery might have a more relevant impact on overall accuracy.

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P094

Erhöhte intraoperative Impedanzwerte während der Implantation von Elektroden für die Tiefe Hirnstimulation
High impedance values during the implantation procedure of leads for deep brain stimulation

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Objective

The implantation of electrodes into basal ganglia nuclei for deep brain stimulation (DBS) is a routine technique in the treatment of movement disorders. As a final step during the implantation procedure, impedance measures document correct technical functioning of the implanted system. Hence, abnormally high or low impedance measures may require extensive troubleshooting. We here present cases of abnormally high impedances and troubleshooting in a series of patients implanted with DBS electrodes.

Methods

We investigated the intraoperatively determined impedance measures of the DBS system in fifty consecutive patients implanted in our department. These measures were correlated to image findings in intra- and postoperative CT scans, to the implanted system, surgical incidents, total operating time, brain side for initial implantation and the number of microelectrodes used for evaluation of the target region.

Results

In all patients, leads and DBS systems were implanted without incident or complication. In 4 of 40 electrodes implanted with segmented directional leads, increased impedance values were measured (see table for example). Operating time, brain side for initial implantation, and the number of microelectrodes did not differ to the patient group with normal impedance measures. The connections from electrodes to the extensions and to the stimulator (IPG) were electrically intact. In one patient, a CT scan directly after surgery revealed intracranial air around electrode contacts which was not apparent in the other patients who received their CT only one day later. In a repeated measurement of impedances, earliest two hours after surgery in one patient, all aberrant impedance values were returned to normal. In 5 of 60 electrodes implanted with electrodes with classical ring contacts, intraoperatively increased impedance values could invariably be solved by readjusting connections between cables and / or cables and IPG.

Conclusion

Intraoperative high impedance values of the DBS system should lead to extensive troubleshooting. If single segments of the directional lead contacts are identified as the most probable cause, surgery may be routinely completed and impedance measurement should be repeated two to four hours later. We found air around the leads in CT scans as the most probable cause of transient high impedance measures.

Fig. 1

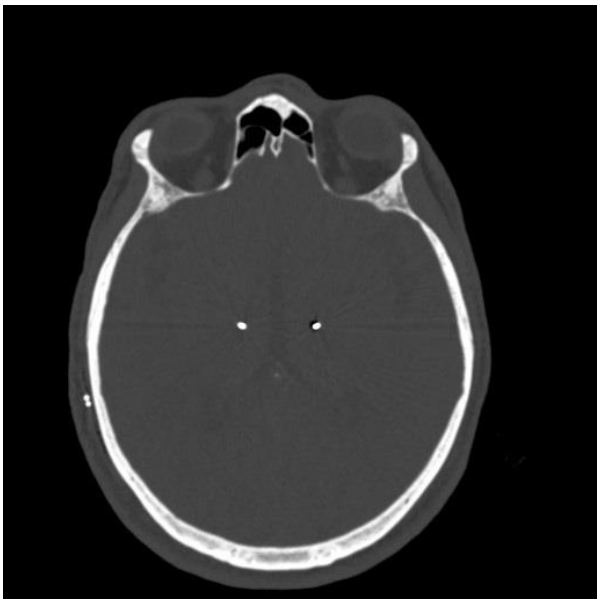

Fig. 2

Configuration

IPG

Device Type:
Vercise Genus™
R16

Model
DB1216

Serial
501147

Implant Date
28 Oct 2020

Firmware
9028506-102-00

Battery Type
Rechargeable

Battery Voltage
3.96 V

Patient Amplitude
OFF

Port: L

Lead Type: DB-2202 | *Impedances(Ω)* | *Last measured 28 Oct 2020 10:29:48*

Hemisphere: Left
Target: STN
Lead Orientation: Anterior

	case	E8	E7	E6	E5	E4	E3	E2
E8	1656							
E7	1904	2964						
E6	1787	2875	2875					
E5	3269	4449	4387	4110				
E4	3166	4429	4384	4410	6046			
E3	2374	3623	3715	3421	5199	4269		
E2	+9999	+9999	+9999	+9999	+9999	+9999	+9999	
E1	2586	3920	4103	3972	5542	5066	4208	+9999

Port: R

Lead Type: DB-2202 | *Impedances(Ω)* | *Last measured 28 Oct 2020 10:29:48*

Hemisphere: Right
Target: STN
Lead Orientation: Anterior

	case	E8	E7	E6	E5	E4	E3	E2
E8	853							
E7	1653	2008						
E6	1803	2155	2690					
E5	2139	2498	3104	3118				
E4	1612	2136	2715	2941	3273			
E3	2251	2761	3427	3486	3900	3157		
E2	1754	2291	2960	3098	3358	2616	3209	
E1	946	1554	2276	2431	2754	2023	2687	2152

Funktionelle Neurochirurgie und Schmerz I, Freie Themen/*Functional neurosurgery & pain I, free topics*

P095

Implantation von direktionalen Elektroden führt zu einer verbesserten Ergebnisqualität der tiefen Hirnstimulation bei Patienten mit idiopathischen Parkinsonsyndrom

Implantation of directional leads improves patient outcome after deep brain stimulation in Parkinson's disease

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Objective

Recent developments of more complex lead designs for deep brain stimulation with a greater number of contacts and the ability to alter the shape of stimulation fields were introduced to enlarge the therapeutic window in deep brain stimulation. We evaluated, whether these directional leads have also an impact on short-term patient outcome.

Methods

Twenty patients in total underwent deep brain stimulation into the subthalamic nucleus (STN-DBS) and were divided to the following two groups: ten patients being operated with non-directional leads (group 1) and further ten patients underwent surgery with directional leads (Boston Scientific) (group 2). The postoperative improvements were measured 3 months after DBS surgery and compared to preoperative conditions. The programming algorithm was equal in both groups. Group 2 was only stimulated directionally.

Results

No hemorrhage or permanent side effects occurred. The Unified Parkinson"s Disease Rating Scale (UPDRS) III (on medication/on stimulation) showed a reduction of 52% in group 1 and 73% in group 2 compared to preoperative UPDRS III (on medication), while the levodopa equivalence dose (LED) could be reduced by 59% (group 1) and 63% (group 2). No differences were observed for UPDRS IV in both groups (reduction of 73% in group 1 and 71% in group 2). The needed stimulation amplitude was 2.5V in group 1 and 2.2V in group 2.

Conclusion

Patient outcome after STN-DBS measured by reduction of UPDRS III and LED was better in patients with implanted directional leads. The impact of directional leads on the outcome of DBS patients should be confirmed with a prospective blinded trial with long-term follow-up.

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P096

Was wissen "Nicht Neurochirurgen" über DBS? – Ergebnisse des DBSurvey
Knowledge about DBS surgery of referring physicians – results of the DBSurvey

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Objective

Deep brain stimulation (DBS) has become an accepted therapeutic alternative for a multitude of neuropsychiatric disorders. Nevertheless, many more patients could be potentially treated with DBS. This raises the question, if clinicians are too reserved regarding DBS treatment and what could be underlying reasons. Therefore, the Swiss physicians and medical students current state of knowledge, experience with and expectations from DBS was evaluated.

Methods

A comprehensive nationwide online survey among referring physicians including general practitioners (GP), neurologists and psychiatrists as well as among students from all medical schools in Switzerland was conducted. The survey web forms consisted of multiple choice and open questions and were available in German, French and Italian language.

Results

Data from 401 responses was analyzed. General knowledge regarding DBS principles was high ("good knowledge" n=140, "heard of it" n=228, "never heard of it" n=32) with mainly positive (34%) and only few negative (4%) experiences reported. The risk of permanent neurological deficit (6%±9%), surgical site infection (6%±8%) and hemorrhage (6%±7%) associated with DBS was estimated as comparable and increased. Expected motor symptoms relief due to stimulation was estimated to be 20-80%, whereas non-motor symptoms were presumed as responding not sufficiently by the majority of participants (90% and 49%, respectively). Parkinson"s disease and tremor were considered as validated indications by most respondents (79% and 55%, respectively). Up to 40% of patients were estimated possible candidates for surgery. For epilepsy patients, most physicians preferred DBS over a classic lesionectomy (n=209 vs. n=71, "don"t know" n=109).

Conclusion

For the majority of physicians and doctors-to-be in Switzerland, the results of this survey revealed a gratifying solid basic knowledge of DBS and its potential, a mainly positive acceptance and relatively realistic expectancies regarding clinical results, response rates and associated risks of DBS therapy.

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P097

Mediation der Tremorreduktion durch den kreuzenden und nicht-kreuzenden Teil des dentato-rubro-thalamischen Trakt (DRTT) bei der tiefen Hirnstimulation bei essentiellem Tremor

Mediation of tremor reduction by the decussating and non-decussating part of the dentato-rubro-thalamic tract (DRTT) in deep brain stimulation in essential tremor

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Objective

Preceding studies found a main influence of the dentato-rubro-thalamic tract (DRTT) in the mechanisms of Essential Tremor. However, the influence of different parts of the DRTT, consisting of a ipsilateral and a decussating part, has not been investigated yet with respect to tremor reduction. Additionally, in only a few studies, probabilistic tractography was used. The aim of this study was to evaluate the influence of the ipsilateral and the intersecting part of the DRTT on clinical tremor improvement in Essential Tremor.

Methods

A cohort of 10 patients having received bilateral DBS of the VIM between 2016 and 2019 was analysed retrospectively. Preoperative DWI scans were performed on patients under general anaesthesia at a 3T MRI scanner with 64 gradient directions. We used a workflow for probabilistic fibre tracking using FSL 6.0.3 (fsl.fmrib.ox.ac.uk/). Electrodes were reconstructed using LeadDBS (lead-dbs.org). We calculated distance maps from the different parts of the DRTT and correlated distances to the pole coordinates with clinical data on tremor reduction derived from neurological single pole testing.

Results

3 patients with current-steered systems were excluded from further statistical analysis due to inadequate comparability. Regarding postural tremor, contacts with good clinical response significantly correlated with lower distances to both parts of the DRTT (non-decussating $p<0,05$; crossing $p<0,01$). Good contacts were located closer to the crossing part of the DRTT. Bivariate correlation analysis showed significant results for both parts of the DRTT with a higher Pearson-coefficient for the crossing part (Pearson 0,295 vs. 0,429). Regarding intentional tremor, contacts with good clinical response significantly correlated with lower distances to the crossing part ($p<0,01$). In contrast, the non-decussating part did not show significant results. Bivariate correlation analysis resulted in significant results for both parts of the DRTT with a higher Pearson-coefficient for the crossing part (Pearson 0,356 vs. 0,405).

Conclusion

Pathophysiologically, growing evidence suggests a disruption of cerebellar-thalamic-basal ganglia-motor cortex networks in Essential Tremor. Therefore, the DRTT is considered to play a major role in these mechanisms. Our data suggest an involvement of both parts of the DRTT in tremor reduction indicating mediation of DBS-effects by both fibre bundles, even if the crossing part showed stronger correlations with good clinical responses.

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P098

Netzwerkaktivität in humanem Kortexgewebe in Mikro-Elektroden Array Recordings – ein potentielles Fenster zu kortikaler Mikrokonnektivität in gesundem und pathologischem Hirngewebe

Network activity in human cortical tissue recordings on micro-electrode arrays – a potential window to cortical micro-connectivity in normal and pathological human brain

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[4]Universitätsklinikum Aachen, Department of Epileptology, Neurology, Aachen, Germany
[5]University of Tübingen, Department of Neurosurgery, Tübingen, Germany
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Objective

Micro-Electrode Arrays (MEAs), novel culturing methods for human brain tissue, and advanced tools in data science enable us for the first time to analyze massive parallel recordings of spike trains in human cortical tissue. Measuring neuronal connectivity on a millimeter scale in real time can help us to understand cortical microcircuits. Here we recorded human tissue of neurosurgical interventions *in vitro* on MEAs to investigate spatio-temporal patterns (STP) in spiking activity.

Methods

Organotypic human cortical slices were prepared from tissue resected from epilepsy patients undergoing surgical treatment. Slices were cultivated as described (Wickham et al. 2020) and the optogenetic actuator Channelrhodopsin-2 was transduced into the slices for specific stimulation. Recordings were obtained using a 256-MEA (electrode spacing: 200µm) combined with optogenetic stimulation. Data analysis was performed using Python including packages numpy, elephant, neo and viziphant. Bursts were detected using an interspike-interval method. Spiketrains were analyzed for STP using SPADE ("Spike Pattern Detection and Evaluation") with a minimum of 30 instances and 3 spikes to qualify as pattern on one exemplary recording (120 seconds). We investigated for optogenetic-induced patterns and spontaneous activity.

Results

On multiple recordings we found massive network bursts with a spatial extent of several 100µm that lasted for seconds seemingly independent of optogenetic stimulation. We detected >80.000 spiking patterns. Specific patterns only observed during network bursts appeared >90 times and could be found with a spatial extent up to 1.8 mm and latency times of 130ms (SPADE p-value=0.047), thus indicating a robust polysynaptic neuronal connection possibly explaining distant tissue epileptogenic micro-foci.

Conclusion

Within network bursts we identified several spatio-temporal patterns with remarkable spatial extent and latencies between spikes. This method is a promising tool for investigations of electrophysiological features of cerebral pathologies such as epilepsy or glioma. These features potentially reveal novel aspects of pathogenesis. Next steps will be to integrate these physiological findings into histo(patho)logical context.

Wirbelsäulenchirurgie/Spinal surgery

P099

Spinale Tumore – eine Diagnose, die man bei SAB nicht übersehen sollte – Literaturrecherche und Fallbericht
Spinal tumour – a diagnosis that shouldn't be missed in SAH – literature review and case report

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Objective

The incidence of SAH is around 6/100 000 people annually. In 15-37% of the cases, no origin of the bleeding is found. Further diagnostics in angio-negative patients can be challenging and are not standardized. Rarely, a spinal pathology is the cause for SAH (0.5-1% of the cases). The aim of this study was to define criteria to identify the patients with a possible spinal origin of the SAH. In those few patients, a spinal axis MRI workup may be useful. We present a literature review and a case of a 61-year old patient with SAH due to spinal Schwannoma. The patient initially presented headache, vomiting and urinary retention. A cranial CT showed a SAH and no source of bleeding. Due to worsened ability to walk a spinal axis MRI was performed. An intradural tumor was found and supposed to be an ependymoma. Surgery was performed without complications, histopathology revealed a Schwannoma WHO°I.

Methods

A literature review was performed based on Pubmed/Cochrane/Google Scholar for SAH & Spinal Schwannoma / SAH & Ependymoma. The review was performed according to the PRISMA guidelines. Out of 297 resulting articles, 32 were included. We analyzed a total of 44 cases of spinal origin SAH with classical cerebral SAH symptoms such as sudden headache and nuchal rigidity between 1951 and 2020. We dichotomized symptoms according to the tumor localization and according to the SAH.

Results

44 patients were included, 14 Schwannomas (31.8%) and 30 ependymomas (68.2%). Men represented 77% of the Schwannoma and 64% of the Ependymoma cohort. Median age was 45 years in the Schwannoma group vs 29 years in the Ependymoma group. Tumors were equally distributed between the cervical and lumbar spine for Schwannomas (cervical 36%, lumbar 29%), Ependymomas were mostly located in the lumbar spine (85%) Clinical symptoms that could topographically be localized to the spine were found in 9 out of 14 patients (65%) of the Schwannoma group: Radicular pain (28%), motor deficit (22%), and incontinence (14.5%) and were found in 93% of the Ependymoma group as: Radicular pain (40%), motor deficit (20%) and incontinence (17%).The SAH was diagnosed in 86.5% by a LP. Spinal pathologies were diagnosed through MRI or Myelogram, 14 (32%) of the cases were reported before the era of MRI and CT.

Conclusion

The key finding of our study was that the presence of any clinical symptom that can topographically be localized to the spine must prompt a complete workup of the spinal axis in patients with SAH and no cerebral source of bleeding.

Wirbelsäulenchirurgie/*Spinal surgery*

P100

Kurz- bis mittelfristige Analyse der Morbiditäts-, Mortalitäts- und Komplikationsrate bei den über neunzig-jährigen Patientinnen, die an einer akuten traumatischen Dens-Fraktur Typ-II mit einer navigierten atlanto-axialen Fusion operiert wurden – eine retrospektive Studie aus einer prospektiven Datenbank

Short- to mid-term analysis of the morbidity, mortality and complications rate in nonagenarians undergoing navigated atlanto-axial fusion for acute traumatic odontoid type II fractures – a retrospective study from a prospective database

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Objective

Odontoid type II fractures are the most common cervical spine injuries in patients over 65 years. The decision for surgical treatment in patients over 90 years of age is still controversially discussed. The aim of this study was to assess early morbidity and mortality and long-term outcome in nonagenarians undergoing atlanto-axial posterior instrumentation.

Methods

Out of 150 patients, a total of 15 patients with an acute traumatic odontoid type II fracture were retrospectively analyzed. Complications, morbidity and mortality rate, as well as length of ICU and hospital stay were determined. Clinical and radiological follow-up was conducted based on available and acquired information based patients" family support.

Results

Mean age was 91.4 years (mean: 90-96 years). No in-hospital mortality was observed. All surgical procedures were performed uneventfully with no new neurological deficits. Five patients died during the follow-up period. Average time to death was 26.6 months. Mean length of hospital stay was 13.4 days and 1.9 days for ICU. Blood transfusion was necessary in three patients. Two patients (13%) developed urinary tract infection and one patient (7%) developed a delirium. Another patient (7%) developed a septic shock with full recovery within several weeks. The average follow-up was 36 months (10–72 months). Implant-related complications occurred in one patient (7%).

Conclusion

Our current study confirms that atlanto-axial fusion by using spinal navigation in nonagenarians is a safe and effective procedure with few complications in multi-morbid patients ages 90 years and older, demonstrating further that surgical treatment of odontoid type II fractures in nonagenarians does not negatively impact survival.

Wirbelsäulenchirurgie/*Spinal surgery*

P101

Die Rolle der intraoperativen Bildgebung (3D Rotation mit dem C-Arm versus O-Arm) in der spinalen Chirurgie – Ergebnisse eines Single-Centers

The role of intraoperative image guidance system (3D C-arm vs. O-arm) in spinal surgery – results of a single-centre study

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Objective

Spinal dorsal instrumentation is an established treatment option for a range of spinal disorders In combination with navigation, intraoperative fluoroscopy reduces the risk of incorrectly placing screws. This study aimed to evaluate the efficacy and validity of fluoroscopy (3D rotation of C-arm *vs.* O-arm) for placing screws and verifying the placement during spinal surgery as compared with postoperative control CT scans.

Methods

In this retrospective single-center study, 240 patients were included between July 2017 and April 2020. Intraoperative images were acquired using a Siemens-Arcadis Orbic 3D C-arm with a dedicated navigation system (Brainlab) or using O-arm (Medtronic) with a dedicated navigation system (S7 StealthStation). The final position of the screws was verified by a postoperative CT scan. Finally, we compared mismatches between intraoperative and postoperative CT imaging results using Rampersaud-grade (A-D)

Results

A total of 1614 screws were included in the evaluation: 94 patients in the C-arm group (cAG) and 146 in the O-arm group (oAG). After implantations, a second scan was performed intraoperatively. In cAG, 3% (n=20) of the screws had to be replaced directly due to inadequate positioning with median or lateral breaches, and 3.5 % of screws in oAG (n=35). An A-score was achieved for 85.7% in the cAG and 87.4% in the oAG. A B-score was found in 11.5% in the cAG and 11.9% in the oAG. In the cAG, a C-score was achieved for 2.5% and in oAG for 0.7%. For 0.3% of the screws a D-score was found in cAG and for none in oAG.

Conclusion

The data of our study shows that placement of screws using intraoperative imaging in combination with navigation tool is accurate. Furthermore, navigation coupled with the O-arm had significant advantages in accuracy over navigation with 3D C-arm fluoroscopy. However, both systems offer a high level of accuracy.

Wirbelsäulenchirurgie/*Spinal surgery*

JM-PSN-02

Der Blutdruck hängt mit ausgewählten Persönlichkeitsmerkmalen in der Gruppe der Patienten zusammen, die wegen Arthrose der Wirbelsäule behandelt wurden – Vorstudie

Blood pressure is related to selected personality traits in the group of patients treated for osteoarthritis of the spine – preliminary study

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Objective

Previous studies suggest a relationship between personality traits and the level of blood pressure. In addition, they indicate a relationship between blood pressure and cardiovascular risk, the occurrence of nervous system diseases (e.g. stroke, dementia) and the occurrence of perioperative and postoperative complications. However, very few of these studies have been conducted among patients operated for spine osteoarthritis. The aim of our preliminary study was to evaluate the relationship between selected personality traits and temperament, as well as blood pressure.

Methods

The study included 33 people (including 17 women) aged approximately 47.1 years (SD = 9.66) and with a mean 13.5 years of education (SD = 3.01): 78.8% were living in the city, 69.7% were working, and 90.9% were married or with a partner. All participants received blood pressure measurements and were evaluated using the personality inventory (NEO-FFI) and the temperament questionnaire (FCZ-KT).

Results

Statistically significant correlations were observed between blood pressure and rate of activity (Alertness, $p < .05$) and the ability to respond adequately to long-term stimulation (Endurance, $p < .05$). Inverse correlations were found between blood pressure and the organization of activities, persistence (Conscientiousness, $p < .05$), openness to new experiences (Openness, $p < .05$), the ability to respond to weak stimuli (Sensitivity, $p < .01$) and the tendency to continue behavior after the end of the situation (Perseverance, $p < .05$).

Conclusion

The results indicate the presence of a relationship between personality and temperamental traits and blood pressure level. This may suggest that the intensification of selected personality and temperamental traits predisposes to the appearance of higher (excessive) blood pressure, and thus an increased risk of cardiovascular complications in the perioperative period. However, this hypothesis requires further prospective studies in patients operated for osteoarthritis of the spine. It would also seem advisable to include psychotherapeutic interactions with patients waiting for surgery and characterized by a specific personality profile.

P102

Komplikationen und Outcome bei Patienten mit Leberzirrhose Stadium Child B&C nach instrumentierten Wirbelsäuleneingriffen

Complications and outcome of patients with liver cirrhosis Child stages B&C after spinal instrumentation

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Objective

With this study we want to share our experience and outcome with patients with liver cirrhosis Child-Pugh stages B and C after instrumented spine surgery. We already know that patients with cirrhosis (Child-Pugh B & C) are high-risk patients due to their coagulation problems, higher infection risk, as well as osteopenia.

Methods

Between 2012 and 2020 we have operated on 14 patients with liver cirrhosis (Child-Pugh B & C) and spinal fractures (spontaneous and traumatic). All these patient underwent instrumented spinal surgery. This retrospective study is based on the patients" conditions, intra- and postoperative complications, and the patient outcome scores.

Results

The study group comprised 14 cirrhotic patients (11 males and 3 females). The average age was 59 years (±26). The average length of stay was 36 days (±27). 4 (29%) patients were admitted with neurological deficits with hypoaesthesia, 10 (77%) patients were admitted with thoracolumbar pain. One patient was stabilised with wire cerclage due to dens fracture, 5 patients underwent dorsoventral instrumentation, and in 5 patients we performed only posterior fusion due to thoracic and lumbar vertebral body fractures. 1 patient received an ACDF with plating. 5 (35.5%) patients experienced postoperative material dislocation. One of these patient suffered postoperative paraparesis and also 5 (35.5%) of this group had to be re-operated on due to postoperative epidural bleeding. 4 of the patients had postoperative wound infections (28.6%) and one of them became septic (7.1%). Postoperative pain reduction was achieved in only three patients (21.4%). 7 (50.0) of the cohort required up-titration of their pain medication postoperatively and one patient had permanent paraparesis. One (7.1%) patient died postoperatively due to drastically deranged coagulation. The overall complication rate was about 78.6%.

Conclusion

In our experience, in most of patients with liver cirrhosis (Child-Pugh stages B & C) we were unable to improve the neurological or pain situation with spinal instrumentation. The risk of neurological complications and infections are markedly higher in patients with cirrhosis. These patients require in-depth and individualised evaluation before undergoing spine surgery with instrumentation.

Wirbelsäulenchirurgie/*Spinal surgery*

P103

Entwicklung eines Maus-Wirbelsäulen-Modells zur Erforschung 3D-gedruckter bioaktiver spinaler Implantate
Development of a murine spine model for 3D printed bioactive spinal implants

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Objective

The development of new materials for spine implants, e. g. with osteoinductive properties, is in the focus of experimental and preclinical research. For *in vivo* examinations, these studies commonly use large animal models, e. g. in sheep, while small animal models are uncommon. However, a murine spine model would be advantageous because of the broad availability of transgenic strains necessary to study osteointegration on the cellular level. In this proof of principle study, the feasibility of a murine model to perform a vertebral body replacement with an individually 3D printed implant was evaluated.

Methods

3 C57BL/6NRj mice were euthanized. The cervicothoracic spine was scanned in a µCT. The scan data was segmented and exported as a 3D model to a 3D software. Next the cervical vertebral bodies C4 and C5 were virtually removed and a tube shaped intervertebral implant with additional plate for fixation was designed. The implant was then fabricated on a stereolithography 3D printer measuring 4100 µm (+/- 40) x 1600 µm (+/- 12). In a next step the implants were implanted into 9 mouse cadavers after removal of 2 cervical vertebrae with a micro drill via an anterior approach and fixed with micro screws. After the preparation, all cadavers received transcardiac and esophageal perfusion with a radiopaque casting agent. The samples then underwent µCT scanning.

Results

The surgical procedure was carried out in 9 murine cadavers. In the first 4 cases, a fracture of the implant or bone occurred during insertion. These cases were excluded from further analysis. In the further cadavers, the surgical procedure was carried out successfully. The aim of implant and screw placement, and µCT scanning was achieved in all 5 cases. Mean surgical time was 35 min +/- 13 min. In 2 of the 5 cases vertebrae C4/5 and in 3 of the 5 cases vertebrae C5/6 were successfully removed. A screw deviation with intraspinal screw position was observed in 7/10 screws (70%). Other gross misalignments of the implants were not observed. Leaking of the contrast agent indicating lesions of the carotid arteries or the esophagus were not observed.

Conclusion

Our study demonstrates that a murine model for spine implants is feasible from the surgical and imaging perspective, while especially the screw fixation of the implants still needs to be improved. Our 3D printing technique allows fast fabrication of individual implants. Animal studies will be needed to test the feasibility of the model for *in vivo* examinations.

Wirbelsäulenchirurgie/*Spinal surgery*

P104

Nachweis von Cutibacterium acnes in gesundem Knochenmehl – Krankheitswert, Kontamination oder Besiedlung?
Presence of cutibacterium acnes in healthy bone specimens of the skull in cranial neurosurgery – pathogenic, contamination or colonisation

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Objective

Cutibacterium acnes (formerly Propionibacterium) has been discussed to provoke low-grade infections leading to aseptic bone resorption in patients undergoing autologous cranioplasty. While its presence has been described in osteolytic processes, its pathogenic role remains a matter of debate. Our aim was to perform a control study investigating the presence of bacteria in the calvaria of patients undergoing cranial surgery without visible signs of high- or low-grade infections.

Methods

We performed a prospective monocentric study enrolling patients prior to an operative neurosurgical treatment including a craniotomy. Informed consent was obtained and the bone meal accumulated during the craniotomy was collected and sent for microbiological analysis. Patients with clinical or radiological signs of septic or aseptic bone infections were excluded. We assessed perioperative data such as antibiotic prophylaxis, comorbidities and complications such as wound healing disorders.

Results

In total, bone specimen from 42 patients were analyzed. Patients were stratified in 2 groups: first surgery (26 patients) and patients undergoing cranial surgery for tumor recurrence (16 patients). In 29/42 patients (69%), the microbiological analysis revealed the presence of bacteria (13/16 preoperated and 16/26 first operated patients). The analysis mainly revealed the presence of Cutibacterium acnes (diagnosed in first surgery patients in 16/16 patients). Findings in the preoperated group included: Cutibacterium acnes (n: 8), Staphylococcus (Staph.) epidermidis (n: 1) and Enterobacter cloacae (n: 2) as well as Staph. capitis and Staph. warneri (both n: 1). In 5/42 patients we detected wound healing difficulties on the further clinical course, 4/5 patients had a Cutibacterium acnes presence. None of the patients suffered from bone resorption on the further course of treatment.

Conclusion

In more than half of the patients, we detected the presence of bacteria in the bone meal extracted without signs of infections. Reoperation did not make a difference. Cutibacterium acnes as the most frequent germ might be causative for a high number of wound healing problems. Whether this can be avoided by early targeted postoperative antibiotics needs to be examined.

Wirbelsäulenchirurgie/*Spinal surgery*

P105

Seltener Fall einer pilz-bedingten Spondylitis in der HWS und BWS – Fallbericht
Rare case of complex fungal spondylitis in the cervical and thoracic spine – case report

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Objective

Spondylitis is an infection of the vertebral column, the incidence of which is increasing due to an increase in the susceptile population and improved ascertainment. This disease has been associated with a wide range of microorganisms. Fungal spondylodiscitis is uncommon (0.5-1.6%) and strongly associated with immunosuppression and diabetes. A rare case of fungal spondylitis in a semi-neutropenic patient because of history of lung cancer is reported herein.

Methods

A case of fungal spondylitis of C3-T10 was diagnosed and suspicious in MR imaging. The woman showed history of treated lung cancer by radiation and chemotherapy in 2015 and 2018 and suffered from immobilizing neck and upper back pain (VAS 10). The diagnosis was finally obtained by twice trans-pedicular biopsies of para-vertebral and intra-vertebral contrast enhancements in T6/7. During the course, multiple blood cultures were provided. Scanty samples of Candida species could be verified, especially in a lung cave via CT punction.

Results

Drug therapy consisted of antimycotic medication (Voriconazol) for 12 months, supporting antibiotic therapy for 3 months (amoxicillin, clavulanacid) because of potential bacterial load, and a 3-level analgetic medication for 6 months. A complex orthesis for cervical and thoracic spine lead to substantial posture and pain relief. Regular MR and CT imaging and blood controls were performed (first every 6 weeks, than every 3 months). The patient recovered well, vertebral bone consolidated and so far, no stabilization surgery was necessary.

Conclusion

Diagnosis of fungal spondylitis/spondylodiscitis is rare and often delayed or missed. Physicians should consider this entity in differential diagnosis of vertebral pain especially in immunosuppressed patients, in order to initiate an adequate therapy and to prevent further spinal lesions and disability.

Fig. 1

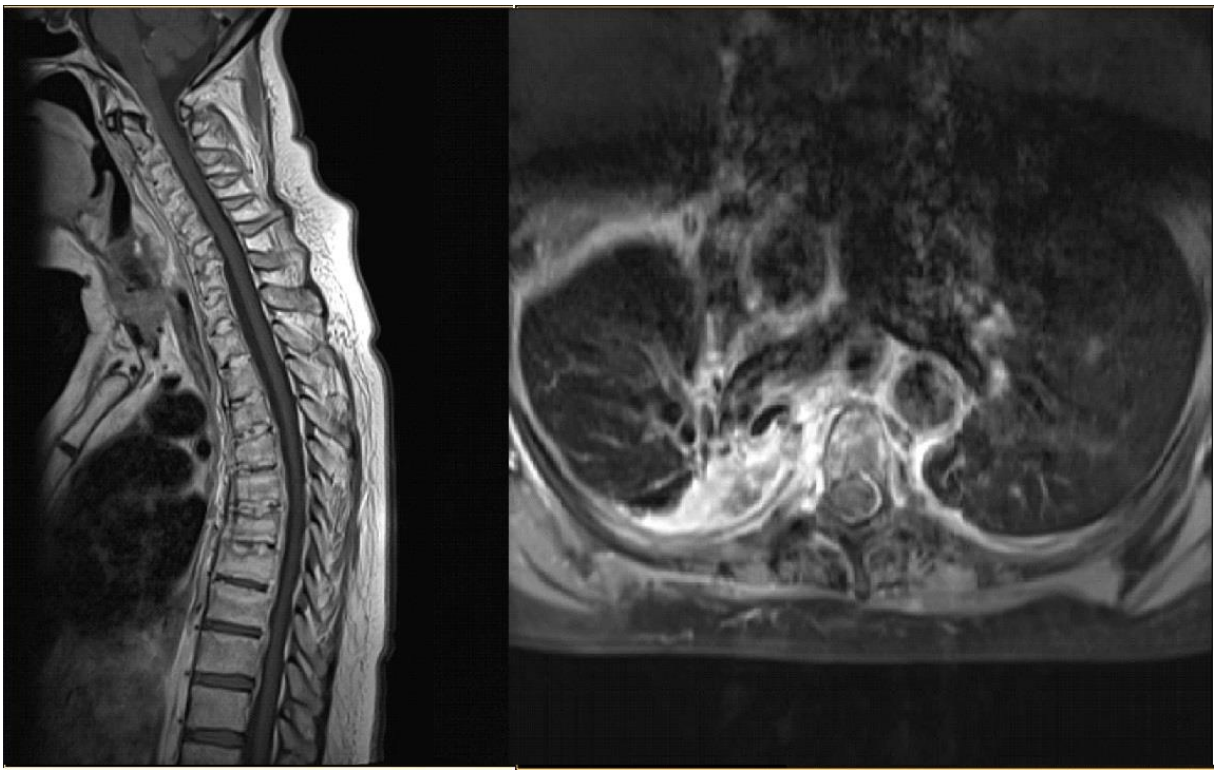
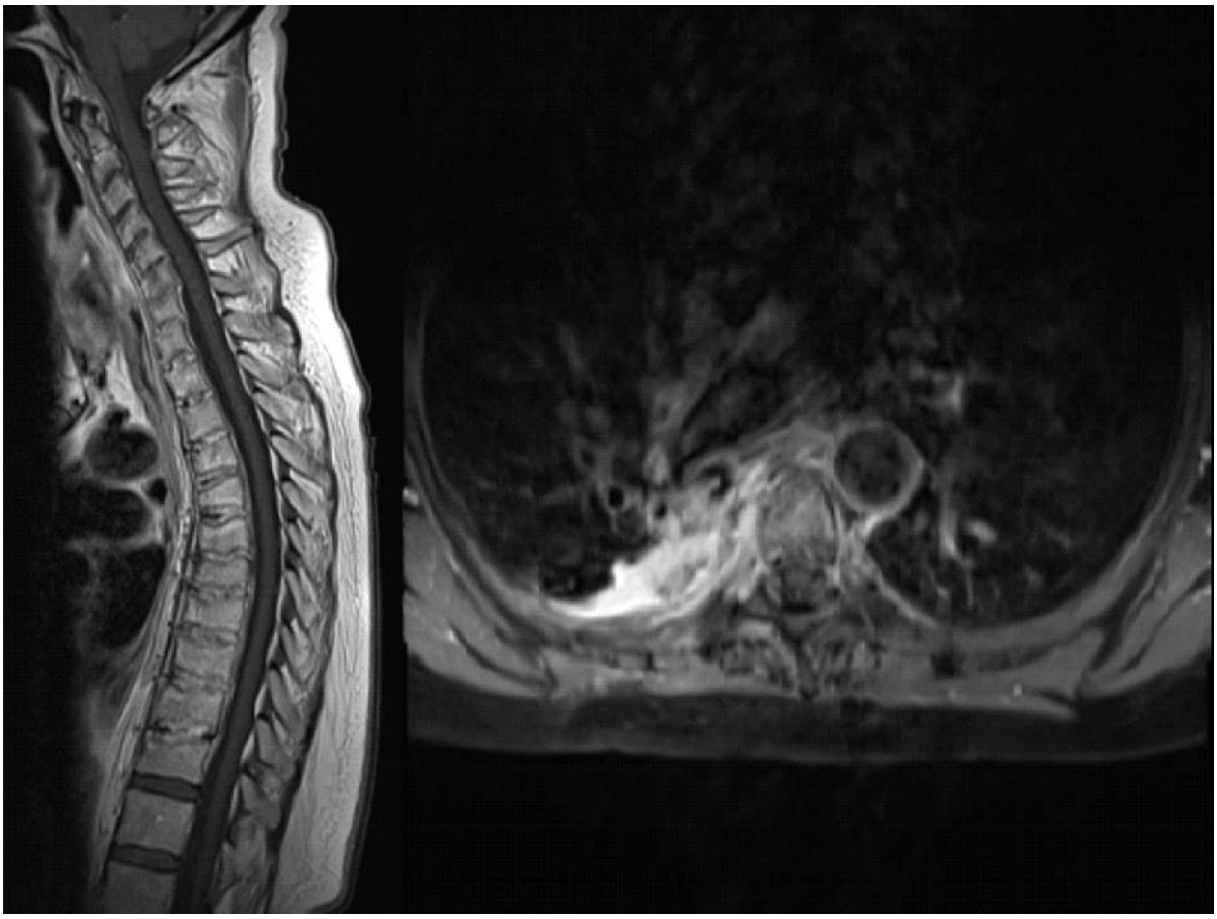


Fig. 2



P106

Sagittale Deformitätenkorrektur mit expandierbaren Wirbelkörperersatz Cages mit großen Endplatten in der thorakolumbalen Wirbelsäule

Sagittal deformity correction with expandable cages with large endplates for thoracolumbar vertebral body replacement

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Objective

Vertebral body replacements (VBRs) with expandable cages with larger endplates allow more distraction due to their larger footprints. Aim of this study was to analyze the rate of segmental correction and subsidence rates in patients with osteoporotic and pathological fractures.

Methods

A retrospective analysis from February 2015 until July 2019 of patients following a staged posterior pedicle screw instrumentation and VBR with expandable cages with large endplates (Samson ®, HumanTech) was performed. Plain radiographs and CT- imaging were performed before and after the surgery and at last follow up. Radiological data such as local sagittal angle and segmental height as well as revision rates were analyzed.

Results

A cohort of 58 consecutive patients were identified. 62% were female and the median age was 68 years. Median follow up was 8 months. There were 22, 20, and 16 cases of osteoporotic fractures, spondylodiscitis and 16 metastases respectively. VBR were performed in 31 and 27 in the thoracic and lumbar spine, respectively. There was a significant gain in segmental height of 8 and 11 mm in the thoracic and lumbar spine, respectively. There was a significant segmental angle correction 4° and 6° degrees in the lumbar and thoracic spine, respectively (p=0.000). These significant differences remained throughout follow up (p=0.001). In spondylodiscitis cases, cage over-distraction (mean 6 mm) was associated with higher subsidence rates (mean 8mm, p=0.013) on follow up examinations, which resulted in revision surgery in 3 cases (5%).

Conclusion

Expandable vertebral body replacements with larger endplates achieve satisfactory correction of sagittal height and angle. However over-distraction, especially in infectious cases, is associated with higher subsidence rate.

Wirbelsäulenchirurgie/*Spinal surgery*

P107

Dyspnoe aufgrund zervikaler Spinalkanal-/Foramenstenose – postoperative Rückbildung nach anteriorer Dekompression – Fallbericht

Severe dyspnea due to cervical spinal/foraminal stenosis C3/4 – postoperative regression after anterior decompression – case report

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Objective

A case of a cervical spinal and foraminal stenosis C3/4 is presented which caused a high-grade exertional dyspnea mimicking congestive heart failure.

Methods

Case report and literature review

Results

We report about a 58-year-old man who presented with progression of exertional dyspnea limiting his walking distance to a maximum of 80 meters. Other signs of radiculopathy such as pain or motor weakness were denied. Respiratory symptoms started one-and-a-half year earlier and were investigated extensively but ruled out cardiac pathologies. A left-sided diaphragmatic elevation resulted from a traffic accident twelve years ago.

Neurography showed no compound muscle action potentials of the left N. phrenicus proving decompensation of prior inapparent phrenic dysfunction. Along being asthmatic and obese (BMI 38.2 kg/m2) he is using nCPAP due to a chronic obstructive sleep apnea. MRI revealed cervical spinal stenosis with foraminal stenosis at the level of C3-C4. We performed an anterior cervical discectomy with uncoforaminotomy on both sides. Three months after surgery his dyspnea resolved completely making him able to walk 3 kilometers. Increase of physical activity made him lose 10 % of his body weight (BMI 32.7 kg/m2).

Our case is a rare example of a cervical spinal stenosis leading to a high-grade exertional dyspnea as the only symptom. Radiculopathies of C3-C4 level most commonly cause radiating pain and sensory deficits. Motor impairment often remains inapparent. Progression of dyspnea on exertion may drastically reduce physical activity level leading to fast fatiguability and weight gain. Mimicking symptoms of heart failure a cardiac pathology should be ruled out primarily along other diseases of respiratory dysfunction. However, MR imaging may identify spinal pathologies and be useful for evaluating possible candidates for neurosurgical intervention.

Conclusion

To our knowledge, this is the tenth case worldwide reporting about a cervical spinal stenosis at the C3-C4 level with accompanying foraminal stenosis leading to severe dyspnea. Our intervention led to complete regression of exertional dyspnea after anterior decompression. Affection of the diaphragmatic innervation is thought to be the underlying mechanism and can be investigated via nerve conduction studies along electromyography. The presented case is rare but has to be kept in mind when progression of respiratory complaints seems to be unrelated to any other cardiorespiratory pathology.

Wirbelsäulenchirurgie/*Spinal surgery*

P108

Die Standard-Antibiotikaprophylaxe ist nicht ausreichend wirksam gegenüber der Kolonisierung von Spondylodesematerial und Endoprothesen mit niedrigvirulenten Bakterien

Standard perioperative prophylactic antibiotics are not effective against colonisation of spinal instrumentation and endoprostheses with low-pathogenic bacteria

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Objective

It remains unclear whether low-grade infection of implants is a consequence of bacterial contamination during surgery or if rather these pathogens are intrinsic commensals residing in the deep tissue. The ability of perioperative single-shot antibiotics to eradicate low-virulent bacteria has not been studied sufficiently. In this study we analysed the rates of positive bacterial cultures from removed spinal implants and endoprostheses of hips and knees. The resistance profile of these bacteria with respect to the prophylactic single-shot antibiotics applied during implantation was studied as well.

Methods

A retrospective single-centre study involving two departments was conducted. From January 1st 2018 till March 31st 2020, 94 patients with removal of spinal implants and 448 with removal of hip and knee endoprostheses were included. Patients with spondylodiscitis, deep wound infection, carbon/PEEK implants and acute infection were excluded.

Results

Swabs and sonication of removed spinal implants showed a high rate of positive bacterial cultures not only for patients with screw loosening (43% positive cultures), but also for patients with implants removed because of adjacent segment degeneration (27 %) or after fracture healing (44 %).

Of patients with implant removal because of endoprosthesis loosening in 30% a bacterium was detected. In cases with mechanical failure of endoprostheses without loosening in 13% a bacterium was cultivated.

Most frequent bacteria cultivated were *Cutibacterium acnes* and *Staphylococcus epidermidis*. While *Cutibacterium acnes* was sensitive to the prophylactic antibiotics in all cases, high rates of resistances where found for *Staphylococcus epidermidis* (45% endoprostheses, 75% spinal implants). When a combination of cefuroxime and vancomycin was used as a prophylactic antibiotic in 23 % a bacterium was detected during implant removal.

Conclusion

Especially for spinal surgery high rates of positive bacterial cultures are found during implant removal for loosened and non-loosened implants. This suggests that low-grade infection as being a major source of implant loosening has to be put in doubt. Moreover, neither standard nor extended perioperative antibiotic regime does prevent colonization of implants with low-pathogenic bacteria.

Ökonomie und Qualität, Komplikationen, Patientensicherheit /*Economics and quality, complications, patient safety*

P110

Ein neues mikrochirurgisches Anastomosen-Trainingsmodel in Kadavern der Ratte

A novel microsurgical anastomosis training model using gradually thawed cryopreserved microvessels of rat cadavers

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Objective

Training operation procedures is essential for patient safety. In consideration of the 3-R-rule (Refine-Replace-Reduce) as a guideline for promoting ethical use of animals for surgical training, we present a novel training model for microvessel anastomosis.

Methods

In a rat cadaveric study, we evaluated the surgical anatomy of the common carotid artery (CCA), external jugular vein (EJV) and femoral vessels (FV) which were then used as templates for the present investigation. Anatomical dissection of 30 rat cadavers was performed. Two residents without prior microsurgical experience were included in the study and performed 5 CCA, 5 femoral artery, 5 EJV and 5 femoral vein anastomoses. Patency and leakage served as qualitative variables and operation time as a quantitative variable for efficiency control.

Results

The average time improved for arterial and venous anastomoses (45 min to 22 and 60 to 32 min, respectively) for both surgeons. While both surgeons experienced patency failure or leakage within the first half of performed arterial and venous anastomoses, they could improve to a 100% patency rate without the occurrence of leakage for the last half of trials. The rat head & neck anatomy presents various characteristics related to the harvest of the vessels of interest.

Conclusion

We provide anatomical knowledge about the topography related to the harvest of the CCA, EJV, and FV. Our model is an easily accessible, low-cost microsurgical simulation model, allowing a realistic and instructive performance of anastomoses.

Ökonomie und Qualität, Komplikationen, Patientensicherheit /*Economics and quality, complications, patient safety*

P111

Ein Standard-Protokoll zur sitzenden Lagerung bei neurochirurgischen Eingriffen – der Umgang mit venösen Luftembolien und der Stellenwert eines Persistierenden Foramen Ovale

A standardised protocol for the sitting position in neurosurgical procedures – management of venous air embolism and the role of patent foramen ovale

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Objective

To describe the clinical and treatment characteristics of the sitting position during neurosurgical procedures and the role of patent foramen ovale (PFO) in the management of venous air embolism (VAE).

Methods

All surgical procedures were performed in the sitting position and under general anesthesia despite a PFO. We used a standardized protocol for 1. the sitting position, 2. preoperative detection of PFO and monitoring of VAE (trans-esophageal echocardiography TEE; capnometry), 3. surgical and 4. anesthesiological management of VAE. VAE episodes were allocated to two groups, based on severity (VAE °I: positive TEE and/or air aspiration; VAE°II: VAE°I plus drop in expiratory CO2 by more than 10% and/or decrease in mean arterial pressure by more than 20%).

Results

During 2012 and 2016, a total 182 patients were included (age 59± 6a, range 16-89a) in the study. Surgical procedures comprised spinal (N=37, 20%) and cranial approaches (N=145, 80%; intraaxial N=51, 35%, extraaxial N=94, 65%). Duration of surgery was 192±85 min (range 48-484min). Twenty-two patients (12%) exhibited a PFO. At least one episode of VAE occurred in 48 patients (26%). A VAE°I occurred in 39 (81%) and a VAE°II in 9 (19%) cases, respectively. All VAE events were managed safely and successfully following our institutional standards. Comparison of patients" postoperative course with and without VAE, VAE°I and °II unveiled no differences in terms of PFO, overall length of stay on intensive care unit and in hospital.

Conclusion

Following a standardized protocol, the sitting position and the management of VAE is safe and effective in experienced surgical and anesthesiological hands. Under consideration of our data, the role of PFO in the sitting position needs a thorough reevaluation, such as the need for a VAE classification.

Ökonomie und Qualität, Komplikationen, Patientensicherheit /*Economics and quality, complications, patient safety*

P112

Komplikationsraten von zwei verstellbaren Shuntventilen bei der Hydrozephalusbehandlung – ein monozentrischer Erfahrungsbericht

Complication rates of two common programmable differential pressure hydrocephalus shunt devices – a single-centre experience

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Objective

Hydrocephalus (HC) requiring cerebrospinal fluid (CSF) flow diversion is observed in a diverse spectrum of neurosurgical diagnoses. Ventriculoperitoneal (VP) shunt placement represents one of the management modalities and is generally regarded as a novice competency neurosurgical procedure. A wide range of devices with programmable or fixed-pressure valves are available on the market, with little knowledge on differences in their specific complication rates.

Methods

A single-center retrospective analysis of all consecutive adult patients with VP shunt placement over a period of four years was performed and details on demographics, shunt devices, surgeries and complications were collected. In a subgroup analysis, the complication rates of the most commonly used programmable shunt devices (Miethke® proGAV (1.0 or 2.0) valve in combination with Miethke® shunt assistant and Codman®Certas Plus valve) were statistically compared ($p < 0.05$ was considered significant).

Results

Between 2015–2019, 463 eligible adult VP shunt patients could be identified (230 males, 233 females, median age 59.9 (18.2–88.5) years). Non-obstructive HC after SAH or TBI was present in 31% of the patients, followed by NPH in 18% and obstructive HC in 15%. A programmable shunt device was used in the majority of cases (85%), with Miethke® devices being implanted in 349 and Codeman® devices in 46 patients. Surgical complications occurred in 24% of cases and were often related to infection (4%) or dysfunction (5%) of the shunt systems, leading to revision surgery in 122 patients. The rate of non-surgical complications (5%) including mortality (2%) was low. A comparison of Miethke® devices with the Codman® device revealed no significant difference in terms of complications. In a "clean" cohort (n=104) of only normal pressure hydrocephalus (NPH) and idiopathic intracranial hypertension (IIH) patients, however, the rate of surgical complications was significantly higher when the Codman® Certas Plus valve was used (55% vs. 19%, p=0.016).

Conclusion

Similar to data published in the literature, VP shunt placement was associated with relevant rates of complications and revision surgeries in our current analysis. A relationship between the different types of programmable shunt devices and the occurrence of surgical complications might exist.

Ökonomie und Qualität, Komplikationen, Patientensicherheit /*Economics and quality, complications, patient safety*

P113

Welcher Überwachung bedarf es nach elektiven Kraniotomien?
How much monitoring is required after elective craniotomy?

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Objective

In most neurosurgical departments patients undergoing an elective craniotomy are postoperatively admitted to an intensive or intermediate care unit (ICU, IMC) for close monitoring until the next morning (i.e. 12-24h). Currently the COVID-19 pandemic requires this valuable resource and especially ICU-beds are re-allocated. In this study we aim to evaluate the occurrence of neurological or cardiopulmonary events in the early postoperative phase to re-define the monitoring algorithm after elective craniotomy.

Methods

Data acquisition was conducted as a single-center retrospective analysis. Patients undergoing elective craniotomy were included in this study. Demographic data, diagnosis, ASA-score, complications, as well as type and duration of monitoring were documented and analyzed.

Results

206 consecutive patients were included in our study. Mean patient age was 60.7years (18 to 61) and 114 (55,3%) patients were female. 63 (30.6%) patients underwent microsurgical extra-axial tumor resection, 131 (64.6%) intra-axial tumor resection, 16 (7.7%) neurovascular surgery, 48 (23.8%) procedures were infratentorial. The mean ASA-score was 2.5 (0.56 SD). The vast majority (139, 67.5%) of patients was admitted to the ICU and 67 (32.5%) to the IMC unit. During the first 24 hours, 32 postoperative incidents occurred, including i) ongoing catecholamine therapy after surgery (n=2), ii) prolonged awakening (n=7), iii) postoperative seizures (n=3), iv) new temporary or permanent focal neurological deficits requiring imaging (n=17), v) postoperative delirium (n=4), vi) postoperative hemorrhage (n=5), vii) malignant brain swelling (n=2). However, 32 patients experienced a postoperative incident detected by close monitoring and requiring ICU monitoring/treatment and 7 patients experienced an incident requiring repeat surgery at a mean duration of 6.4 hours after surgery. 2 of these cases were very complex surgeries where ICU treatment would have been out of any question. The mean age of patients with postoperative incidents was 65.7 years (24 to 86).

Conclusion

In our study, the ASA-score and age did not correlate with occurrence of complication during early postoperative phase. Neurological deterioration mostly leads to immediate imaging and further conservative therapy. Considering premorbidity and surgery-associated complication to identify patients at risk, a more precise algorithm with a rapid transfer to the normal ward apart from the undisputed gold standard of ICU monitoring should be established.

Ökonomie und Qualität, Komplikationen, Patientensicherheit /*Economics and quality, complications, patient safety*

P114

Gibt es einen Wochenend-Effekt bei der Behandlung von rupturierten Hirnaneurysmen mittels Clipping bei Patienten mit Subarachnoidalblutung?

Is there a "weekend effect" for microsurgical clipping of ruptured intracranial aneurysms in patients with subarachnoid haemorrhage?

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Objective

The "weekend effect" describes that emergency hospital admissions and/or procedures performed at night and on weekends may be associated with a worse clinical outcome when compared to admissions during regular working hours. This study evaluates, whether admission of patients with subarachnoid haemorrhage (SAH) out of regular working hours and microsurgical clipping at nighttime are associated with a worse patient outcome.

Methods

Consecutive patients that underwent microsurgical clipping of an acutely ruptured aneurysm at a single institution between 2010 and 2019 were retrospectively reviewed. Patients admitted during 1) regular working hours (Monday – Friday, 08:00 – 17:59) and 2) on-call duty and microsurgical clipping performed during a) daytime (Monday – Sunday, 08:00 – 17:59) and b) nighttime were compared regarding the following parameters: baseline patient and aneurysm characteristics, timing and duration of surgery, procedural complications, clinical outcome and angiographic results.

Results

Out of 157 included patients, 53 (34%) were admitted during regular working hours and 104 (66%) during on-call duty. Clipping was performed during daytime in 109 cases (69%) and at nighttime in 48 (31%). Baseline patient and aneurysm characteristics were comparable between the subgroups. Admission during on-call duty did not affect the admission-to-surgery time (8±7 h vs. 10±6 h, p=0.3), overall cerebral infarction (43% vs. 49%, p=0.5), mortality (12% vs. 17%, p=0.3), 6-month favourable outcome (47% vs. 59%, p=0.2) and complete aneurysm occlusion rates (72% vs. 76%, p=0.7). In the univariate analysis, microsurgical clipping at nighttime was associated with higher odds of unfavourable outcome at discharge (OR: 2.3, 95%CI: 1.0 – 5.1, p=0.039). However, this difference did not remain significant after multivariable adjustment (OR: 2.1, 95%CI: 0.7 – 6.2, p=0.2). The operation time (261 ± 70 min vs. 274 ± 84 min, p=0.3), procedure-related cerebral infarction (23% vs. 21%, p=0.8), and complete aneurysm occlusion rates (70% vs. 74%, p=0.9) were comparable between nighttime and daytime surgery.

Conclusion

Admission out of regular working hours and clipping at nighttime were not independently associated with a poor clinical outcome. The adherence to standardized treatment protocols might mitigate the "weekend effect" in clinical practice, as suggested previously for ischemic stroke.

Ökonomie und Qualität, Komplikationen, Patientensicherheit /*Economics and quality, complications, patient safety*

P115

Obligatorische Morbiditäts- und Mortalitätskonferenzen (MMK) im zertifizierten Hirntumorzentrum und Wirbelsäulenzentrum der Maximalversorgung – Die strukturierte Durchführung genügt der Form, aber welche Maßnahmen folgen daraus?

Mandatory morbidity and mortality conferences (MMC) at a certified brain tumour centre and certified spine centre – The structured implementation may fulfil the requirements, but what are the consequences of the proposed measures?

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Objective

DKG (German Cancer Society, neuro-oncology) or DWG (German Spine Society, spine) certified centres are obligated to carry out a minimum number of annual MMCs. Studies on how they influence healthcare quality and safety in neurosurgery are inconsistent. This study examines MMCs with focus on derived measures, their implementation, relation to quality indicators (QI) and possibilities of improvement.

Methods

Retrospective evaluation of all MMC cases 2014-11/2020 presented at the spine and brain tumour centre of a teaching hospital (severity, derived measures, implementation, possible reasons for non-implementation, relation to QI).

Results

In 34 MMCs, 41 cases (24 brain tumour centre, 17 spine centre) were analysed. The MMCs were further grouped into postoperative complications (66%), operative indications (7%), follow-up care (17%) and diagnostics (10%). In 23 of 41 cases (56%) the MMC topic had a possible influence on public/ non-public quality indicators (Initiative Qualitätmedizin e.V., DKG / Onkozert). 55 proposals for measures derived from the MMCs. At the time of evaluation, 33 of those proposals were implemented (degree of implementation 60%). In 70% of the implemented measures, new guidelines (SOPs) were created or existing ones were adapted. 30% of the implemented measures led to further educational training. 40% of planned measures were not implemented, 16% due to a lack of evidence. The implementation of the other measures (24%) was not precisely defined or followed up.

Conclusion

In addition to an educational aspect, MMCs have a high potential to identify improvement measures in patient care. In this analysis, we observed that the implementation of some measures had to be postponed due to a lack of evidence. Conversely, MMCs could be used as a tool to identify significant scientific questions. A major number of analysed cases and measures were related to quality indicators (QI). Therefore, a higher degree of implementation of measures should be achieved (e.g. via Plan-Do-Check-Act cycle). Prospective studies could be useful to investigate the effect of MMCs on established QI.

Ökonomie und Qualität, Komplikationen, Patientensicherheit /*Economics and quality, complications, patient safety*

P116

TTFields beim anaplastischen Meningeom – Surveillance-Analyse zur Verträglichkeit
TTFields in anaplastic meningioma – surveillance safety analysis

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Objective

Anaplastic meningioma is the most malignant type of meningioma, characterized by aggressive intracranial growth. Only few treatment options exist to date for patients suffering from this tumour. For another malignant intracranial tumour with limited treatment options – glioblastoma – an additional treatment modality has been established in recent years: alternating electric fields, called TTFields, generated by a portable device and applied to the tumour via arrays attached to the scalp. The effect of this treatment modality has been studied already in patient-derived meningioma cells and demonstrated decreased cell proliferation. Clinical trials are currently under way to analyse safety and efficacy of TTFields in meningioma patients. This analysis aims at collating data on safety of TTFields in anaplastic meningioma patients monitored within the scope of post-marketing surveillance.

Methods

Unsolicited safety data of anaplastic meningioma patients treated with TTFields were evaluated in the context of post-marketing surveillance and were systematically analyzed for this study. The MedDRA body system (system organ class (SOC) and preferred terms) was utilized. Data cut-off was October 31, 2020

Results

Out of more than 17,000 TTFields-treated patients, 34 patients were treated with TTFields for anaplastic meningioma diagnosis in Germany, Israel, and the USA to date. Ten patients were female (29%), 24 were male (71%); their median age was 57 years (range 26-74 years). In total, 61 adverse events (AE) were reported, with 18 patients reporting at least one AE. Of those 61 AEs, 39 were assessed to be potentially related to TTFields therapy. The most commonly reported AEs were electric sensation (9 patients, 26%) and skin reactions (7 patients, 21%). There were no serious adverse events related to TTFields reported.

Conclusion

This safety surveillance analysis of patients with anaplastic meningioma treated with TTFields revealed no serious systemic adverse events associated with TTFields and no new safety signals, supporting safe use of TTFields in this tumour type. Prospective, randomized clinical trials are needed to further shed light on safety and efficacy of TTFields in anaplastic meningioma.

Ökonomie und Qualität, Komplikationen, Patientensicherheit /*Economics and quality, complications, patient safety*

P117

Strahlungs-Dosis des sliding gantry CTs im Vergleich zum mobilen cone-beam CT bei der navigierten Anlage von Pedikel-Schrauben in einer homogenen Kohorte

Radiation doses of sliding gantry CT-based as compared to mobile cone-beam CT-based navigated pedicle screw placement in a homogenous cohort

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Objective

Today, multiple solutions for navigation-guided pedicle screw placement are available. For the present study, we compared the applied radiation doses of sliding gantry CT-based (SGCT) and mobile cone-beam CT-based (CBCT) pedicle screw placement for spinal instrumentation.

Methods

We analyzed 183 and 54 patients who underwent SGCT-based using an automated radiation dose adjustment or standard CBCT-based pedicle screw placement for spinal instrumentation at our department between 06/2019 and 01/2020, respectively.

Results

Baseline characteristics including the number of screws per patient and the number of instrumented levels did not differ between the two groups. Although the accuracy of screw placement according to Gertzbein-Robbins classification did not differ between the two groups, more screws had to be revised intraoperatively in the CBCT group (SGCT: 39, 2.7% vs. CBCT: 23, 6.0%; p=0.0036). Mean ± standard deviation radiation doses [mGy*cm] for the first (SGCT: 484.0±201.1, CBCT: 687.4±188.5; p<0.0001), second (SGCT: 515.8±216.3, CBCT: 658.3±220.1; p<0.0001), third (SGCT: 531.3±237.5, CBCT: 641.6±177.3; p=0.0140), and the total of all scans (SGCT: 1216.9±699.3, CBCT: 2000.3±921.0; p<0.0001) were significantly lower in the SGCT group. The same applies to radiation doses per level (SGCT: 461.9±429.3, CBCT: 1004.1±905.1; p<0.0001) and radiation doses per screw (SGCT: 172.6±110.1, CBCT: 349.6±273.4; p<0.0001).

Conclusion

The present results show that the applied radiation doses are significantly lower using a SGCT for navigated pedicle screw placement in spinal instrumentation. A modern CT scanner on a sliding gantry leads to lower doses, especially through automated 3D radiation dose adjustment.

Ökonomie und Qualität, Komplikationen, Patientensicherheit /*Economics and quality, complications, patient safety*

P118

Risikofaktoren für die Prädiktion der In-House-Mortalität bei Patienten nach Hirntumor-Operation, basierend auf Krankenhaus-Routine-Daten – die Rolle des Stausberg Scores

Risk factors based on routine administrative hospital data for the prediction of in-house-mortality in brain tumour surgery – Stausberg Score

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Objective

Indicators for treatment quality (quality indicator, QI; e.g. outcome) are prone to inaccuracies. For longitudinal intra- or cross-sectional inter-departmental comparison, input variables as risk factors, other than age and gender, seem to be multiple and their share of the value of a QI is difficult to quantify. Stausberg and Hagn developed a score for the QI In-House-Mortality based on 42 ICD-10 categories, which can be easily drawn from routine hospital administrative data. We analyzed its applicability for patients having undergone brain tumor surgery.

Methods

We analyzed a retrospective mono-center cohort of patients (n=411) being operated upon a brain tumor from 2015 to 2018 on In-House-Mortality as the primary outcome. Age, gender, PCCL, relative weight (RW), length of stay (LOS), nosocomial infection (NI), type of admission (emergency room (ER), non-ER), event of re-operation and complications and the Stausberg Score on demission were retrieved from routine hospital data banks. Univariate and multivariate binary regression analyses were performed. Statistical significance was set as the probability of Type 1 error below 5% ($p<0.05$).

Results

In-House-Mortality in surgically treated patients with brain tumors was 2,9%. Univariate regression identified LOS, PCCL, RW, Stausberg Score, NI and type of admission as significant risk factors. Multivariate analysis revealed only Stausberg Score as a significant risk factor (OR 1,150 (95%CI 1,022 – 1,295); p=0,021; Nagelkerke´s R2: 0,403) with an 15% increase in odds per higher score point with a meaningful predictive effect (AUROC 0,85 (95%CI 0,74 – 0,93)).

Conclusion

Events with low prevalence are difficult to model and to predict. Stausberg Score seems to be a promising candidate for the prediction of In-House-Mortality in surgically treated brain tumor patients.

Ökonomie und Qualität, Komplikationen, Patientensicherheit /*Economics and quality, complications, patient safety*

P119

Klinische Effizienz und Qualität des OP-basierten sliding gantry CTs im Vergleich zum mobilen cone-beam CT für die navigierte Anlage von Pedikel-Schrauben – eine Observations-Kohorten-Studie an 853 Patienten und 6733 Schrauben

Clinical efficiency and quality of operating room-based sliding gantry CT as compared to mobile cone-beam CT-based navigated pedicle screw placement – an observational cohort study on 853 patients and 6733 screws

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Objective

Today, multiple solutions for navigation-guided pedicle screw placement are available. For the present study, we analyzed the efficiency of an operating room (OR)-based sliding-gantry CT (ORCT) and a mobile cone-beam CT (CBCT)-based approach for spinal instrumentation.

Methods

We analyzed all patients who underwent ORCT-based or CBCT-based pedicle screw placement for spinal instrumentation at our department between 11/2015 and 01/2020.

Results

Intra- and postoperative complications as well as number of navigated screws and levels per case did not differ between the two groups. Although the accuracy of screw placement according to Gertzbein-Robbins classification did not differ between the two groups, more screws had to be revised intraoperatively in the CBCT group (ORCT: 98, 2.8% vs. CBCT: 128, 4.0%; p=0.0081).

The median time of patients inside the OR (*Entry – Exit*) was significantly shorter for the ORCT group (ORCT: median, [95% CI] 237.5, [247.8, 264.3] min, CBCT: 267, [274.4, 291.5] min; p<0.0001) based on shorter times for *Positioning - Incision* (ORCT: 17, [18.1, 19.9] min, CBCT: 32, [32.2, 35.5] min; p<0.0001) and *Suture - Exit* (ORCT: 22, [23.6, 26.1] min, CBCT: 25.5, [27.5, 30.7] min; p<0.0001).

Conclusion

The present results show that the choice of assistive technology for navigated pedicle screw placement has significant impact on standard spine procedures even in a high-volume spine center. Particularly with regard to cost-effectiveness and the duration of surgeries, the shorter time needed for preparation and de-positioning in the ORCT group made the main difference, while the quality of accuracy was even higher.

Ökonomie und Qualität, Komplikationen, Patientensicherheit /*Economics and quality, complications, patient safety*

P120

Einflussfaktoren für Komplikationen der externen ventrikulären Liquor-Drainagen – eine prospektive Evaluation der Komplikationen und der standarisierten Präventionsmaßnahmen sowie vergleichende Untersuchung von Metallnadel und Polyurethan-Katheter als ventrikuläre Liquor-Drainagen-Systeme

Factors which influence the complications of external ventricular cerebrospinal fluid drainage – a prospective evaluation of complications & standardised preventive measures & a comparative investigation of metal needles & polyurethane catheters as ventricular cerebrospinal fluid drainage-systems

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Objective

Initiales Ziel der Studie ist herauszufinden, welche Faktoren einen Einfluss auf das Auftreten von Komplikationen bei und nach der Anlage externer ventrikulärer Liquor-Drainage (EVD) haben und mit welcher Häufigkeit diese Komplikationen vorkommen. Weitere Ziele sind die Analyse der standarisierten Präventionsmaßnahmen und die vergleichende Untersuchung von Metallnadel und Polyurethan-Katheter als EVD-Systeme.

Methods

Durchführung einer prospektiven Beobachtungsstudie anhand 200 konsekutiver Patienten (100 Patienten mit Metall-Drainage und 100 Patienten mit Polyurethan-Katheter), die mittels EVD therapiert werden. Einschlusskriterien sind Ersteinlage einer präkoronaren EVD über Bohrlochtrepanation (Bohrlochdurchmesser 1.4mm–16mm) und Alter>18Jahre. Ausschlusskriterien sind die offene Einlage der EVD (Kraniotomie-Durchmesser>16mm) und/oder eine vorbestehende Infektionserkrankung des Zentralnervensystems. Neben den Parametern deskriptiver Statistik erfolgte die Überprüfung der statistischen Signifikanz durch den χ^2-Test nach Pearson und den exakten Test nach Fisher (Signifikanzniveau p≤ ,05).

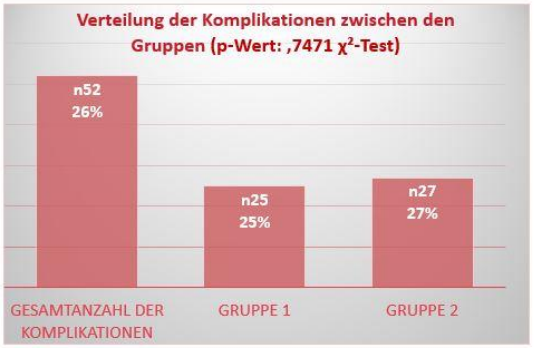
Results

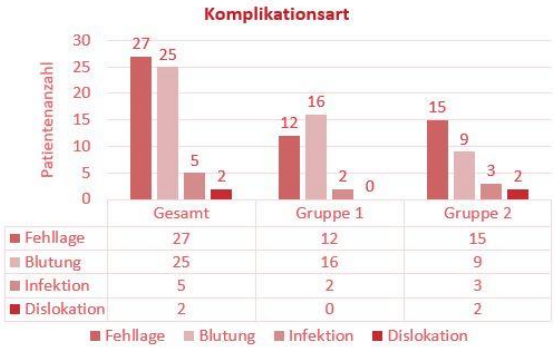
200 Patienten wurden inkludiert. 100 Patienten mit EVD aus Metall (Gruppe1) und 100 Patienten mit Polyurethan-Katheter (Gruppe2). Bei 52 Patienten (26%) traten Komplikationen auf (n25 in Gruppe1 & n27 in Gruppe2). Die Komplikationen waren Fehllage, Blutung, Infektion und Dislokation. Fehllage bei 27 Patienten (13,5%) (n12 (12%) Gruppe1 & n15 (15%) Gruppe2). Blutungen durch die EVD-Einlage bei 25 Patienten (12,5%) (n16 (16%) in Gruppe1 & n9 (9%) in Gruppe2); davon waren 4 Blutungen OP-würdig. Es traten 5 Infektionen (2,5%) auf (n2 (2%) in Gruppe1 & n3 (3%) in Gruppe2). Bei 2 Patienten (1%) traten Dislokationen auf (beide Fälle (2%) in Gruppe2). Es lag kein statistisch-signifikanter Unterschied im Auftreten von Komplikationen zwischen beiden Gruppen vor (p-Wert: ,7471 χ^2-Test). Das Vorliegen einer Mittellinienverschiebung war statistisch-signifikant für das Auftreten von Fehllage (p-Wert: ,0114 Exakter Test nach Fisher). Die Einnahme von Antikoagulantien war statistisch-signifikant für das Auftreten von Blutungen (p-Wert: ,0018 χ^2-Test; ,0059 Exakter Test nach Fisher).

Conclusion

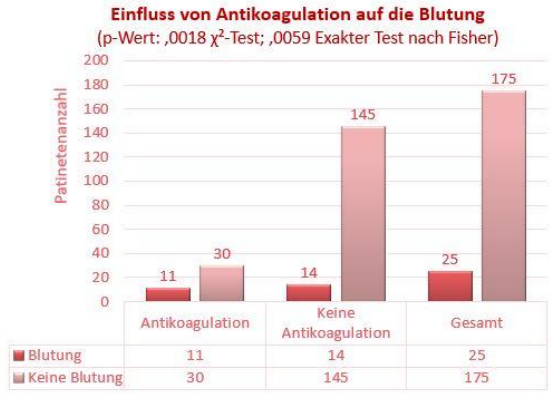
Es liegt kein statistisch-signifikanter Unterschied zwischen beiden EVD-Systemen bezüglich des Auftretens von Komplikationen vor. Die Mittellinienverschiebung scheint einen Einfluss auf das Auftreten von Fehllagen zu haben und die Antikoagulation einen großen Einfluss auf das Auftreten von Blutungen.

Fig. 1


Verteilung der Komplikationen zwischen den Gruppen (p-Wert: ,7471 χ²-Test)
n52 26%
n25 25%
n27 27%
GESAMTANZAHL DER KOMPLIKATIONEN
GRUPPE 1
GRUPPE 2


Komplikationsart
Patientenanzahl
Gesamt
Gruppe 1
Gruppe 2
Fehllage 27 12 15
Blutung 25 16 9
Infektion 5 2 3
Dislokation 2 0 2


Einfluss von Mittellinienverschiebung auf die Fehlage
(p-Wert: ,0114 Exakter Test nach Fisher)
Patientenanzahl
Mittellienienverschiebung
Keine Mittellienienverschiebung
Fehllage 8 19
Keine Fehllage 18 155


Einfluss von Antikoagulation auf die Blutung
(p-Wert: ,0018 χ²-Test; ,0059 Exakter Test nach Fisher)
Patinetenanzahl
Antikoagulation
Keine Antikoagulation
Gesamt
Blutung 11 14 25
Keine Blutung 30 145 175

Neuroonkologie III/Neurooncology III

V109

Entschlüsselung des genetischen und epigenetischen Hintergrunds von stillen und nicht-stillen ACTH-Adenomen
Deciphering the genetic and epigenetic background of silent and non-silent ACTH adenomas

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Objective

Corticotroph adenomas express adrenocorticotrophic hormone (ACTH) and may result in Cushing"s disease (CD) if elevated ACTH blood levels are present. Silent ACTH adenomas (SCA) that express ACTH but do not cause hypercortisolism, might exhibit a more aggressive course and are classified as "aggressive pituitary gland tumors". Here we show that genetic and epigenetic profiling can distinguish ACTH adenomas from SCA.

Methods

23 SCA patients and 49 CD patients that underwent transsphenoidal resection were included. Tumor size was measured by MRI. Tumor histology included immunstaining for ACTH and GATA3. Sanger sequencing was performed to analyse mutational burden within the ACTH and USP8 locus. Genome-wide DNA methylation profiling was performed using a 850k and 450k Illumina arrays and classified by the DKFZ brain tumor classifier as well as Prinicipal component (PCA) and copy number variation (CNV) analysis using R (n=36).

Results

Patients with SCA had significantly larger tumors ($p < 0.0001$). USP8 mutations were only found in CD, while GATA3 expression exclusively appeared in SCA. CNV analysis inferred from the methylation data revealed cytogenetic aberrations across all analyzed samples. tSNE analysis further supported that SCA and CD can be distinguished by their epigenetic profile, also seen in the CNS reference cohort from Capper et al.

Conclusion

SCA show a strong expression of ACTH without causing hypercortisolism. The reason for this is not yet known. Our data suggest that genome-wide DNA methylation profiles allow subgrouping of SCA and CD adenomas that might not be achievable by standard endocrinological testing or histopathology

Neuroonkologie III/*Neurooncology III*

V110

Direkte orale Antikoagulantien vs. niedermolekulares Heparin zur Behandlung der Lungenembolie im Glioblastom
Direct oral anticoagulants vs. low-molecular-weight heparin for pulmonary embolism in glioblastoma

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Objective

Glioblastoma (GBM) is a cancer type with high thrombogenic potential and GBM patients are therefore at a particularly high risk for thrombotic events. To date only limited data on anticoagulation management after pulmonary embolism (PE) in GBM is available and the use of DOACs remain off-label

Methods

A retrospective comparative cohort analysis of patients with GBM and postoperative, thoracic CT-scan confirmed, PE was performed. Clinical course, follow-up at 6 and 12 months and overall survival (OS) were evaluated using medical charts and neuroradiological data.

Results

Out of 584 GBM patients, 8% suffered from postoperative PE. Out of theses, 30% received DOACs and 70% LMWH for therapeutic anticoagulation. There was no significant difference in major intracranial hemorrhage (ICH), re-thrombosis or re-embolism between the two cohorts. Although statistically non-significant, a tendency to reduced mRS at 6- and 12- months was observed in the LMWH cohort. Furthermore, patients receiving DOACs had a statistical benefit in OS.

Conclusion

In our analysis DOACs showed a favourable safety profile in terms of major ICH, re-thrombosis and re-embolism in GBM patients with postoperative PE. Prospective, randomized trials are urgent to evaluate DOACs for therapeutic anticoagulation in GBM patients with PE.

Neuroonkologie III/*Neurooncology III*

V111

Dissoziation des strukturellen und funktionellen Konnektoms bei Gliompatienten
Dissociation of the structural and functional connectome in glioma patients

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Objective

Functional integrity is believed to be tightly bound to structural integrity in the healthy brain. Diffuse infiltrative glioma however disrupts structural white matter integrity and may impact on functional connectivity, both of peritumoral and distant brain regions. Whether structural and functional connectivity (SC, FC) are interdependent in glioma patients, diverge regionally, or differ depending on tumor growth dynamics remains unclear. We analyzed potential correlations of FC and SC in glioma patients under consideration of tumor site and IDH mutation status.

Methods

27 glioma patients (15 IDH_{mut}, 12 IDH_{wt}) and 27 healthy controls underwent diffusion-weighted imaging and resting-state-fMRI. Patients were enrolled preoperatively. Whole-brain (WB) and default-mode network (DMN) parcellations were based on the Brainnetome atlas, and corresponding SC and FC matrices were determined for each subject. SC measures comprised the number of fibers (NF), and the mean fractional anisotropy (FA) of fibers connecting two regions, based on free-water corrected probabilistic tractography. FC measures comprised the correlation between the mean time-series of structurally connected regions. SC as well as FC submatrices of ipsi-, contra-lesional and interhemispheric connectivity were compared across groups, and partial correlations ($p<0.05$, uncorrected) analyzed for corresponding SC and FC submatrices.

Results

Patient groups and healthy controls differed neither in FC nor in NF. By trend, however, mean FA values were lower in IDH_{wt} as compared to IDH_{mut} patients across all submatrices. Correlation analyses revealed intramodal associations within SC and FC matrices, both for patients and controls. But while in controls, FA and NF were associated across all submatrices, only few associations were found in IDH_{mut} patients (FA_{contra} and FA_{inter} with NF_{ipsi} and NF_{contra}), but none in the IDH_{wt} group. Furthermore, healthy subjects showed SC-FC correlations for WB as well as within the DMN, while neither IDH_{mut} nor IDH_{wt} patients showed any association between SC and FC measures.

Conclusion

Microstructural integrity of the structural connectome seemed to be altered in the prognostically less favorable IDH_{wt} patients, even in tumor distant regions. While FC may not yet be altered, the dissociation of SC and FC might be an early indicator of network desintegration in glioma patients.

Neuroonkologie III/*Neurooncology III*

V112

Meclofenamat sensitiviert primäre Glioblastomzellen für einen durch Lomustin vermittelten Zelltod
Drug repurposing of meclofenamate as a potent gap junction inhibitor sensitises primary glioblastoma cells for lomustine

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[3]Universitätsklinikum Bonn, Institut für Neuropathologie, Bonn, Germany
[4]Universitätsklinikum Bonn, Klinik für Neurologie, Bonn, Germany
[5]Universitätsklinikum Bonn, Institute of Experimental Immunology, Bonn, Germany
[6]University Medical Center Ulm, Department of Pediatrics and Adolescent Medicine, Ulm, Germany
[7]Medical Center, University of Freiburg, Translational NeuroOncology Research Group, Freiburg, Germany
[8]Medical Center, University of Freiburg, Faculty of Medicine, Freiburg, Germany
[9]Medical Center, University of Freiburg, Department of Neurosurgery, Freiburg, Germany
[10]Universitätsklinikum Bonn, Klinik für Neurologie, Abteilung für klinische Neuroonkologie, Bonn, Germany

Objective

Sine inhibition of a syncytial intercellular communication via gap junctions has been shown to sensitize glioblastoma cells to temozolomide-mediated antitumoral effects, the idea of gap junction-targeted therapies has been proposed as a promising novel therapeutic strategy within translational glioblastoma research. However, the impact of gap junction inhibition in the context of lomustine therapy, that has recently been shown to markedly improve survival of glioblastoma patients in combination treatment with temozolomide, has not been examined, so far. By repurposing of meclofenamate (MFA) - a clinically approved nonsteroidal anti-inflammatory drug - as a potent gap junction inhibitor, the present study aimed at investigating the effects of a gap junction-targeted therapy on primary human glioblastoma cells in the context of lomustine administration.

Methods

In order to quantify the extent of gap junction inhibition, Realtime-Imaging fluorescence-guided measurements of calcein cell-to-cell cytoplasm transfer were performed. We used RNA-sequencing and proteome profiling to study the downstream signalling due to meclofenamate treatment. DNA-fragmentation served as readout for cell death and was assessed by flow cytometric analysis of propidium iodide-stained nuclei.

Results

We observed a significant reduction of calcein cytoplasm transfer in MFA-treated cells. Pharmacological inhibition of gap junctions profoundly increased the percentage of lomustine-mediated cell death. Gap junction inhibition was associated with elevated activity of the JNK signalling pathway.

Conclusion

This study is the first to show that inhibition of intercellular comunication via gap junctions profoundly sensitizes primary glioblastoma cells to lomustine-mediated cell death therefore constituting a promising new therapy strategy for patients suffering from this disastrous and currently incurable cancer. With regard to MFA as a clinically-approved drug, MFA might harbour the potential of bridging the idea of gap junction-targeted therapeutic approaches into an instant subsequent clinical implementation.

Neuroonkologie III/*Neurooncology III*

V113

Eloquente Hirnmetastasen – Eine No-Go-Zone für den Neurochirurgen oder eine übersehene Gelegenheit zur lokalen Tumorkontrolle?

Eloquent brain metastases – A neurosurgeons no-go-zone or an overlooked opportunity for local tumour control?

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Objective

Brain metastases (BM) have traditionally been regarded as an ominous development in the natural history of cancer patients. Between 1985 and 2005, median survival of patients with BM was 7 months. Over the past decade, developments in neurosurgical techniques, stereotactic radiosurgery, and targeted therapies have increased median survival in BM to 12 months. However, patients with BM located in eloquent regions are seldomly considered candidates for neurosurgical resection due to the risk of postoperative neurological deficits.

Methods

We conducted a a post hoc analysis on data from a prospective study (MetastaSys) of patients undergoing BM resection at our institution between 2013-2016. Patients with eloquent BM underwent neurosurgical resection with intraoperative neuromonitoring, including transcranial motor evoked potentials and cortical/subcortical stimulation for motor-eloquent BM, and awake craniotomies for speech-eloquent BM. We then compared patients with eloquent and non-eloquent BM in terms of postoperative neurological deficits, local recurrence, and overall survival with a log-rank test.

Results

A total of 168 patients were included in the analysis. Of these, 43 (26%) had eloquent BM. No statistically significant difference (p=.921) was observed in the incidence of postoperative neurological deficits (9% in both cohorts). Similarly, local control was achieved in both cohorts, with 13% of local recurrence in the non-eloquent group vs. 9% in the eloquent group, p=.541. No statistically significant difference was observed in median progression free survival (25 months in the non-eloquent group vs. 29 months in the eloquent one, p=.194) and overall survival (11 months in the non-eloquent group vs. 15 months in the eloquent group, p=.260) in both groups.

Conclusion

Patients harboring eloquent BM should not be excluded from surgical therapies, as current neurosurgical techniques can provide local control without increased neurological morbidity.

V114

Neurogene Dysphagie in Subduralhämatom
Neurogenic dysphagia in subdural haematoma

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Objective

Dysphagia is a common and severe symptom of traumatic brain injury (TBI) affecting up to 78% of patients. It is associated with pneumonia, increased morbidity and mortality. Although subdural hematoma (SDH) accounts for over 50%, the occurrence of dysphagia in this subtype of TBI has not been widely investigated. The aim of the study was to evaluate the overall frequency, clinical predictors and functional outcome of dysphagia in SDH.

Methods

A retrospective analysis was conducted including all patients admitted to the neurosurgical department of the authors´ institute between 2007 and 2020 with SDH. All patients with clinical suspicion for dysphagia received a clinical swallowing assessment by a speech and language pathologist. Functional outcome was evaluated by Glasgow outcome scale (GOS).

Results

Of 545 patients, 71 patients had dysphagia (13%). Independent predictors for dysphagia were GCS <13 at admission (OR 4.17), pneumonia (OR 2.88) and cardiovascular disease (OR 2.29). The only protective factor for dysphagia was surgical treatment (OR 0.23). After surgical treatment of SDH, the incidence of dysphagia was significantly lower compared to those with conservative treatment (11.8% vs 21.8%; OR 0.23; p=0.02). Furthermore, patients with dysphagia had significantly worse outcome compared to those without dysphagia (48.8% vs 26.4%; p<0.001).

Conclusion

Dysphagia is a frequent and relevant symptom in patients with SDH. Surgical treatment is effective in preventing dysphagia and consequently leads to improved clinical course and outcome. GCS at admission might prove useful in clinical decision pathways to risk-stratify identify patients in need of a thorough swallowing assessment by an SLP after surgery.

Traumazentren/*Trauma centres*

V115

Je schneller desto besser? – Dauer bis zur ersten CT-Untersuchung nach Aufnahme bei Patienten mit mittelschweren und schweren Schädel-Hirn-Trauma und deren Einfluss auf die Mortalität

The faster the better? – time to first CT scan after admission in moderate to severe traumatic brain injury and its association with mortality

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[3] Krankenhaus Köln-Merheim, Klinikum der Universität Witten/Herdecke, Klinik für Orthopädie, Unfallchirurgie und Sporttraumatologie, Köln, Germany
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Objective

Fast acquisition of a first computed tomography (CT) scan after traumatic brain injury (TBI) is recommended. This study aims to investigate whether the length of the period preceding initial CT scan influences mortality in patients with leading TBI.

Methods

A retrospective cohort analysis of patients registered in the TraumaRegister DGU® was conducted. Adult patients with TBI, defined as Abbreviated Injury Scale (AIS) $_{Head}$ ≥3 and GCS ≤13 who had been treated in level 1 or 2 trauma centers between 2007 and 2016 were included. Patients were grouped according to time intervals either from trauma to CT or from admission to CT. In order to explore the influence of CT timing on mortality, standard mortality ratios (SMRs) were calculated for the different groups.

Results

A total of 6,904 patients met the inclusion criteria. Mean time period from trauma to hospital admission was 68.8min. From admission to first CT a mean of 19.0min elapsed. Trauma severity was higher in groups with a longer duration from trauma to CT as represented by a mean (± standard deviation) Injury Severity Score (ISS) of 19.8±9.0, 20.7±9.3 and 21.4±7.5 and similar distribution of mortality of 24.9%, 29.9% and 36.3% in the ≤60min-, 61-120min- and ≥121min-group, respectively. An adjusted multivariable logistic regression model showed a significant influence of the level of the trauma center (p=0.037) but not for interval from admission to CT (p=0.528).

Conclusion

TBI patients with a longer time span from trauma to first CT were more severely injured and demonstrated a worse prognosis, but received a CT scan faster when duration from admission is observed. The duration until the CT scan was obtained showed no significant impact on the mortality. It may be concluded that time management of TBI patients is adequate leading to timely initial diagnostic measures without causing harmful delay.

Traumazentren/*Trauma centres*

V116

Frühe vs. späte Kranioplastik nach SHT – eine Single-Center-Analyse von 129 Fällen hinsichtlich perioperativer Modalitäten, postoperativer Komplikationen und neurologischen Ergebnissen

Early vs. late cranioplasty after TBI – a single-centre analysis of 129 cases with regard to perioperative modalities as well as postoperative complications and neurological results

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Objective

Cranioplasty (CP) after decompressive craniectomy (DC) is an elective procedure that serves to reconstruct and restore the cranial vault from a functional and aesthetic perspective. Although it is a routine procedure, the optimal timing of CP remains an object of discussion. The traditional time of delayed CP (3-6 months after DC) is more and more questioned by neurosurgeons, while trying to find advantages for early CP (1-3 months after DC). We conducted this study to compare both timings in TBI patients with regard to perioperative modalities, postoperative complications and neurological results.

Methods

This retrospective single-center study was conducted on 129 cases undergoing cranioplasty following TBI. Early cranioplasty patients (73/129) and late cranioplasty patients (56/129) were observed from 01/2005-12/2018. All patients were followed based on medical, operative and digital records. Postoperative complications were divided into short-term (< 30 days) and long-term (> 30 days). Neurological results (GOS, GOSE) were collected via telephone interview.

Results

Patients with early CP had a shorter surgery time, lower intraoperative blood loss and shorter postoperative hospitalization compared to late CP. The total re-operation rate was 10.2%, with late CP patients having to be revised in 17.9% of cases, while early CP patients were re-operated in 4.2% of cases. This represents a significant difference (p = 0.016) in favor of early CP. Moreover, late CP patients developed a significantly higher rate of postoperative epidural hematoma (p = 0.010). Even considering the minor complications, late CP patients showed a higher rate than early CP patients. In contrast, detailed examination of the minor complications revealed that early CP patients had a higher number of CSF pads. Furthermore, VP-Shunt-dependent postoperative hydrocephalus rates were significant higher in the early CP group (p = 0.036). The neurological outcome in GOS and GOSE were almost identical in the early and late CP group and represented a moderate disability.

Conclusion

The study showed that early CP patients had superior intra- and postoperative results compared to late CP patients. However, especially postoperative hydrocephalus CSF pad rates were higher at early CP patients, which differed from the results of other studies. This shows the need for further research to confirm the results of the present study and to contribute to the discussion for optimal timing of CP.

V117

Angeleitetes Valsalva Manöver nach Bohrlochtrepanation und Blutungsevakuation des chronischen Subduralhämatoms – eine prospektive Kohortenstudie

Supervised valsalva maneuver after burr hole evacuation of chronic subdural haematomas – a prospective cohort study

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Objective

Research on chronic subdural hematoma (cSDH) management has primarily focused on potential recurrence after surgical evacuation. Herein, we present a novel postoperative/non-invasive treatment that includes a supervised Valsalva maneuver (SVM) which may serve to reduce SDH recurrence. Accordingly, the aims of the study were to investigate the effects of SVM on SDH recurrence rates and functional outcomes.

Methods

A prospective study was conducted from December 2016 until December 2019 at our institution. Of the 204 adult patients with surgically treated cSDH that had subdural drains placed, 94 patients were assigned to the SVM group and 82 patients were assigned to the control group. The SVM was performed by having patients blow into a self-made SVM-device at least 2 times/hour for 12 hours/day. The primary endpoint was SDH recurrence rate whilst secondary outcomes were morbidity and functional outcomes at 3-months of follow-up.

Results

SDH recurrence was observed in 16 of 94 patients (17%) in the SVM group which was a significant reduction as compared to the control group which had 24 of 82 patients (29.3%; p=0.05) develop recurrent SDHs. Furthermore, the infection rate (e.g.pneumonia) was significantly lower in the SVM group (1.1%) compared to the control group (13.4%; p<0.001; Odds ratio [OR] 0.1). At the 3-month follow-up, 85 of 94 patients (90.4%) achieved favorable outcomes in the SVM group compared to 62 of 82 patients (75.6%) in the control group (p=0.008; OR 3.0). Independent predictors for favorable outcome at follow-up were age (OR 0.9) and infection (OR 0.2).

Conclusion

SVM appears to be safe and effective in the postoperative management of cSDHs, reducing both recurrence rates and infections after surgical evacuation thereby resulting in favorable outcomes at follow-up.

Traumazentren/*Trauma centres*

V118

Das deutsche Schädel-Hirn-Trauma Register – Ergebnisse aus der Pilotphase
The German National TBI-Registry – results from the pilot period

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Objective

Nationwide data on the epidemiology, treatment characteristics, and long-term outcome of severe traumatic brain injury (TBI) in Germany is, unfortunately, nonexistent. Neurosurgeons from the German Neurosurgery Society (DGNC) and traumatologists from the German Trauma Society (DGU), therefore, joined forces in 2016 to conceptualize a TBI module for the well-established Trauma Register of the DGU (TR-DGU). Since then, funding for this "German National TBI registry (GNTR)" has been secured, a consensus has been reached on its dataset and workflow, ethical approval has been obtained, a test period has been successfully concluded, and finally, in February 2019, a pilot period has been initiated. Here, we report on the pilot period of the GNTR, which has been completed in December 2020.

Methods

During the pilot period of the GNTR, over a period of 23 months, TBI patients were prospectively enrolled in ten neurosurgical and traumatological departments across Germany. Inclusion criteria were treatment on the ICU ≥ 24h, or an ISS score ≥ 16. A variety of clinical, imaging and laboratory parameters were collected, and the outcome was assessed by the GOSE score at discharge and 6- and 12 months follow-up.

Results

Details on the structure and dataset of the GNTR and associated milestones and pitfalls during the conception and implementation phase are outlined. Demographic and clinical, imaging, and radiological characteristics of the TBI patients enrolled during the pilot period of the GNTR are presented. Also, mortality and an early functional outcome following severe TBI in the GNTR patients are described. Factors associated with an unfavorable outcome (GOSE 1-4) are assessed using uni- and multivariate regression analyses. Furthermore, the nine participating centers' experience in the GNTR pilot period is summarized, and problems and future directions are discussed.

Conclusion

National registries are needed to collect high quality, prospective data on devastating diseases such as severe TBI. The pilot period of the GNTR helps optimize its dataset and workflow while offering a first glance at the current characteristics of severe TBI in Germany. Opening of the GNTR to all German trauma centers will lead to a better understanding of TBI in Germany and might ultimately help to improve its treatment.

V119

Hirnnervenverletzungen bei Patienten mit moderatem bis schwerem Schädelhirntrauma – Analyse von 91, 196 Patienten des TraumaRegisters der Deutschen Gesellschaft für Unfallchirurgie zwischen 2008 und 2017

Cranial nerve injuries in patients with moderate to severe head trauma – analysis of 91, 196 patients from the Trauma Registry of the German Trauma Society between 2008 and 2017

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Objective

Traumatic brain injury (TBI) constitutes a major cause of trauma-related disability and mortality. The epidemiology and implications of associated cranial nerve injuries (CNI) in moderate to severe TBI is largely unknown. We aimed to determine the prevalence of CNI in TBI as well as clinical differences between TBI patients with and without concomitant CNI (CNI vs. control group) by means of a large multinational trauma registry.

Methods

The Trauma Registry of the German Trauma Society was evaluated for trauma patients with head injuries ≥2 Abbreviated Injury Scale, who had to be treated on intensive care units after emergency admission to European hospitals between 2008 and 2017. CNI and control cases were compared with respect to demographic, clinical, and outcome variables.

Results

1.0% (946 of 91,196) of TBI patients presented with additional CNI. On average, CNI patients were younger than control cases (44.3±20.6 vs. 51.8±23.0 years), but did not differ regarding gender distribution (CNI 69.4%; control 69.1%). Traffic accidents were encountered more frequently in CNI cases (52.3% vs. 46.7%; p<0.01; chi-square test) and falls more commonly in the control group (45.2% vs. 37.1%; p<0.01). CNI patients suffered more frequently from concomitant face injuries (28.2% vs. 17.5%; p<0.01) and skull base fractures (51.0% vs. 23.5%; p<0.01). Despite similar mean Injury Severity Score (CNI 21.8±11.3; control 21.1±11.7) and Glasgow Coma Scale score (CNI 10.9±4.2, control 11.1±4.4), there was a considerably higher rate of anisocoria in CNI patients (20.1% vs. 11.2%; p<0.01). Following primary treatment, 50.8% of CNI and 35.5% of control cases showed moderate to severe disability (Glasgow Outcome Scale score 3-4; p<0.01).

Conclusion

CNI as rare adjuncts to TBI should raise the suspicion of complicating skull base fractures and indicate higher rates of functional impairment following primary care.

Notice: TR-DGU project ID 2019-021. Data provision was carried out by TraumaRegister DGU®. Evaluation and interpretation are in the author"s responsibility and haven"t yet accomplished the review process of TraumaRegister DGU®.

Neuroonkologie III/*Neurooncology III*

V120

Infrarotspektroskopie zur schnellen, operationsbegleitenden Analyse von nativen Hirntumorbiopsien – eine Studie mit 821 Patienten

Infrared spectroscopy for rapid analysis of native brain tumour biopsies during surgery – a study with 821 patients

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Objective

Optical biopsies were suggested for intraoperative brain tumor delineation and diagnosis. Particularly, infrared spectroscopy was shown to identify primary and secondary brain tumors, and is well compatible with clinical routines, as it is fast, label-free and robust. However, studies have been limited to analysis of cryosections and small sample numbers. Here, we aim to assess to potential of infrared spectroscopy for clinical exploitation by approximation of future *in situ* applications and investigation of the influence of interpatient variability.

Methods

We analyzed fresh biopsies of 821 patients (primary and secondary brain tumors, and non-tumor brain samples from surgery for the treatment of pharmacoresistant epilepsy). Infrared spectra were acquired within minutes after removal, reduced to the water-free range (1000-1480 cm-1) and normalized. Principal component (PC) analysis was performed on the training set consisting of spectra obtained on GBM IV (n=173) and non-tumor tissue (n=45) and the PC scores were used to develop a classification strategy based on linear discriminant analysis. For all other spectra (test set), PC scores were calculated based on the PC loadings of the training set. Subsequently, those were subjected to the classification developed on the training set (GBM versus non-tumor).

Results

The selection of principal components 1, 2, 3, 7, 10, 11, 12, 13, 14, 15 resulted in maximal correct rates for reclassification of the training set and those were therefore used for our approach. Correct rates for discrimination of samples of the test set were 84% for GBM (220 patients), 90% for brain metastases (n=177) and 84 % for a mixed group of less frequent tumor entities (n=88). Importantly, all samples of non-tumor brain tissue were correctly recognized (12 patients). Glioma WHO I-III (n=135) were not reliably recognized; possible causes are the inter-patient variability and the limited availability of non-tumor tissue.

Conclusion

Here, we show that infrared spectroscopy can help to identify tumor borders during surgery. Interestingly, a large range of different tumors was recognized using only spectra of GBM and non-tumor brain as training for the classification strategy. However, to what extent the technology is able to address infiltrative glioma remains an open question and requires in situ studies that will allow the comparison spectral signatures of non-tumor and tumor tissue of the same patient.

Neuroonkologie III/*Neurooncology III*

V121

Hemmung von extrazellulären Carboanhydrasen inhibiert Glioblastom Zell-Invasion
Inhibition of extracellular carbonic anhydrases inhibits glioblastoma cell invasion

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Objective

Malignant gliomas metabolize glucose preferably by glycolysis which is in accordance with the Warburg effect. This induces a high demand of glucose combined with a significant lactic acid load. The hypoxia-inducible carbonic anhydrase (CA) IX has been shown to moderate the extrusion of hydrogen ions into the extracellular space. Since the acidification of the extracellular environment contributes to host tissue invasion due to activation of proteolytic enzymes, we hypothesized that CA IX plays an important role in malignant glioma Recently, specific small molecule inhibitors of this enzyme have been developed and may provide an innovative strategy for anti – invasive treatment.

Methods

Two established and 4 primary GBM cell lines (2 with mesenchymal and 2 with proneural transcriptional profile) were exposed to the CAIX inhibitor U104 under normoxic and hypoxic conditions. Cell toxicity was measured by ATP and crystal violet assay. For invasion assessment, a matrigel invasion chamber system with 8 µm pore size polycarbonate filter was used. CAIX expression was analyzed by quantitative RTPCR and Western Blot.

Results

Hypoxia significantly induced CAIX expression in all cell lines. Invasiveness increased significantly under hypoxic conditions in the mesenchymal cells ($p < 0.01$). Regardless of oxygenation status, the mesenchymal group displayed significantly higher invasiveness compared to the proneural group ($p = 0.006$). Looking at all cell lines, invasion is significantly inhibited by U104, both under normoxic and hypoxic conditions ($p < 0.01$). However, while the mesenchymal group showed the highest susceptibility to CAIX inhibition followed by the proneurally differentiated group, the established cell lines were entirely refractory to CAIX inhibition.

Conclusion

Our data demonstrate that CAIX inhibition can effectively inhibit invasion in malignant glioma cells independent from oxygenation status, however the effects are significantly influenced by cell type specific biological features.

Neuroonkologie III/*Neurooncology III*

V122

Gibt es einen Zusammenhang zwischen der Gesamtmenge an verabreichtem Nimodipin und dem Erhalt der Funktionen der Hör- und Fazialisnerven nach der Resektion von Vestibularis-Schwannomen – eine retrospektive Analyse einer randomisierten und multizentrischen Studie

Is there an impact of total nimodipine dosage on postoperative hearing preservation/cranial nerve function after vestibular schwannoma resection – a retrospective analysis of a randomised, multicentre trial

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Objective

This study aims to evaluate the relationship of total nimodipine dosage, tumor size, hearing and facial nerve preservation in vestibular schwannoma surgery.

Methods

In a retrospective analysis the data of 93 patients out of 112 patients of a randomized, multicenter trial that investigated the efficacy of prophylactic nimodipine treatment in vestibular schwannoma surgery were examined. Logistic regression analysis was applied in order to observe the correlation between total nimodipine dosage and postoperative hearing preservation and facial nerve function with respect to tumor size.

Results

Logistic regression analysis showed significant correlation of total nimodipine dosage and postoperative hearing preservation (p=0.049), tumor size (p=0.023) as well as their interaction with postoperative hearing preservation (p=0.043). Comparable analysis of postoperative function of the facial nerve did not correlate significantly with the total nimodipine dosage.

Conclusion

It can be proposed that a higher total nimodipine dosage and a lower tumor size describe better chances for postoperative hearing preservation. Moreover, the positive effect on the preservation of hearing due to higher total nimodipine dosage can especially be seen/ is especially relevant in patients with bigger tumor sizes.

Neuroonkologie III/*Neurooncology III*

V123

Screening mit FDA-zugelassenen, antineoplastischen Medikamenten identifizierte Ixabepilon für die Behandlung von aggressiven Meningeomen

Large-scale drug screening of FDA-approved antineoplastic drugs identifies Ixabepilone for the treatment of aggressive meningiomas

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Objective

The management of aggressive meningiomas remains challenging due to limited treatment options beside surgical removal and radiotherapy. High recurrence rates and lack of effective chemotherapies may be reasons for unfavorable prognosis of these patients. Consequently, there is an urgent need to identify effective therapeutic agents.

Methods

For this purpose, we performed a large-scale drug screening utilizing a drug library consisting of 119 FDA-approved antineoplastic drugs (AOD VI) on the anaplastic meningioma cell line NCH93 using CellTiter-Glo (Promega). Based on the lowest half-maximum inhibitory concentrations (IC50), top 4 drugs were selected. Validation of candidate compounds was performed in Ben-Men-1 (WHO°I), NCH93, and IOMM-Lee (WHO°III) cells using crystal violet assay. Proliferation assay was done by manual counting. Cell cycle and cell death analysis using Annexin V/PI were measured by flow cytometry. A heterotopic xenograft mouse model was established by injecting NCH93 cells in the flank of nude SCID mice. After reaching tumor volume of 200 mm^3, mice were randomized intro treatment groups and drugs were administered intraperitoneally.

Results

Large-scale drug screening resulted in the identification of Carfilzomib, Omacetaxine, Ixabepilone, and Romidepsin as potent drugs. Dose-curve analysis revealed IC50 values in the lower nanomolar range for all compounds and all cell lines (0.2 – 16.2 nM). To further substantiate our findings, cell proliferation was significantly reduced by up to 90% by each candidate drug at 10xIC50 after 48h. Furthermore, cell migration was inhibited up to 60% by all candidate drugs at the respective IC50. However, colony formation was only significantly reduced by Carfilzomib. All candidate drugs induced cell cycle arrest at G0/G1 or G2/M phase and subsequently induced apoptosis. Among them, Ixabepilone and Romidepsin profoundly induced apoptosis by up to 70%. Furthermore, all drugs inhibited tumor growth *in vivo,* with the most pronounced effect for Ixabepilone, reducing tumor volume by 86% compared to control (p<0.001).

Conclusion

In summary, by utilizing a large-scale drug screening library of FDA-approved drugs we were able to identify Carfilzomib, Omacetaxine, Ixabepilone, and Romidepsin as potent antineoplastic agents of which Ixabepilone showed the most pronounced effect. These promising preclinical results warrant further clinical investigation of Ixabepilone for the treatment of aggressive meningiomas.

Neuroonkologie III/*Neurooncology III*

V124

Monozentrische Auswertung von mikrochirurgisch behandelten Chordomen und Chondrosarkomen der Schädelbasis
Monocentric follow-up of microsurgically treated skull base chordomas and chondrosarcomas

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Objective

To get an assessment of the microsurgical treatment of patients presenting with chordomas and chondrosarcomas of the scull base

Methods

Symptoms, endocrinological deficits, tumor location/extension were documented as well as the surgical approach and prior therapies. The direct postoperative clinical condition was assessed regarding neurological and endocrinological deficits and perioperative complications. A broad panel of neuropathological examinations was conducted (Keratin, EMA, D2-40, Brachyury, S 100, Ki67). Patients were followed for adjuvant therapies, clinical status, regular MRI, the overall survival rate with time to recurrence and subsequent therapies

Results

27 patients were treated between March 2004 and June 2020. 55,6% (15) were female. 55,6% (15) presented with histologically diagnosed chordoma, 11.1% (3) with chondroid chordoma and 33.3% (9) with chondrosarcoma. Mean age was 42.9 ± 19.8 years. 22.2% (6) were operated using a transcranial approach, the others by the transsphenoidal route. A planned biopsy for histological confirmation of extensive lesions was taken in 18.5% (5), intended partial resection in 63% (17) and 14.8% (4) total resection. For 1 patient grade of resection was not classified. Frozen section was performed in 13 cases, 2 of those did not prove the later diagnosis. Surgery associated complications were seen in 4 patients (18.2%, p=0.21 Fisher"s exact). CSF leaks were seen in 3 of 20 patients with transsphenoidal surgery (15.0%), no leaks were recorded in transcranial operations (p=0.50). 1 patient died due to a severe hemorrhage after transcranial surgery. Follow up was 2.7 (range 0-6) years mean. 63% (17) showed postoperative tumor mass and 14.8% (4) were reoperated during follow up. 7,4% (2) received conventional radiotherapy, 18.5% (5) did not receive adjuvant therapy, 11,1% (3) were treated using heavy ion irradiation and 44,4% (12) received proton irradiation. 3,7% (1) required a VP-Shunt. An adjuvant therapy was initiated in 47.2% of all chordomas and 100% of all chondroid chordomas and chondrosarcomas. 2 more patients died within follow-up

Conclusion

Curative surgery for skull base lesions from the chordoma/chondroid chordoma/chondrosarcoma group by microsurgery alone is hard to achieve. The majority of patients requires adjuvant radiation treatment which can control the disease. Intraoperative frozen section is helpful to guide surgical aggressiveness for these difficult lesions

Fig. 1

Histological Markup

Diagnosis	Keratin	EMA	D2-40	Brachyury	S100	Ki67 <1%	Ki67 <5%	Ki67 <10%
Chordoma	100%	100%	25%	92.3%	86.7%	72%	18%	9%
Chondroid Chordoma	100%	100%	0%	100%	100%	0%	67%	33%
Chondrosarcoma	20%	25%	100%	0%	100%	50%	50%	0%

Neuroonkologie III/*Neurooncology III*

V125

Die nTMS gestützte Traktografie bei Hirnstammtumoren – Risikostratifizierung und klinisches Potenzial
NTMS based tractography in brainstem tumours – risk stratification and clinical potential

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Objective

Neurosurgical interventions in the brainstem have a high risk for new postoperative deficits due to the close spatial relation and density of vital neuronal structures. Reliable preoperative methods to evaluate factors that correlate with these risks are necessary for informed therapeutic decision making. The nTMS based tractography has already taken an important role in preoperative planning in brainstem cavernoma surgery, but has not been investigated in brainstem tumors yet. The aim of this study is to establish a reliable methodology to visualize the descending motor fibers in patients with brainstem tumors and to evaluate the potential for presurgical risk stratification of this method.

Methods

All patients with brainstem tumors, diagnosed by means of MRI, were examined preoperatively with navigated transcranial magnetic stimulation (nTMS) and diffusion tensor imaging (DTI). [TP1] The MEP-positive spots were used as seed points for the DTI fiber tracking of the descending motor tracts. Somatotopic fiber tracking was performed at a fractional anisotropy (FA) value of 75% of the individual FA threshold. Then, distance measurements between the brainstem tumor and the corticospinal tract (CST) and corticobulbar tract (CBT) were performed.

Results

18 patients were enrolled in this study, with 11 patients undergoing surgical resection and 6 receiving stereotactic biopsy. The diagnoses consisted of glioma (WHO I-II° 28%, III-IV°: 44%), meningioma (22%) and metastasis (5%). Mapping of the motor cortex and tract reconstruction for hand, leg, and facial function was successful in all patients. The somatotopy of corticospinal and corticobulbar tracts was also clearly depicted on the brainstem level. In all the patients with a CST to tumor distance of 0-1mm, only a partial resection due to MEP loss during surgery could be accomplished. None of the patients developed a new motor deficit postoperatively.

Conclusion

NTMS-based fiber tracking allows for an individually tailored surgical planning and risk stratification. The somatotopic tract visualization on the brainstem level might serve as a valuable instrument to increase safety in brainstem tumor surgery and expand surgical indication in these patients.

Digitale und KI-basierte Anwendungen II/*Digital and AI-based implementations II*

V126

Datengetriebene Vorhersage des postoperativen klinischen Outcomes unter Verwendung des Neurologic Assessment in Neuro-Oncology (NANO)-Scores bei Glioblastompatienten – die klinische Nützlichkeit eines Black-Box Machine Learning Models

Data-driven prediction of postoperative clinical outcome using the Neurologic Assessment in Neuro-Oncology (NANO) score in glioblastoma patients – the clinical usefulness of a black-box machine learning model

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Objective

For patients with glioblastoma (GBM), postoperative neurological deterioration can markedly compromise the quality of life and reduce overall survival. The Neurologic Assessment in Neuro-Oncology (NANO) score was proposed for the standardized assessment of neurologic function, but its accurate prediction remains challenging. Artificial intelligence-based methods offer patient-tailored predictive analytics for outcomes in neurosurgery, but they often remain black-box models for the sake of maximizing performance over interpretability. We compare a logistic regression (LR) with a neural network (NN) for *clinically relevant* outcome predictions and discuss their usefulness in personalized medicine.

Methods

Data included 229 patients (mean [SD] age 62 [11] years; 88 female) in total, with a preoperative NANO score of mean 2.3 [2.1], and mean 2.4 [2.4] postoperatively. Clinically relevant postoperative deterioration was defined as NANO≥3. Data were randomly split into a development set (80%) and a validation set (20%). Generalizability was evaluated in 1000 bootstrap iterations on the validation set.

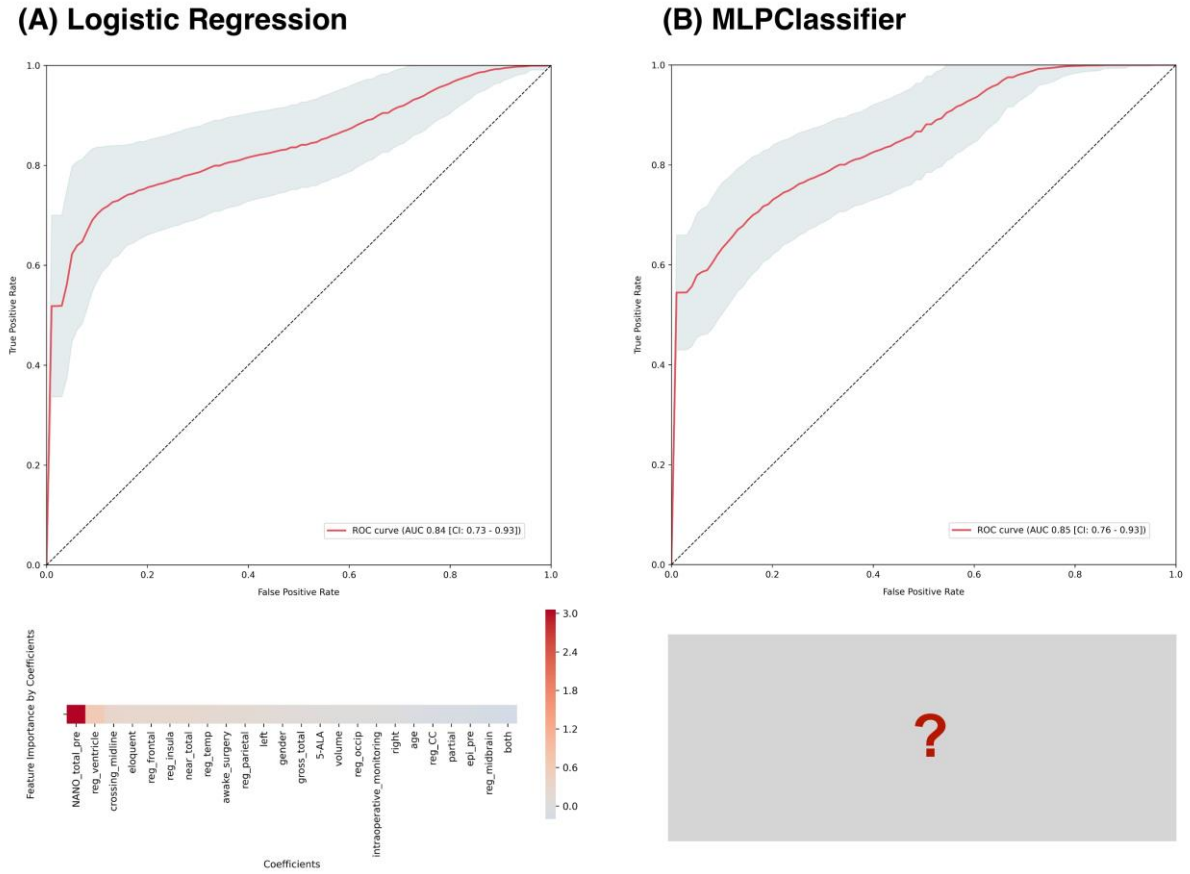
Results

The predictive performance was determined by comparing the predicted with the actual neurologic deterioration, which resulted in an area-under-the-curve (AUC) value of 0.84 [95% CI 0.73- 0.93] for LR (Fig. 1A), with a precision and recall of 0.85 [0.76-0.92] and 0.83 (0.74-0.91). The NN performed better: AUC 0.85 [0.76 - 0.93], precision 0.78 [0.69-0.88] and recall 0.76 (0.67-0.87) (Fig. 1B). Based on AUC alone, the NN is superior; however, considering precision and recall it is outperformed by the LR. Further, only the LR is inherently interpretable and offers insights into the inference of the included features (Fig. 1A lower part). This makes it more useful in the clinical setting and highlights the influence of preoperative NANO, ventricular and midline infiltration, as well as eloquence for postoperative predictions.

Conclusion

An AI-based neuronal network was successfully applied to predict postoperative NANO after GBM resection. While maximizing performance, the NN lacks measures of interpretability, and can generally be seen as a *black-box model*. In contrast, LR offers insights into the model"s generative process and performs almost equally. As high-stake clinical decisions require both accuracy and understanding of how the prediction works, the usefulness of black-box models seems to be limited and needs further development for successful clinical application.

Fig. 1


(A) Logistic Regression
(B) MLPClassifier
True Positive Rate
False Positive Rate
ROC curve (AUC 0.84 [CI: 0.73 - 0.93])
ROC curve (AUC 0.85 [CI: 0.76 - 0.93])
Feature Importance by Coefficients
NANO_total_pre
reg_ventricle
crossing_midline
eloquent
reg_frontal
reg_insula
near_total
reg_temp
awake_surgery
reg_parietal
left
gender
gross_total
5-ALA
volume
reg_occip
intraoperative_monitoring
right
age
reg_CC
partial
epl_pre
reg_midbrain
both
Coefficients
?

Digitale und KI-basierte Anwendungen II/*Digital and AI-based implementations II*

V127

Datengesteuerte chirurgische Entscheidungsfindung – Vorhersage der Resektabilität bei Glioblastompatienten mittels Machine Learning

Data-driven surgical decision-making – prediction of resectability in patients with glioblastoma using machine learning

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[2]Universitätsklinikum Aachen, Neurosurgical Artificial Intelligence Laboratory Aachen (NAILA), Aachen, Germany
[3]University Medical Center Hamburg-Eppendorf, Department of Neurosurgery, Hamburg, Germany
[4]University Hospital Cologne, University of Cologne, Department of Neurosurgery, Köln, Germany

Objective

Surgical decision-making in patients with glioblastoma (GBM) remains challenging as it aims at achieving maximal resection without causing neurological deterioration. Computational approaches leveraging novel artificial intelligence and machine-learning methods may enhance the decision-making process in a "*data-driven*" fashion – realizing a step towards personalized medicine.

Methods

We conducted a machine learning-based examination of multicentric data from four sites, including 480 patients with GBM (mean [SD] age 62 [12] years; 191 female) in total, of which 47% were found to have complete excision of the contrast-enhanced tumour area. Resection was classified as gross-total versus partial. Data were randomly split into a development set (80%) and a validation set (20%). The model selection included AdaBoost, GradientBoost, Logistic Regression, and Random Forest. L2-penalized Logistic Regression was selected as most competitive and hence evaluated on the validation set in 1000 bootstrap iterations.

Results

The overall accuracy of the learned predictive model was determined by comparing the predicted resectability with the actual rate of removal, which resulted in an area-under-the-curve (AUC, Fig. 1) value of 0.70 (95% CI 0.61- 0.79) on the validation set, confirming the generalizability of the approach. Precision and recall of 0.68 (95% CI 0.60-0.77) and 0.67 (0.58-0.75) were observed, respectively. Based on the coefficient weights of the predictive machine learning approach (Fig. 2), the use of intraoperative monitoring and the application of 5-ALA, positively impacted the rate of gross-total resection, while unfavorable locations, as well as overall tumor volume, had a negative impact.

Conclusion

The proposed machine learning-based framework allows for reliable prediction of gross-total resectability in patients with GBM and is hoped to complement and ease surgical decision-making, highlighting the benefits of intraoperative fluorescence and monitoring, as well as unfavorable topographical tumour patterns.

Fig. 1

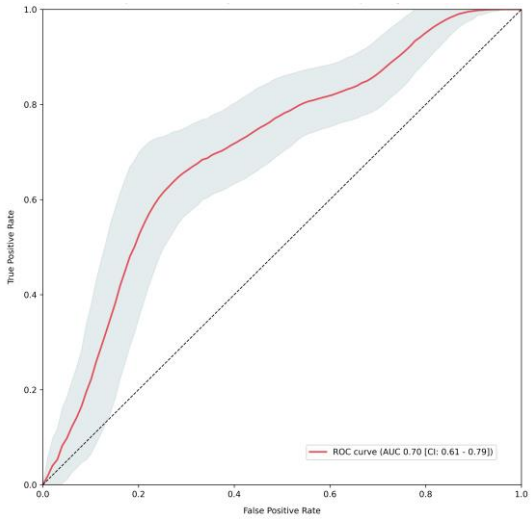
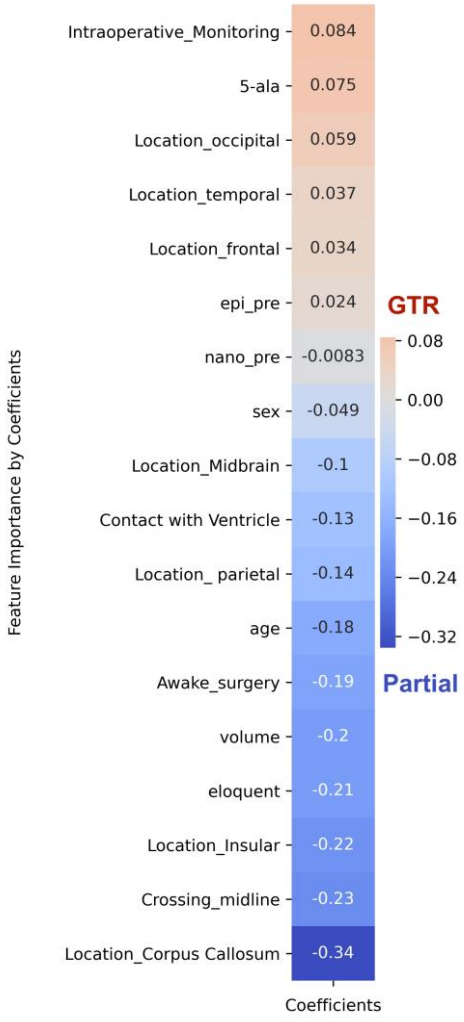

True Positive Rate
False Positive Rate
ROC curve (AUC 0.70 [CI: 0.61 - 0.79])

Fig. 2


Intraoperative_Monitoring 0.084
5-ala 0.075
Location_occipital 0.059
Location_temporal 0.037
Location_frontal 0.034
epi_pre 0.024
nano_pre -0.0083
sex -0.049
Location_Midbrain -0.1
Contact with Ventricle -0.13
Location_ parietal -0.14
age -0.18
Awake_surgery -0.19
volume -0.2
eloquent -0.21
Location_Insular -0.22
Crossing_midline -0.23
Location_Corpus Callosum -0.34
Feature Importance by Coefficients
Coefficients
GTR
0.08
0.00
−0.08
−0.16
−0.24
−0.32
Partial

Digitale und KI-basierte Anwendungen II/*Digital and AI-based implementations II*

V130

Vollautomatische Planung navigierter lumbosakraler Pedikelschrauben mittels künstlicher Intelligenz
Automated screw planning of navigated lumbosacral pedicle screws using artificial intelligence

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[2]DKFZ Heidelberg, Medical Image Computing, Heidelberg, Germany
[3]Universitätsklinikum Heidelberg, Neuroradiologie, Heidelberg, Germany

Objective

Use of navigation for spinal instrumentation has gained traction in recent years but preoperative trajectory-planning is a time-consuming task. We sought to develop and validate an automated planning tool for lumbosacral pedicle screws using a convolutional neural network (CNN).

Methods

We used planning data from random 155 CT-navigated instrumentations and extracted screw parameters from 1052 pre-planned pedicle screws covering L2-S1 levels, which served as training data for a CNN. A vertebra instance-based approach employing a state-of-the-art U-Net framework was developed and trained followed by internal 5-fold cross-validation. The retrieved net was evaluated on an external test-set of 30 cases not involved in training. Automatic screw parameters were compared to corresponding pre-planned screws in the test-set by mean absolute difference (MAD) of screw head and tip points, length and diameter, respectively. Clinical acceptability of algorithm-generated screws was evaluated by experts using the Gertzbein-Robbins (GR) classification.

Results

Automated planning was feasible for all targeted 198 screws. Compared to pre-planned screws, MAD was 4.3±2.1mm for screw head, 4.2±2.4mm for tip points, 4.6±3.1mm for length and 0.4±0.3mm for diameter. In ANOVA followed by Dunn"s multiple comparison, MAD for head and tip points was significantly greater at L5 and S1 compared to other segments ($p<0.001$), reflecting increasing degrees of freedom in caudal screw placement. No difference between segments was found for screw length and diameter. Upon expert rating, screws were predominantly classified grade A (189, 95%) with only 9 grade B screws (5%) according to GR indicating that screws showed either no, or only minor (<2mm) cortical breach. All planned screws were classified clinically acceptable. Algorithm generated screws were not inferior to their manually planned companions.

Conclusion

We derived a fully automated planning tool for lumbosacral pedicle screws using CNN. Validation showed sufficient accuracy to facilitate screw planning with high potential to increase time-efficiency in navigated spinal instrumentation when integrated into commercial navigation systems.

Digitale und KI-basierte Anwendungen II/*Digital and AI-based implementations II*

V131

Das Verhältnis von peritumoralem Ödem zu Tumorvolumen lässt auf den *KLF4*^{K409Q} Mutationsstatus in Meningeomen schließen

High peritumoral oedema relative to tumour volume predicts KL4*^{K409Q} *mutation in meningioma

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[2]Universitätsklinikum Köln, Radiologie, Köln, Germany
[3]Universitätsklinikum Magdeburg, Neuropathologie, Magdeburg, Germany

Objective

In Meningioma, several Non-NF2 driver mutations (*KLF4, TRAF7, SMO, AKT1E17K*) have been shown to correlate with certain pathological subtypes, tumor locations and clinical features. Specifically, we have recently shown that the *KLF4*^{K409Q} mutation may cause enhanced hypoxia signalling and correlates with increased peritumoral edema. While mutation-specific treatment options are still lacking, preoperative identification of the mutational status of meningioma could facilitate selection of pre- and perioperative medical treatment options in the future. The objective of this study was to evaluate the relationship of preoperative MRI features and the *KLF4*^{K409Q} mutation in meningioma patients

Methods

Clinical, pathological and preoperative imaging data on 96 patients who previously underwent meningioma resection between 2013 and 2018 were collected and frozen tumor samples sequenced for the *KLF4*^{K409Q} mutation. Different imaging characteristics were collected (i.e. tumor surface, arachnoid plane, T2 intensity) and semiautomatic volumetric analysis of tumor size and peritumoral edema (PTE) was performed. In addition, the edema index (EI) (ratio of PTE to tumor volume) was calculated and all factors were correlated with the mutational status of KLF4. Receiver operating characteristic (ROC) curve analysis was performed to identify cut-off EI values to predict the mutational status of *KLF4*.

Results

13 (13.5%) of the analysed tumors carried the mutation and the mutation was significantly associated with a secretory subtype ($p<0.001$) and sphenoid wing location ($p<0.005$). Increased EI ($p<0.005$), as well as a large PTE ($p<0.05$) proved to be significantly associated with the *KLF4*^{K409Q} mutation. In receiver operating characteristic (ROC) curve analysis, EI was the most sensitive and specific parameter to predict a *KLF4*^{K409Q} mutation with an AUC of 0.767. The optimal cut-off value at >1.7 provided a sensitivity of 69.2% and a specificity of 85.5%.

Conclusion

EI can be used as a specific and sensitive parameter to predict the *KLF4*^{K409Q} mutation in meningioma, providing a useful tool for improvement of pre- and perioperative medical management.

Fig. 1

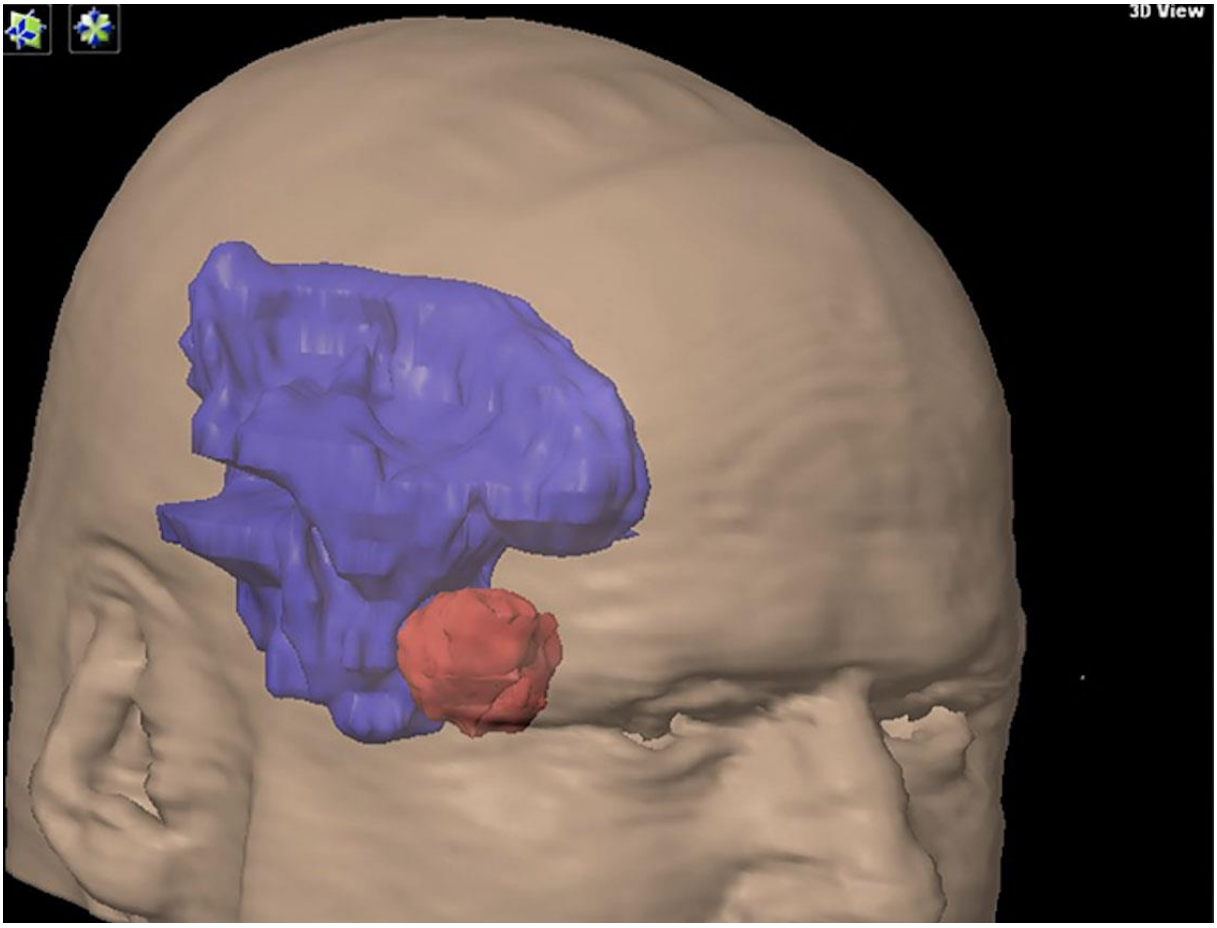
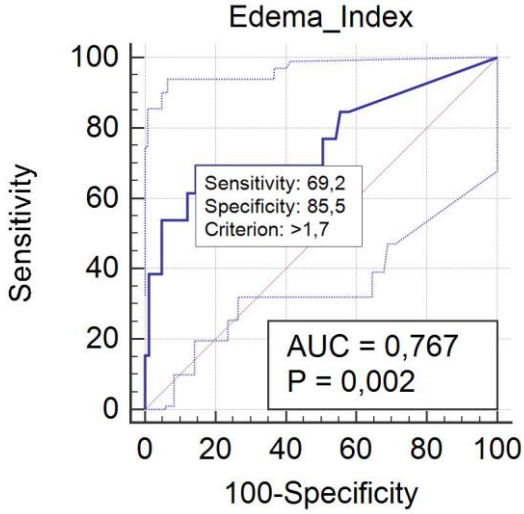

3D View

Fig. 2


Edema_Index
Sensitivity
100
80
60
40
20
0
0
20
40
60
80
100
100-Specificity
Sensitivity: 69,2
Specificity: 85,5
Criterion: >1,7
AUC = 0,767
P = 0,002

Qualitätssicherung und Komplikationsmanagement I/*Quality assurance and complication management I*

V132

Verhindert die antibiotische Therapie eine erneute Schraubenlockerung nach initialer aseptischer Schraubenlockerung und mikrobiologischer Besiedlung? – eine prospektive Beobachtungsstudie

Does antibiotics therapy prevent recurrent screw loosening after low-virulent colonialisation? – a prospective observational study

D. Tkatschenko[1], J. Onken[1], V. Prinz[1], T. Finger[1], A. Trampuz[2], P. Vajkoczy[1], S. Bayerl[1]

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[2]Charité Universitätsmedizin, CMSC, Berlin, Germany

Objective

Screw loosening after spondylodesis represents a common postoperative complication after spine surgery with heavy burden on both patients and healthcare stakeholders. Low-virulent microorganism colonialization exposed by sonication was identified as a possible cause for symptomatic implant ease. However, the role of antibiotics administration for de novo screw loosening prevention remains unclear. The aim of our study was to determine whether antibiotics administration after positive sonication prevents de novo screw loosening.

Methods

After positive ethics vote (EA2/047/19) all patients from January 2015 – July 2018 were identified undergoing revision surgery and examination of explanted screws for microorganism colonialization with sonication. All identified patients were invited for clinical and radiographic follow-up. Screw loosening was evaluated in CT-scans carried out at least 12 months after revision surgery. Subdivision into three groups was conducted: Group 1a included all patients with positive sonication results and postoperative antibiotics treatment, Group 1b involved all patients with positive sonication results without postoperative antibiotics treatment and Group 2 served as reference cohort containing all patients with negative sonication results.

Results

79 patients (51 female, mean age 65.12 years) were identified. 25 patients agreed to participate in follow-up (31.6%). Eligible CT-scan for screw loosening evaluation was available in 42 patients (51.2%). This patient population was segregated into the three groups (Group 1a - n=5, 12%, Group 1b - n=8, 19% and Group 2 - n=29, 69%). In 10 out of 13 patients with positive sonication (Group 1a + Group 1b) de novo screw loosening occurred (76.9%) whereas antibiotics administration had no influence on screw loosening rates (4 out of 5 patients in Group 1a and 6 out of 8 patients in Group 1b). In the reference Group 2 in 11 out of 29 patients de novo screw loosening was identified (37.9%).

Conclusion

Low-virulent microorganism colonialization plays an important role in the incidence of screw loosening. No benefit for antibiotics administration in patients with positive sonication could be depicted. New ways of biofilm formation prevention have to be established.

Fig. 1

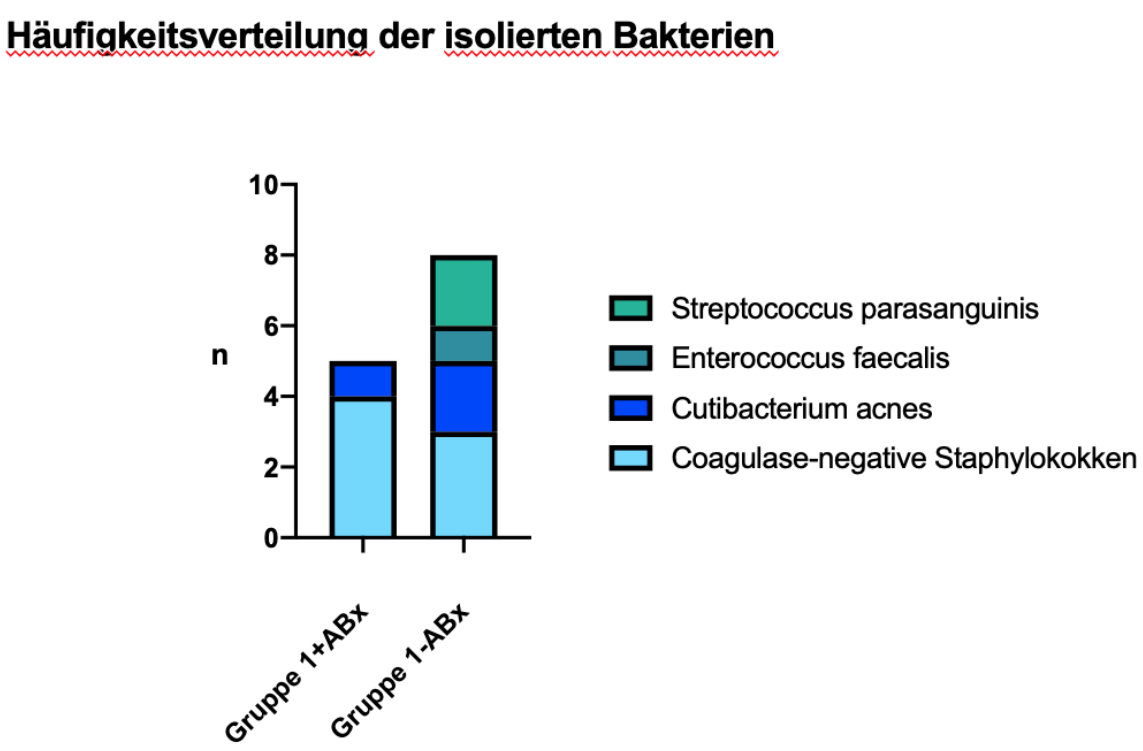
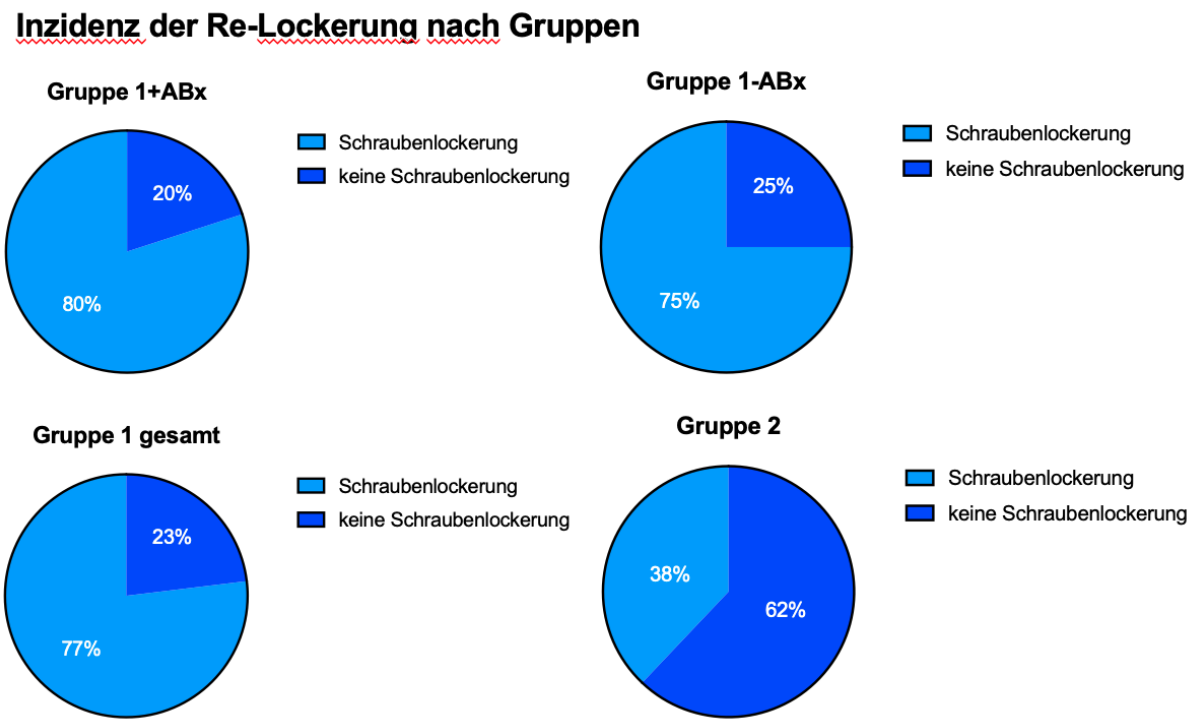

Häufigkeitsverteilung der isolierten Bakterien
10
8
6
4
2
0
n
Gruppe 1+ABx
Gruppe 1-ABx
Streptococcus parasanguinis
Enterococcus faecalis
Cutibacterium acnes
Coagulase-negative Staphylokokken

Fig. 2


Inzidenz der Re-Lockerung nach Gruppen
Gruppe 1+ABx
20%
80%
Schraubenlockerung
keine Schraubenlockerung
Gruppe 1-ABx
25%
75%
Schraubenlockerung
keine Schraubenlockerung
Gruppe 1 gesamt
23%
77%
Schraubenlockerung
keine Schraubenlockerung
Gruppe 2
38%
62%
Schraubenlockerung
keine Schraubenlockerung

Qualitätssicherung und Komplikationsmanagement I/*Quality assurance and complication management I*

V133

Endoskopische ICG-Angiographie – Ist ein Routineeinsatz in der Aneurysmachirurgie durch technische Verbesserungen möglich?
Endoscopic ICG angiography – Routine tool during aneurysm surgery by technical advancements?

D. Mielke[1], X. Hautmann[1], V. Malinova[1], C. Bettag[1], B. Schatlo[1], V. Rohde[1]

[1]Georg-August-Universität Göttingen, Neurochirurgie, Göttingen, Germany

Objective

It has been shown that endoscopic indocyanin green (ICG) angiography in aneurysm surgery provides the neurosurgeon with additional information in 50 % of the cases, if compared with microscopic ICG angiography. However, insufficient illumination of the operative field and a substantially poorer contrast than in microscopic ICG angiography hindered a more widespread use. The aim of the present investigation was to test if new software releases for image processing in combination with better light transmission improved this technique.

Methods

In six patients with unruptured aneurysms, endoscopic ICG angiography was performed after clip placement, using two imaging processing software solutions combined (I: dynamic brightening of dark areas of the endoscopic image; II: color contrast enhancement) and one software solutions alone (III: spectral color shift and color exchange). For each patient and each software/software combination, illumination of the operative field and intensity of contrast was rated by 4 neurosurgeons not involved in the treatment as poor (1 point), moderate (2 points) or good (3 points). In a second step, the neurosurgeons compared the image quality with that of video-taped endoscopic ICG angiographies that had been performed before the recent soft- and hardware release and of microscopic ICG angiographies in 3 patients each.

Results

Better results in terms of contrast were obtained with the combination of software I and II (6.5 versus 5), whereas software III scored better in terms of illumination (6.75 versus 4). If compared with the “old” endoscopic ICG angiographies, the image quality was constantly rated as being better irrespective of the applied software. If compared with microscopic ICG angiography, the image quality of endoscopic ICG angiography is as good (contrast: 6.5 versus 7.25, illumination: 6.75 versus 6) as microscopic ICG angiography.

Conclusion

Recent software releases together with improved light transmission substantially improved the quality of endoscopic ICG angiography, being now as good as microscopic ICG angiography. At latest now, endoscopic ICG angiography can considered being a useful tool during aneurysm surgery.

Qualitätssicherung und Komplikationsmanagement I/*Quality assurance and complication management I*

V135

Die Entscheidung lebensverlängernde Maßnahmen nach Hemikraniektomie bei Schlaganfallpatienten einzustellen – eine Analyse von Mortalität und Entscheidungsfindung

Mortality re-visited – end of life decisions after decompressive hemicraniectomy in patients with ischemic stroke

X. Hautmann[1], S. Hernández-Durán[1], C. von der Brelie[1], V. Rohde[1]

[1]Universitätsmedizin Göttingen, Neurosurgery, Göttingen, Germany

Objective

Decompressive hemicraniectomy (DC) in ischemic stroke is often indicated in an emergency setting and decision making is challenging. Postoperatively patients might remain in a critical condition and the clinical course might be complicated. As clinicians, we often arrive at a point where we feel obliged to challenge and re-evaluate the achievable therapeutic goal. In this study, we performed an analysis on the reasons of mortality and the frequency, reasons and content of "end of therapy" / "end of life" (EoL) decisions.

Methods

We retrospectively analyzed the postoperative course of 109 patients who underwent DC for ischemic stroke at our department between January 2011 and March 2019. We checked if an EoL decision was made and which patient-related factors, CT findings and neurological findings played a role in the EoL decision. We furthermore looked at congruency of the EoL with the alleged patients will.

Results

39 patients (33%) died during their hospital stay. An EoL decision prior to death was documented in 92.3 % (36 patients) of all deaths. The mean duration between DC and an EoL decision was 9.4 days (range 2-29 days). Higher age was associated with a higher rate of EoL decisions (p=0.005). There was no significant association between CT findings (brain edema, midline shift, brain herniation) and EoL decisions. Postoperative hemorrhagic transformation of the infarction led to a significantly longer duration until an EoL decision was made (p=0.025). Postoperative complications (such as wound problems, hematoma formation) and the side of infarction did not correlate with the rate of EoL decisions. Interestingly, EoL decisions were made more often in men (p=0.031). Male sex correlated highly significant with a higher rate of involvement of relatives in decision making (p=0.01). The alleged patient´s will was evaluated in 75% of all cases. 97.2% of all EoL decisions were taken unanimously between physicians, nurses and relatives. An ethics committee was involved in one case.

Conclusion

The rate of EoL decisions after DC in ischemic stroke was suprisingly high. Our study shows that particular clinical or radiological criteria did not contribute to decision making, while the evaluation of the alleged patient´s will, higher age and interdisciplinary decisions play an important role.

Qualitätssicherung und Komplikationsmanagement I/*Quality assurance and complication management I*

V136

Neuropsychologisches Outcome nach Wach-Operationen von Hirntumoren in der sprachdominanten Hemisphäre
Neuropsychological outcome after awake surgery of brain tumours in the language-dominant hemisphere

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[1]University Hospital Frankfurt, Department of Neurology, Frankfurt am Main, Germany
[2]University Hospital Frankfurt, Department of Neurosurgery, Frankfurt am Main, Germany

Objective

Preserving patients" cognitive performance during surgical therapy is of special importance for their future participation and professional ability. Therefore, we aimed at evaluating the neuropsychological outcome in patients after awake brain tumour surgery in language-relevant areas.

Methods

In 27 patients with gliomas in language-relevant areas of the left dominant hemisphere comprehensive neuropsychological assessment was performed before (T0) awake surgery as well as ≤9 months (T1) and >9 months (T2) thereafter. A neuropsychological test battery evaluating attention, verbal fluency, verbal memory, working memory, executive functions, and mood disturbances was applied. Differences in pre- and postsurgical cognitive performance were analysed by paired samples t-tests, and Cochran tests.

Results

At T1, impairments in all cognitive domains were noted, with significant deteriorations in verbal fluency (t^{0vs1}=-2.824, p=0.010), and working memory (t^{0vs1}=-2.668, p=0.014). At T2, all cognitive functions, particularly verbal fluency (t^{1vs2}=5.200, p<0.001) and verbal memory (t^{1vs2}=3.407, p=0.004) had recovered. Defining a z-score <-1.5 as an objectified deficit, we found significant changes in deficit rates for verbal fluency (Cochran"s Q=9.333, p=0.009) with a pronounced increase to T1 and a subsequent return almost to the preoperative level (T0: 7.7%, T1: 36.4%, T2: 10.5%), for executive functions (Q=6.000, p=0.049) with also higher values for T1 (T0: 14.8%, T1: 34.8%, T2: 5.0%), but also a decrease in the rate of mood impairments (Q=7.000, p=0.030; T0: 66.7%, T1: 34.8%, T2: 35.0%). In summary, at T2, 5% of patients still had deficits in attention, working memory and executive functions, 10.5% deficits in verbal fluency, 20% disorders of verbal memory, and 35% still showed impaired mood.

Conclusion

Our results indicate that the cognitive status of patients with tumours in language-relevant areas initially worsened significantly after awake surgery. These deficits consistently recovered after the subsequent months, but a relevant number of patients with persistent impairments remained (especially in language-related functions and mood). Therefore, caution is advised regarding the assumption of full recovery of cognitive performance after awake surgery, in order to identify individual needs for neuropsychological rehabilitation and psychotherapeutic support in this subset of patients.

Qualitätssicherung und Komplikationsmanagement I/*Quality assurance and complication management I*

V137

Veränderung des Outcome in der elektiven chirurgischen Versorgung von Aneurysmen der vorderen Strombahn durch technische Verbesserungen

Outcome changes in elective anterior circulation aneurysm surgery over the last two decades due to technical improvements

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[2]University Hospital, Ludwig-Maximilian-University Munich, Anesthesiologic Clinic, München, Germany

Objective

Over the last 20 years, several periprocedural adjuncts for elective surgical aneurysm treatment have been introduced to increase safety and efficacy, notably the spread of intraoperative neurophysiological monitoring in the late-1990s, implementation of ICG-videoangiography (ICG-VAG) in the mid-2000s, and introduction of intraoperative CT-angiography/-perfusion (iCT-A/-P) in the mid-2010s. These technical achievements were accompanied by improved anesthesiologic and standardized OR-procedures. Although the benefit seems intuitively obvious, it has never been shown whether patient outcomes improved in parallel with introducing these techniques.

Methods

Patients undergoing microsurgical clip occlusion for anterior circulation aneurysms between 1999–2018 were included, with IONM routinely used since 1999, ICG-VAG routinely since 2009, and iCT-A/-P since 2016 in selected cases. We analyzed patients" characteristics, imaging/surgical parameters, treatment-related morbidity, and outcomes, focusing on differences between three distinct cohorts.

Results

543 patients were included, all treated by a specialized vascular team, which changed over time. 192 patients were operated before 2008 (cohort I). Since 2009, 284 patients were operated with ICG-VAG, but without iCT-A/-P (cohort II), and 67 patients with ICG-VAG and iCT-A/-P (cohort III). While mean age was younger in cohort I (52 vs. 55 resp. 57yrs; $p<0.01$), there was no difference between the three cohorts concerning gender distribution (m/f: 1/3) and predominant aneurysm location (MCA: 61%, ICA: 19%, AcomA: 20%). Mean aneurysm size was larger in cohort I (9.3 vs. 7.5 resp. 7.0mm; $p<0.01$). Both the rate of radiologically detected postoperative ischemia (15.6 vs. 12.0 vs. 9.0%) and the rate of postoperative new deficits (12.5 vs. 7.7 vs. 7.5%) were improved in cohort II and III compared to I; however, the differences did not reach significance. Yet, the incomplete aneurysm occlusion rate was significantly improved at last follow-up (mean: 12months) between cohort I and cohort II resp. III (29.7 vs. 16.4 resp. 6.8%; $p=0.05$). For cohort III, however, radiologically described aneurysm remnants (4 of 67 cases) were only considered clinically relevant in one patient requiring re-surgery.

Conclusion

(Peri)procedural achievements in elective anterior circulation aneurysm surgery seem to have improved surgical outcomes during the past 20 years.

Neurovaskuläre Chirurgie I/*Neurovascular surgery I*

V138

In vivo Induktion von Vasospasmen mit Hilfe von Ultraschall im CAM-Modell
In vivo vasospasm induction by ultrasound application in the chicken chorioallantoic membrane model

K. Döring[1], H. Schroeder[2], S. Sperling[3], M. Ninkovic[3], F. Streit[4], L. Binder[4], V. Rohde[3], V. Malinova[3]

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Objective

Cerebral vasospasm is the most investigated phenomenon in the context of aneurysmal subarachnoid hemorrhage (aSAH), its pathophysiology however is still not fully understood. Experimental models are irreplaceable for the evaluation of new drugs for vasospasm resolution. In this study, we assessed the reliability of in-vivo vasospasm induction by means of ultrasound in the chicken chorioallantoic membrane (CAM) model as an alternative to animal models.

Methods

After incubation of the fertilized chicken eggs for four days, a fenestration was performed to enable examination of the CAM. On the thirteenth day continuous wave ultrasound (3 MHz, 1 W/cm^2, maximum effective area of 5 cm^2) was applied on the CAM vessels for 60 seconds. The ultrasound effect on the vessels was recorded by life imaging (5 MP HD-microscope camera, Leica®). The induced vasospasms were evaluated based on the vessel diameter in a defined time interval of 10 minutes using a Fiji macro. The vessel diameter before and after the ultrasound application was measured and the relative diameter reduction was calculated.

Results

The experiment was performed on 10 embryo eggs. A first reduction of vessel diameter was observed after three minutes. The maximum reduction in vessel diameter was reached eight minutes after the ultrasound treatment (mean relative vessel diameter reduction of 46%, range 44-56%). The ultrasound-induced vasospasm was reliably reproducible in all 10 eggs. The vasospasm persisted for all ten recorded minutes post induction. Longer ultrasound application (more than 60 seconds) did not lead to an increase in vasospasm-intensity.

Conclusion

Vasospasm can be reliably induced by direct short application of low frequency ultrasound in the CAM model. This might be a suitable in-vivo model for the evaluation of drug effects on vasospasm in an experimental setting and could serve as an alternative to animal models.

V139

Aspirin Einnahme schützt vor übermässiger Entzündung in tierexperimentellen Bifurkationsaneurysmen unter Betrachtung verschiedener Wandcharakteristika

Aspirin treatment protects again inflammation in experimental bifurcation aneurysms with different wall conditions in New Zealand white rabbits

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Objective

In the past decades endovascular therapies have become increasingly popular in treating unruptured and ruptured intracranial aneurysms. Aneurysm wall degeneration is linked to aneurysm growth and rupture in preclinical and clinical studies. The aim of this study was to analyze the impact of aspirin (ASA) on the natural course of aneurysms with different wall conditions (vital, decellularized, elastase degraded) in a rabbit bifurcation model.

Methods

Bifurcation aneurysms were created in New Zealand White rabbits by suturing the right on the left carotid artery by end-to-side anastomosis with interposition of an arterial pouch (allograft or autograft). Study groups comprised vital, decellularized and elastase degraded aneurysms either with or without additional ASA treatment (n = 6). Animals were randomly allocated to one of these groups using a web-based randomization system. Primary outcomes were aneurysm patency and growth within 28 days. At follow-up contrast enhanced magnetic resonance and fluorescence angiography were performed. After harvesting the aneurysm underwent macroscopic and histological evaluation. Inflammation was assessed by semiquantitative cell count for neutrophils.

Results

We observed that none of the aneurysms ruptured during follow-up. Intraoperative fluorescence angiography revealed aneurysm patency in all cases (n = 44/44). After 28 days, patency of the aneurysm was confirmed in 92 % (n = 33/36) with magnetic resonance imaging. The vital (without ASA) and elastase (with and without ASA) groups revealed a significant increase in aneurysm size measured macroscopically. The decellularized series without ASA showed complete aneurysm thrombosis in only 50 % of cases (n = 3/6). Histological analysis revealed a significant reduced inflammation of the aneurysm complex in all groups receiving ASA.

Conclusion

Continuous ASA intake prevented inflammation of the periadventitial tissue layers as well as of the aneurysm wall, irrespective of initial wall condition. In aneurysms with vital walls, ASA significantly prevented aneurysm growth, whereas this preventive effect did not seem to play an important role in elastase degraded

pouches. Considering these results, ASA intake in humans might have a potential preventive effect in the early phase of aneurysm formation in cases with healthy vessels but not if highly degenerative aneurysm wall is present.

V140

Brain natriuretic Peptide als Prädiktor der früh postoperativen Krampfanfälle nach chirurgischer Behandlung traumatischer akuter Subduralhämatome – eine prospektive Studie

Brain natriuretic peptide as predictor of early postoperative seizure in patients with traumatic acute subdural hematoma – a prospective study

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Objective

Brain natriuretic peptide (BNP) is known as a reliable biomarker in the acute phase of traumatic brain injury, related to its severity, presence of increased intracranial pressure and unfavorable outcome. The purpose of this study was to analyze the plasma BNP level in patients with traumatic acute subdural hematoma (aSDH) and assess its clinical implications.

Methods

Patients with unilateral traumatic aSDH that were surgically treated in our department between July 2017 and April 2020 were included in the study. Plasma BNP levels were preoperatively measured. Early postoperative seizure (EPS) was assessed. Neurological condition and functional status of the patients were prospectively recorded using the Glasgow Coma Scale (GCS) at admission, at the seventh postoperative day, and the modified Rankin Scale (mRS) at discharge and follow-up (at 2-3 months), respectively. An unfavorable outcome was defined by a mRS>3.

Results

In total, 104 patients were included in the study (median age: 74.5 years, range: 23-91 years). In-hospital mortality occurred in 31.7% of the cases (n=33). At follow-up, 83.1% of the survivors were assessed. EPS (median: 3 days, IQR: 1 day) occurred in 19.2% of the patients (n=20), and was recurrent in 80% (16/20) of the cases. The univariate analysis showed a statistically significant association between poor GCS score at the seventh postoperative day and EPS, but no association between EPS and functional outcome at discharge and last follow-up. The multivariate analysis revealed higher plasma BNP levels (cutoff ≥ 95.4 pg/ml, aOR=5.9, p=0.004), left-sided aSDH (aOR=4.4, p=0.017) and female sex (aOR=3.8, p=0.024) as independent predictors of EPS.

Conclusion

Preoperative plasma BNP level is a reliable predictor of EPS in patients with traumatic aSDH. EPS is common and is known to worsen the postoperative neurological status of the patients, affecting the short and long-term functional outcome by delaying the recovery. Whether the postoperative prophylactic use of antiepileptic drugs in patients with higher risk of EPS can improve their neurological and functional outcome, needs further investigations.

Neurovaskuläre Chirurgie I/*Neurovascular surgery I*

V141

Contralateral inhibition of the motoric language area in left sided ischemia and its effect on language performance – a model for neurosurgical patients with aphasia

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Objective

Repetitive transcranial 5Hz-magnetic stimulation (rTMS) supports and 1Hz rTMS impairs neuronal depolarization of cortical neurons. Both techniques are used to reinforce speech therapy (ST) and were tested by us in 2 randomized double blind sham controlled protocols.

Methods

Protocol 1:

Right handed patients with left sided brain infarcts were treated over 2 weeks with daily ST, preceded by 20 min of inhibitory rTMS to the contralateral (right hemisphere) homologous Broca area. 15 pts. received sham stimulation and 15 verum rTMS at 1 Hz. Clinical speech capacity was tested before and after the protocol with the Aachener Aphasia Test (AAT).

Protocol 2:

63 pts. suffering from sub-acute ischemic stroke aphasia of the Cologne-Canadian randomized, double blind placebo controlled protocol (1, details see Europ Stroke J, 10.1177/2396987320934935) were divided into 3 groups and treated within 45 days after stroke over 2 weeks with either inhibitory rTMS (N = 20) (same protocol as in study 1), cathodal transcranial direct current stimulation (ctDCS) (N = 24) or sham (N = 19) over the right-hemispheric homologous Broca area as preceding adjuvant therapy to daily ST.

Test on progression at three language primary outcomes were performed on days 0 and 30 using the Boston Naming Test (BNT), Token Test (sentence comprehension) and Semantic Fluency test.

Results

In both protocols pts. treated with daily ST plus rTMS had at end of protocol a better speech performance (Naming, sentence comprehension) as pts. with sham treatment.

At day 30 there was a difference for naming ($p = .010$) and sentence comprehension tasks ($p = .033$). Naming scores of rTMS patients improved significantly more than Naming-scores of tDCS patients. The tDCS group improved more on the Token test. Per-protocol analyses (N=48) confirmed the beneficial effect of rTMS on naming recovery at Day 30 post-treatment.

Conclusion

In left sided ischemic aphasia of the postacute state speech therapy plus preceding repetitive transcranial magnet inhibition of the right sided homologous Broca area is an effective treatment. Cathodal direct current stimulation seems to be an alternative to rTMS. It seems possible that patients with neurosurgical interventions suffering from pre- or postoperative aphasia will also benefit. This should be evaluated in studies with aphasic patients suffering from craniectomy, posttraumatic state, subarachnoid hemorrhage, and other intracerebral lesions.

Neurovaskuläre Chirurgie I/*Neurovascular surgery I*

V142

Gibt es eine Zukunft für die dekompressive Kraniektomie? – Ergebnisse des German Cranial Reconstruction Registry (GCRR)

Is there a future for decompressive craniectomy? – Results of the German Cranial Reconstruction Registry (GCRR)

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Objective

The benefit of decompressive craniectomy (DC) in cerebral infarction (CI) and traumatic brain injury (TBI) is an ongoing debate in which the aspect of a reduced mortality seems to ignore the procedural complication rate accompanied by clinical disability. Here, we report an interim analysis of the German Cranial Reconstruction Registry (GCRR) with special regard to the timing and technique of DC and perioperative complications.

Methods

A subgroup analysis of the GCRR, a prospective multicenter database for DC and subsequent cranioplasty,was performed. All patients enrolled at the time of DC were included in the analysis and perioperative complications as well as in-hospital neurologic outcome were analyzed.

Results

A total of 217 patients out of 502 registered in the GCRR were included. Depending on the diagnosis we divided five groups: 1. TBI (37.6%), 2. Malignant CI (25.2%), 3. aneurismatic Subarachnoid Hemorrhage (aSAH, 12.8%), 4. Intracerebral Hemorrhage (ICH, 7.8%) and 5. Other (16.5%). Patients in group 2 and 4 showed a significant worse neurological outcome (mRs 4.7±0.4 and 4.63±0.9) at discharge compared to patients in group 1 (mRs 2.8±4) or 5 (1.5±2.7). In addition, size of DC were different between the five groups with significant larger DC"s in group 1 and 2. The overall in-hospital mortality rate was 12.4% whereas the overall complication rate after DC was 40.6% (88/217 patients). Most common complications were wound healing disorders (23.5%), CSF-fistulas (12.2%) and postoperative hemorrhage (6.8%). A revision surgery was necessary in 31.3% of patients.

Conclusion

High complication rates of more than 40% require a critical reevaluation of previous DC studies and call our daily management into question. Upcoming analyses of the GCRR will further sharpen our understanding of this treatment.

Neurovaskuläre Chirurgie I/*Neurovascular surgery I*

V143

Levosimendan als therapeutische Strategie zur Vorbeugung von Neuroinflammation nach aneurysmaler Subarachnoidalblutung?

Levosimendan as therapeutic strategy to prevent neuroinflammation after aneurysmal subarachnoid haemorrhage?

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Objective

Poor patients' outcome after aneurysmal subarachnoid haemorrhage (SAH) is owed a multifactorial process, mainly including cerebral inflammation (CI), breakdown of cerebral autoregulation, delayed cerebral vasospasm (DCVS) and delayed cerebral ischemia (DCI) followed by neurodegeneration. CI is mainly triggered by enhanced synthesis of serotonin (5-HT), prostaglandin F2alpha (PGF2a) and cytokines such as interleukines. Levosimendan (LV), a calcium-channel sensitizer, was already shown to display anti-inflammatory effects in patients with severe heart failure. Therefore, we wanted to elucidate its potential anti-inflammatory role on cerebrovasculature after SAH.

Methods

Experimental SAH was inducted by using a modified double-haemorrhage rat model. Autologous blood was taken and injected into the cisterna magna on day 1 and 2. Sham animals received injection of isotonic 0.9 % saline, instead. Sprague-Dawley rats were sacrificed on day 3 and 5 after SAH or sham operation. The vasospastic basilar artery was carefully dissected from the brain stem and further used for isometric investigations of the vessel tone in an organ bath. Vessel segments were either preincubated with LV (10-4 M) or without. Precontraction was performed with 5-HT (10-9 M – 10-5 M) or PGF2a (3 x 10-5 M) followed by application of an acetylcholine- (ACh) (10-8 M – 10-4 M) or LV-series (10-8 M – 3 x 10-4 M).

Results

After preincubation with LV and 5-HT-precontraction ACh-series showed a strong vasorelaxation. Interestingly, SAH D3 and D5 vessel segments showed a higher vasorelaxation compared to sham-operated animals. The application of a LV-series after prior PGF2a precontraction of the arterial ring segments showed a significant enhanced relaxation in sham- ($p = 0.004$) and SAH-animals ($p = 0.0008$), compared to a solvent control group without LV.

Conclusion

LV administration after SAH seems to beneficially influence DCVS by antagonizing inflammatory microenvironment characterized by 5-HT and PGF2a. A 5-HT- and PGF2a-mediated vasocontraction was notably reduced after experimental induced SAH. Considering these spasmolytic and anti-inflammatory effects, LV might possess a role in the treatment of SAH, even more in the treatment of Tako-Tsubo-Cardiomyopathy, where the use of catecholamine inotropes is contradicted.

Starke Frauen, starke Männer – Schaffen wir die Gleichstellung?

V210

Eine steigende Flut bringt alle Boote zum Schwimmen? – die Evolution der Frauenbeteiligung in der Deutschen Gesellschaft für Neurochirurgie

A rising tide lifts all boats? – evolution of female participation in the German Society of Neurosurgery

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Objective

Neurosurgery has traditionally been a male-dominated field, with both U.S.-American and European studies demonstrating a disproportionally small recruitment of women into the specialty when compared to their male counterparts. In this study, we aimed to determine the evolution of female participation in the German Association of Neurosurgery (DGNC) and establish a trend on female recruitment.

Methods

We conducted a retrospective study evaluating the membership of the DGNC from its creation until present, assessing the amount of female members and their academic degrees. We then performed a scatter-plot charting of their numbers throughout the years for trend estimation.

Results

In 1969, the first woman joined the DGNC. Since then, the amount of ordinary members has exponentially risen to 170 in 2020 (b=86). The first two female associate professors (PD) joined the DGNC in 1981, constituting 29% (2/7) of all female ordinary members. Since then, the percentage of PD among female members of the DGNC has steadily decreased (y= -0.31), making up 10% of the current female ordinary membership. On the other hand, the first female professor in the DGNC appeared in 1985, making up 14% (1/7) of all female ordinary members in that year. Since then, the proportion of professors among female ordinary members has also steadily decreased (y= -0.17), yet at a slower rate than PD, constituting 11% of the current female ordinary membership.

Conclusion

While female participation in the DGNC has grown exponentially since the first woman joined the association in 1969, our study suggests that there is an academic glass ceiling for women in German neurosurgery, for the proportion of female PD and professors has not followed the trend of female ordinary membership throughout the decades.

Fig. 1

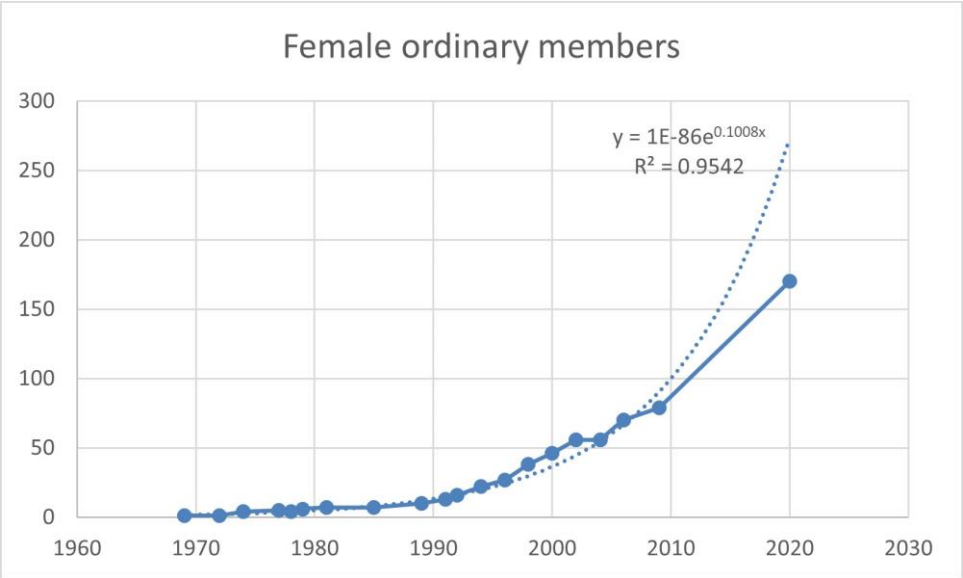
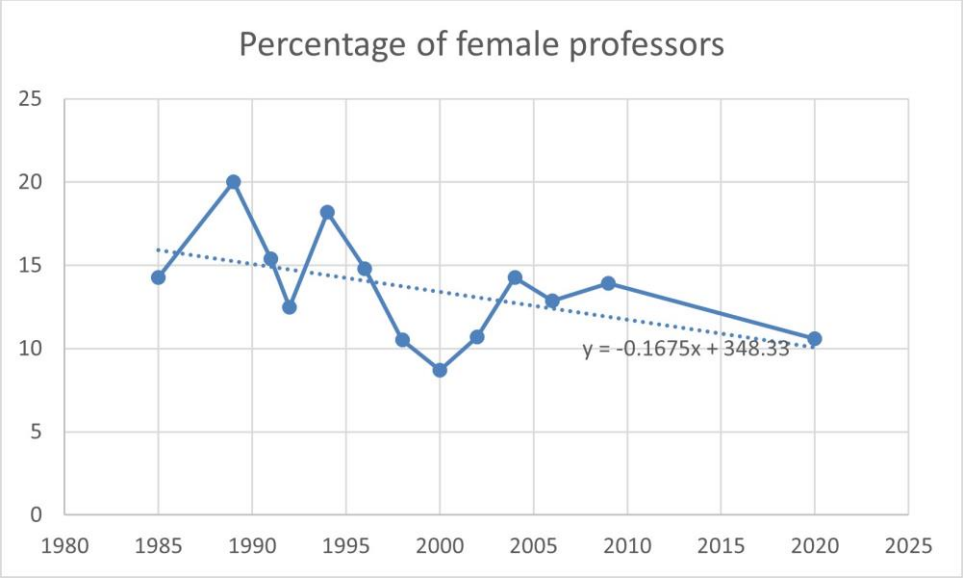

Female ordinary members
y = 1E-86e^0.1008x
R² = 0.9542
300
250
200
150
100
50
0
1960
1970
1980
1990
2000
2010
2020
2030

Fig. 2


Percentage of female professors
y = -0.1675x + 348.33
25
20
15
10
5
0
1980
1985
1990
1995
2000
2005
2010
2015
2020
2025

Starke Frauen, starke Männer – Schaffen wir die Gleichstellung?

V211

Geschlechterdiversität in deutschen neurochirurgischen Kliniken
Gender diversity in German neurosurgery

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Objective

Despite the rising number of women in higher education and leadership positions the rise of female neurosurgeons still lags behind. Therefore, his study evaluates the gender distribution across all career levels in German neurosurgical departments, aiming at heightening the awareness of the possibility for improving gender equality and its related opportunities.

Methods

Data on gender distribution across all professional levels in German neurosurgical departments were obtained from departmental websites as well as by email and telephone request. Results were additionally analyzed in regard to ownership type of neurosurgical departments.

Results

A total of 141 German neurosurgical departments employing 2312 neurosurgeons were evaluated. Analysis revealed a clear preponderance of men in leadership positions. Among 145 department directors 9 (6.21%) female directors were identified. Of 42 deputy directors and 149 senior physicians 1 (2.38%) and 21 (14.09%) were female, respectively. Women accounted for 167 (23.3%) consultant positions. Board-certified neurosurgeons not holding a consultant position and residents were female in 33.8% and 34.8%, respectively.

Of note, the highest proportion of female department directors (16.1%) and senior physicians (19%) was found in private hospitals.

Conclusion

The number of women in leadership positions in German neurosurgical department is dramatically low, and with hierarchy gender disparity increases. Mentorship, recruitment, the perception of benefits offered by diversity and programs facilitating gender equality, job sharing, parental leave policies and on-day child care programs are needed in order to turn German neurosurgical departments into modern medical departments reflecting the gender profile of our patient population.

Starke Frauen, starke Männer – Schaffen wir die Gleichstellung?

P237

Geschlechterunterschiede in der Wahrnehmung und Einstellung von Medizinstudierenden gegenüber der Neurochirurgie – eine bundesweite umfragenbasierte Analyse

Gender differences in perceptions and attitudes of medical students towards neurosurgery – a nationwide survey-based analysis

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Objective

Despite advances in gender equity, the paucity of women neurosurgeons still remains. In Germany, women accounted for only 24% of the specialists who completed their neurosurgical training in 2019. We sought to explore the perceptions of medical students in Germany towards a neurosurgical career, focusing on gender-specific differences which may underlie the gender gap.

Methods

A digital comprehensive 26-item questionnaire with a Likert 4-point scale and open-ended questions was distributed to the German Medical School student bodies. Data was analysed to determine intra-group variability between female and male respondents.

Results

210 medical students participated in the survey. The majority of respondents were in the clinical part of their studies. Female and male students were equally interested in brain pathologies (38% vs. 47%, *strongly agreed*), whereas interest in neurosurgery was significantly greater in males (12% vs. 26%, *strongly agreed*). In contrast, a significantly greater number of male students believed neurosurgical residency would negatively impact their wellbeing (12% of females vs. 37% of males, *strongly agreed*). Further, male students were less likely to believe that female neurosurgery residents would face inequality at work. They were also less likely to support a gender quota in neurosurgery. Yet, both female and male students were convinced that a rise in the number of women would positively impact the field (51% vs. 48%, *strongly agreed*). No gender-dependency was seen in students" strive for success and prestige. Male students felt discouraged from pursuing neurosurgery because they feared an unpleasant work environment whereas female students were concerned about neurosurgery not being family-friendly. Regardless of gender, the greatest factor deterring students from neurosurgery was poor work-life balance.

Conclusion

Awareness must be raised concerning gender inequity and possible gender-specific discrimination in our specialty. A multifaceted approach is imperative to develop our field into a profession where gender becomes less important than the overarching fact that we all share the same mission.

Fig. 1

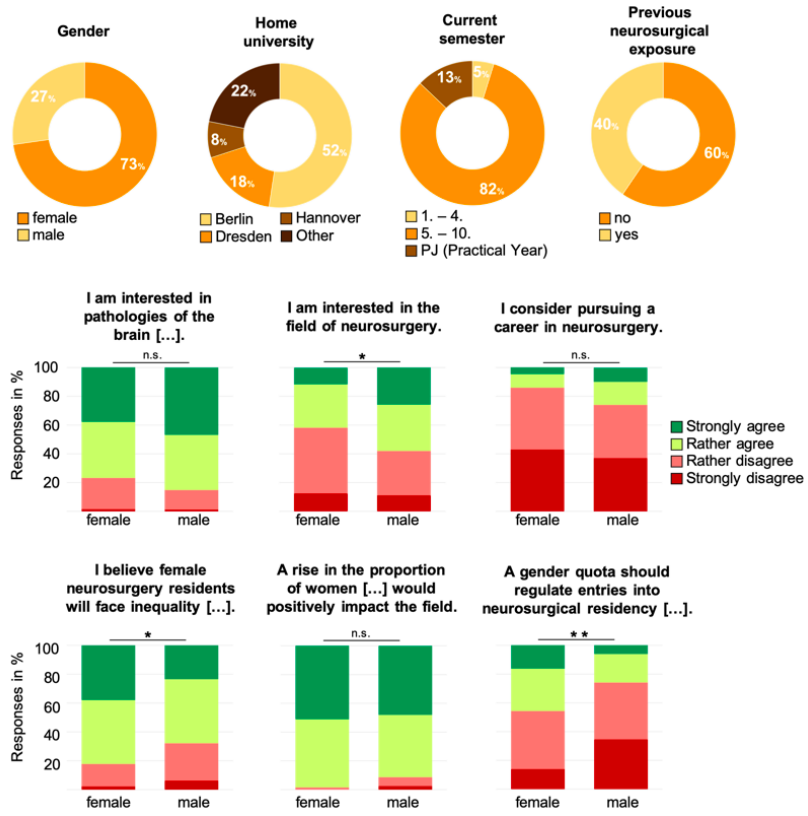

Fig. 2

Item	Gender	Strongly disagree	Rather disagree	Rather agree	Strongly agree	*p*
I am interested in pathologies of the brain […].	Female	1.6%	21.7%	38.8%	38.0%	.429
	Male	1.2%	13.6%	38.3%	46.9%	
I am interested in the field of neurosurgery.	Female	12.4%	45.7%	30.2%	11.6%	**.032**
	Male	11.1%	30.9%	32.1%	25.9%	
I consider pursuing a career in neurosurgery.	Female	43.0%	43.0%	9.4%	4.7%	.195
	Male	37.0%	37.0%	16.0%	9.9%	
I believe female neurosurgery residents will face inequality […].	Female	2.3%	15.5%	44.2%	38.0%	**.047**
	Male	6.2%	25.9%	44.4%	23.5%	
A rise in the proportion of women […] would positively impact the field.	Female	0.0%	1.6%	47.3%	51.2%	.084
	Male	2.5%	6.2%	43.2%	48.1%	
A gender quota should regulate entries into neurosurgical residency […].	Female	14.0%	40.3%	29.5%	16.3%	**.001**
	Male	34.6%	39.5%	19.8%	6.2%	
Family-friendly residency […] should be established in neurosurgery […].	Female	0.8%	2.3%	23.3%	73.6%	.726
	Male	1.2%	4.9%	24.7%	69.1%	
I do not mind a rigorous and unpredictable work schedule.	Female	23.3%	38.0%	29.5%	9.3%	.492
	Male	22.2%	32.1%	29.6%	16.0%	
I am career-oriented and strive for prestige.	Female	9.3%	34.1%	38.8%	17.8%	.722
	Male	11.1%	27.2%	44.4%	17.3%	
[…] neurosurgical residency would negatively impact my […] wellbeing.	Female	8.5%	38.8%	40.3%	12.4%	**.000**
	Male	4.9%	24.7%	33.3%	37.0%	

Pearson's chi-squared test

Neuroonkologie IV/Neurooncology IV

V144

Evaluierung von wichtigsten prognostischen Faktoren für OS bei 202 Patient*Innen mit diffusen Gliomen
Evaluation of key prognostic factors for overall survival in 202 patients with lower-grade gliomas

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Objective

According to unremitting research in recent years, different groups of prognostic factors – molecular features, tumor volumes and epidemiological data – have been proposed for outcome evaluation in patients with lower-grade gliomas. We compared the integrative impact of these factors in terms of overall survival.

Methods

All consecutive patients with diffuse (WHO °II) or anaplastic glioma (WHO °III), who underwent surgery between 2010 and 2019, were included. The pre- and postoperative MRI volumes in T1 CE, T2 and diffused weighted imaging were measured. IDH, ATRX and EGFR status was assessed during neuropathological routine examination or using FFPE tissue from our biobank. Clinical and follow-up data were gained from the institutional neurooncological database.

Results

202 patients (115 men, 87 women) with a median age of 47 years (IqR 36 – 57) were included. Advanced WHO grade (HR 9.0, CI95% 2.3 – 34.2), IDH wild-type (HR 2.1, CI95% 1.0 – 4.4), preoperative (HR 1.028/cc, CI95% 1.004 – 1.052) and postoperative T1 CE volume (HR 1.209/cc, CI95% 1.063 – 1.375), as well as postoperative T2 positive remnant tumor and oedema volume (HR 1.013/cc, CI95% 1.003 – 1.023) showed a significant influence on OS in multivariate Cox analysis.

The OS was decreased in case of anaplasia: 100 months (CI95% 91 – 108) vs. 50 (CI95% 39 – 61), as well as IDH wild-type: 55 months (CI95% 44 – 71) vs. 94 (CI95% 85 – 103). Gliomas with preoperative CE showed an OS of 57 months (CI95% 47 – 67) versus 98 (CI95% 88 – 107) in those without CE. Similar results could be shown for postoperative CE with 90 (CI95% 81 – 98) vs. 46 (CI95% 28 – 64) months correspondingly.

Conclusion

The prognosis for patients with diffuse and anaplastic glioma should be based on integrative evaluation of neuropathological and radiological parameters. Despite the increasing importance of molecular features, the value of WHO grade and contrast enhancement for the OS should not be underestimated.

Neuroonkologie IV/Neurooncology IV

V145

Halbsitzende Lagerung bei Kindern unter 3 Jahren zur Entfernung von Tumoren der hinteren Schädelgrube
Feasibility of the semi-sitting position in children younger than 3 years of age for resection of posterior fossa tumours

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Objective

The semi-sitting position for resection of posterior fossa tumors offers several surgical advantages in comparison with the prone or lateral position like easier anatomical orientation, gravity aided drainage of irrigation and clearer vision, avoidance of venous congestion by cerebellar retraction and minimization of the need for bipolar coagulation. Nevertheless, it harbors some risks, with the most dreaded beeing venous air embolism (VAE).

Methods

We analysed the datasets of children younger than 3 years of age operated in our institution over a 20-year period. Persistent foramen ovale was excluded preoperatively. Seventeen patients were intraoperatively monitored for VAE, 15 by transthoracal echography (TTE) and 2 by transoesophageal echography (TEE). Intraoperative incidents were recorded and patients course followed postoperatively with a special focus on possible complications.

Results

A total of 20 operations in 19 children were performed. There were 12 boys and 7 girls with a mean age of 31 months (range, 9 to 36 months). The histopathological diagnoses included malignant ependymoma (3), pilocytic astrocytoma (6), glioblastoma (1), medulloblastoma (6), ganglioglioma (3) and atypical rhabdoid tumor (1). No major intraoperative complications occurred. VAE was detected in 6 patients. According to the Tuebingen VAE Grading Scale, a grade 1 VAE occurred in two of them without cardiovascular or respiratory signs or symptoms. In one patient a grade 2 VAE was detected managed by intracardial aspiration of the air. In two patients a grade 4 VAE occurred with arterial hypotension with reduction of pCO2, and it was treated successfully with chatecholamin infusion and intracardial aspiration of the air. Postoperatively all children had pneumocephalus and one of them needed a permanent subduroperitoneal shunt. In two children small asymptomatic impression skull fractures due to the Mayfield pin occured.

Conclusion

The semi-sitting position in children under 3 years of age entails certain risks but it can be successfully performed taking special caution to detect and treat potential complications in an interdisciplinary teamwork.

Neuroonkologie IV/*Neurooncology IV*

V146

Neuroonkologische DKG (Deutsche Krebsgesellschaft)-Zertifizierung – Lohnt sich der Aufwand? 5-jährige Erfahrungen eines zertifizierten, regionalen, nicht-universitären Zentrums

Neuro-oncological certification by DKG (German Cancer Society) – Is it worth time and effort? 5-year experiences of a certified regional non-university centre

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Objective

We analysed our 5 years experiences with a DKG - certified regional non-university neuro-oncological centre (NOC) to find out whether the support of extra personnel, costs and time will justify the effects of NOC regarding quantitative and qualitative data.

Methods

From 2014-2019, we systematically evaluated the number of all neuro-oncological cases, the percentage of cases presented and discussed in the weekly interdisciplinary brain tumor board, the percentage of psycho-oncological and of socio-medical care, the percentage of patients enrolled into clinical trials, the number of brain tumor operations and biopsies as well as their complication rates. Baseline was the numbers in 2014 compared with the data in 2019 (audit 2019, key numbers 2018).

Results

Cases presented in the weekly interdisciplinary brain tumor board raised by 15,1%. Psycho-oncological cases raised by 66,6%, socio-medical cases by 9,6%. The number of patients enrolled into clinical studies decreased by 41,3%. The number of brain tumor operations raised by 16,3%. Infection rate was reduced by 82,0%, postoperative clinically relevant hemorrhage by 17,3% and revision surgery by 67,1%.

Conclusion

So far, NOC has resulted in improvement of qualitative and quantitative data concerning number and results of neuro-oncological patients. In our opinion, this justifies the required extra personnel for documentation, costs for the certification procedures and time investment of the neuro-oncological staff even in a regional non-university NOC. For non-university NOCs, participation in clinical studies is still difficult.

Neuroonkologie IV/*Neurooncology IV*

V147

Die Belastung neuroonkologischer Patienten und deren Angehörige während der COVID-19 Pandemie – eine prospektive Untersuchung mit qualitativer Inhaltsanalyse

Neuro-oncological patients' and caregivers' psychosocial burden during the COVID-19 pandemic – a prospective study and qualitative content analysis

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Objective

Neuro-oncological diseases are associated with psychosocial burden, which might be reinforced by the COVID-19 pandemic. We aimed to determine 1) burden caused by the pandemic and disaese, 2) how patients and caregivers cope with the situation, 3) we established items relevant for patients and caregivers in this situation.

Methods

Patients and caregivers were prospectively assessed (04-06/2020) by a 10-item encompassing interview over the phone after given informed consent. The qualitative questions were evaluated using Kuckartz's[1]structured content analysis to find relevant items and main/subcategories.

Results

A total of 69 patients and 20 caregivers were interviewed, n= 36 of the patients were female (49%). Mean age of the patients was 53y (range 32-81). Most patients had the diagnosis of a glioblastoma (31%), the mean KPS was 85%. Patients" mean score on the Distress Thermometer (DT) was 4 (range 0-9; SD= 2.9), n=22 (32%) scored >/=6 showing relevant distress. A total of 25 (36%) had no additional burden due to the pandemic. Main inductive determined categories were 1) "changes in the past four weeks", 2) "burden by the pandemic", 3) "coping strategies" and 4) "requests to the hospital". 21 subcategories were derived deductively from the interviews with the patients, most frequently mentioned were "restrictions in public and private affairs" (28%), "changes in the psychological well-being" (23%) "social interaction by contact restriction"(25%). Main coping strategies were "changes in personal attitude" (58%), and "adaption of behavior to the current situation" (39%). A total of 18 subcategories relevant for caregivers were identified, similar to those of the patients. Regarding burden due to disease vs. pandemic, caregivers perceived a higher burden due to the disease (tumor: DT score 7.5; range 2-10, SD=2.2 vs. pandemic: DT score 3.7 (range 0-10, SD= 3.1). A relevant request to the hospital were telephone consultations instead of face-to-face-contact.

Conclusion

During the pandemic, the needs profile of brain tumor patients is still unique. During COVID-19 pandemic, adaption of the psychosocial assessment is required (e.g., electronic assessment, adaption of questionnaires). We provide main and subcategories covering burden by disease itself but also by the pandemic and focusing on coping strategies and resources, which might be useful in clinical routine.

[1]Kuckartz U. Qualitative Content Analysis: From Kracauer´s Beginnings to Today´s Challenges. Qual Soc Research. 2019.

Neuroonkologie IV/*Neurooncology IV*

V148

Mapping der räumlichen Heterogenität der metabolischen Bildgebung bei Gliomen mittels MR-Spektroskopie
Mapping of spatial heterogeneity of metabolic imaging in glioma using MR-spectroscopy

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Objective

In neuro-oncology, the necessity to examine the biological and molecular properties of glial brain tumors for accurate diagnosis has become crucial. In our prospective study, we aimed to investigate the predictive value of MR-spectroscopy in order to establish a solid automated preoperative molecular characterization of these tumors. We developed a novel MR-spectroscopy-based algorithm that allows the specific molecular analysis of these tumors through a radiomics analytics pipeline.

Methods

90 patients with assumed high- and low-grade brain lesions were enrolled in our prospective imaging trial from 2016 to 2019 and received preoperative anatomical and multi-voxel MRS (5x5x15mm^3 voxel size). Tumor regions were segmented and co-registered to corresponding spectroscopic voxels. Investigation of spatial diversity in tumor-associated metabolic architecture was performed by high-dimensional computational approaches implemented in an innovative R-based package of MRS data analysis. For prediction of molecular profiles based on MRS imaging, we used the bottleneck layer of a deep autoencoder in a multi-layer linear discriminant analysis to predict the molecular profile based on MRS imaging.

Results

Cluster analysis of all spectra revealed 10 different clusters, 6 clusters contained predominantly normal appearing matter, 4 clusters contained FLAIR hyperintense regions, 2 of which were defined as tumor-associated. In the FLAIR hyperintense regions, tumor-infiltrative regions marked by altered choline intensity were separated from edema with a defined signal depression due to increased water peeks. A deep learning model showed high accuracy in differentiating tumor and non-malignant spectra (97.3%). Prediction of the molecular subtype of glioma was 83.4% with the weakest performance in oligodendroglioma (76.7%). Considering the prediction within a spatial resolved MRS dataset, we combined the single-voxel prediction with an MRS-based classifier score which revealed an overall accuracy of 91.2%.

Conclusion

Our data suggest that MRS imaging is a powerful tool to distinguish infiltrative and edema regions and predict non-invasively the molecular profile of brain tumours. The second part of our prospective imaging trial will focus on the validation of our MRS-based classifier.

Neuroonkologie IV/*Neurooncology IV*

V149

Lebensqualität von Patienten nach mikrochirurgischer Entfernung eines Vestibularisschwannoms – ein Langzeit-Follow-Up ≥ 10 Jahre

Patients' quality of life after microsurgery of a vestibular schwannoma – a long-term follow-up ≥ 10 years

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Objective

Long term data about patient health-related quality of life (HRQoOL) following surgery of vestibular schwannomas (VS) is rare. Patients have a favourable prognosis, it is important to evaluate how they fair in the long-term. The aim of our project is to evaluate QOL of patients who underwent surgery in long-term follow up (FU).

Methods

A total of 304 patients who underwent surgery for first diagnosis in 2004-2009 were approached by mail to complete the Dizziness Handycap Scale (DHS), Penn Acoustic Neuroma Quality of Life (PANQOL, disease specific for VS with 8 domains, a score reaching from 0 (worst) to 100 (best), higher scores indicating better function resp. lower symptom load) and Short Form Health Survey-36 (SF-36). We present data descriptively and compared patient groups by treatment or disease related deficits with Mann-Whitney-U-Test.

Results

Responses of n=67 patients were analyzed (22.0%). Mean age at surgery was 50y, n= 39 (58%) are female. Mean FU was 12 years (range: 10-16). Mean domain PANQOL scores were: Anxiety (ANX) 79 (±19), Facial Dysfunction (FAC), 82 (±21), Balance (BAL) 65 (±23), Hearing Loss (HEA) 57 (±25), Energy (ENE) 67 (±21), Pain (PAI) 75 (±28), General Health (GEN) 65 (±19), Total Score (TOT) 70 (±17). An age-adapted comparison of the SF-36 data to the German general population via z-test showed no significant differences (Physical Functioning (PHY) 84 (±19), Role Limitation Physical (RLP) 77 (±38), Bodily Pain (BOP) 83 (±24), General Health (GEN) 69 (±18), Vitality (VIT) 57 (±19), Social Functioning (SOF) 79 (±23), Role Limitation Emotional (RLE) 76 (±39), Mental Health (MH) 68 (±19)). Problems in balance assessed by the DHS were significantly associated with lower HRQoL regarding all subscales of the SF-36, and also for BAL, PAI, ANX, HEA, ENE and TOT on the PANQOL. Facial nerve paresis (House & Brackman °I-II vs. °III-V) was significantly associated with worse disease specific QoL according to PANQOL (FAC $p<0.001$, ANX $p=0.002$ and TOT $p=0.007$).

Conclusion

Although a certain selection bias has to be taken into account, we assume that long-term HRQoL in patients who underwent surgery for VS is not significantly different to the general populations´ HRQoL. However, as measured by the disease specific questionnaire PANQOL, neurological deficits (balance and facial nerve paresis) were associated with reduced HRQoL more than 10 years after surgery.

Neurovaskuläre Zentren III/*Neurovascular centres III*

V150

Epilepsie nach aneurysmatischer Subarachnoidalblutung – Inzidenz, Zeitpunkt und Risikofaktoren
Epilepsy after aneurysmal subarachnoid haemorrhage – incidence, timing and risk factors

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Objective

Aneurysmal subarachnoid hemorrhage (SAH) is a severe type of stroke accompanied with a number of early and late complications resulting in considerable morbidity and mortality. Several studies have already pointed to a delayed risk of post-SAH epilepsy, which is associated with poor outcome. We sought to analyze the risk factors related to the occurrence and timing symptomatic epilepsy after SAH.

Methods

All consecutive SAH cases treated between 01/2003 and 06/2016 were included from our institutional SAH register. Occurrence of epilepsy during the whole documented post-SAH period was followed up to 03/2020. Demographic characteristics and previous medical history of the patients, parameters of initial severity, performed treatments, certain early and late complications of SAH, as well as daily routine laboratory and vital parameter measurements were collected for further assessment with the epilepsy risk in univariate and multivariate analysis.

Results

During the 2811.65 patient-years of post-SAH follow-up (median: 8.93 months/patient), 85 of 948 individuals (9%) in the final analysis developed a symptomatic epilepsy (median: 3.43 months after ictus). In the majority of the cases, epilepsy was diagnosed >3 weeks after SAH (n=61, 71.8%) and in survivors with poor outcome at discharge (mRS=4-5, 15.8% vs. 5.3%, p<0.0001). Patients with epilepsy were at higher risk for functional disability at 6 months after SAH (mRS>2, 61.2% vs. 44.8%, p=0.004). Of over 100 analyzed potential predictors, the following parameters were independently associated with the risk of symptomatic epilepsy after SAH: history of thyroid dysfunction (aHR=1.81, p=0.029), need for decompressive craniectomy (aOR=2.32, p=0.011) and shunt placement (aHR=1.94, p=0.022), persistence of tachycardia (>3 days, aOR=2.06, p=0.025), as well as anemia signs (mean erythrocytes count < 3.6x106 /mcL [aOR=2.4, p=0.015] and mean hematocrit <31% [aOR=2.13, p=0.044]) during first 2 weeks after SAH.

Conclusion

Symptomatic epilepsy occurs predominantly in individuals with poor outcome at discharge and after the acute phase of SAH. The knowledge on the risk factors for SAH-related epilepsy might help in early identification and treatment of compromised individuals, and therefore, help to improve their outcome.

Neurovaskuläre Zentren III/*Neurovascular centres III*

V151

Ursachenfindung bei atypischer intracerebraler Blutung – klinische und radiologische Unterscheidung zwischen cerebraler Amyloidangiopathie und gemischt-lokalisierten atypischen Hirnblutungen

Finding the reason for atypical intracerebral haemorrhage: clinical and radiological differences between patients with probable cerebral amyloid angiopathy and mixed location haemorrhage

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Objective

The key imaging features of cerebral amyloid angiopathy (CAA) are lobar, cortical, or cortico-subcortical microbleeds, macrohaemorrhages and cortical superficial siderosis (cSS). In contrast, hypertensive angiopathy is characterized by (micro) haemorrhages in the basal ganglia, thalami, periventricular white matter or the brain stem. Another distinct form of haemorrhagic microangiopathy is mixed cerebral microbleeds (mixed CMB) with features of both CAA and hypertensive angiopathy. Patients regularly present to neurosurgical and neurological departments with atypical hemorrhages, but clinical differentiation between both entities is often difficult. The distinction between the two entities (CAA and mixed CMB) is clinically relevant because the risk of relevant haemorrhage and stroke should be well balanced if oral anticoagulation is indicated in CAA patients. We aimed to comprehensively compare these two entities.

Methods

Patients with probable CAA according to the modified Boston criteria and mixed CMB without macrohaemorrhage, who presented to the neurovascular service between 2014 and 2019, were retrospectively identified from our database. Comprehensive comparison regarding clinical and radiological parameters was performed between the two cohorts.

Results

96 patients were included into the study. Patients with CAA were older (78±8 vs. 74±9 years, p=0.036) and had a higher prevalence of cSS (19% vs. 4%, p=0.027) but a lower prevalence of lacunes (73% vs. 50%, p=0.018) and deep lacunes (23% vs. 51%, p=0.0003) compared to patients with mixed CMB. Logistic regression revealed an association between the presence of deep lacunes and mixed CMB. The other collected parameters did not reveal a significant difference between the two groups.

Conclusion

CAA and mixed CMB demonstrate radiological differences in the absence of macrohaemorrhages. Susceptibility-based sequences can be used to depict considerably more microbleeds and cortical siderosis compared to GRE T2* sequences. However, more clinically available biomarkers are needed to elucidate the contribution of CAA and hypertensive angiopathy in mixed CMB patients.

V152

Behandlung von rupturierten Arteria Cerebri Media Aneurysmen mit asssoziierten intrazerebralen Hämatom durch ein Team aus Neurochirurgen mit endovaskulärer und mikrochirurgischer Expertise

Managing ruptured middle cerebral artery aneurysms with concomitant intracerebral haematoma in a setting of hybrid capability

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Objective

The management of ruptured middle cerebral artery aneurysms with a concomitant large intracerebral hematoma remains a subject of debate. The rapid evolvement of endovascular techniques and availability has led to studies in the past decade, suggesting a multi-disciplinary approach with coil embolization prior to hematoma evacuation, as an alternative to the conventional purely microsurgical management. However, a multi-disciplinary set up presupposes an efficient cooperation between microsurgeons and interventional radiologists. Hybrid capability on the other hand integrates microsurgical and endovascular ability within a single team of neurosurgeons. It is the objective of this study to analyze if hybrid capability facilitates the management of this subgroup of patients possibly with a superior outcome, in comparison to published multi-disciplinary or purely microsurgical treatment approaches in the literature.

Methods

We retrospectively reviewed 28 cases of ruptured MCA aneurysms with associated ICH, treated in our institution with hybrid capability between January 2006 and December 2019. All patients were initially treated with coil embolization followed by decompressive craniotomy with or without hematoma evacuation. Clinical and radiological features were assessed and the total time to treatment documented. The outcome of patients was followed up at 6 months after discharge according to the Glasgow Outcome Score (GOS).

Results

85.7% of the patients (n= 24) had a poor Hunt and Hess score of 4 or 5 on admission. The mean total treatment time was 238 minutes (range, 130 – 475). The overall in-hospital mortality rate was 21.4% (n= 6). Favorable clinical outcome (GOS 4 or 5) was achieved in 25.9% (7/31) at 6 months. 2 Patients were lost to follow-up.

Conclusion

Hybrid capability efficiently reduces the total treatment time in comparison to published series of multi-disciplinary or purely microsurgical approaches. A positive effect on favorable outcome was not observed.

Neurovaskuläre Zentren III/*Neurovascular centres III*

V153

Zisternale und ventrikuläre Blutmenge verlieren ihre Bedeutung als Risikofaktoren für schlechtes Outcome nach Subarachnoidalblutung durch Einführung von Zisternenlavage-Verfahren

Mitigation of cisternal and ventricular blood load as risk factors for poor outcome after subarachnoid haemorrhage by implementation of cisternal lavage

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Objective

The initial amount of subarachnoid and ventricular blood is an important predictor for outcome in patients with aneurysmal subarachnoid hemorrhage (aSAH). In this comparative study of an unselected aSAH-population we assess the modifiability of these risk factors by implementation of blood clearance by cisternal lavage.

Methods

All patients with aneurysmal subarachnoid hemorrhage (aSAH) treated in our department between 10/2011 and 10/2019 (8 years, n=458) were included in our study. In the first 4-year period (BEFORE), patients with aSAH were treated according to international guidelines. In the second 4-year period (AFTER), cisternal lavage methods were available (n=221) and applied in 72 high-risk patients (31%). The initial cisternal and ventricular blood load was recorded by the Hijdra score. Multivariable regression models were used to assess the prognostic significance of risk factors, including blood load, in relation to common aSAH characteristics in both study groups.

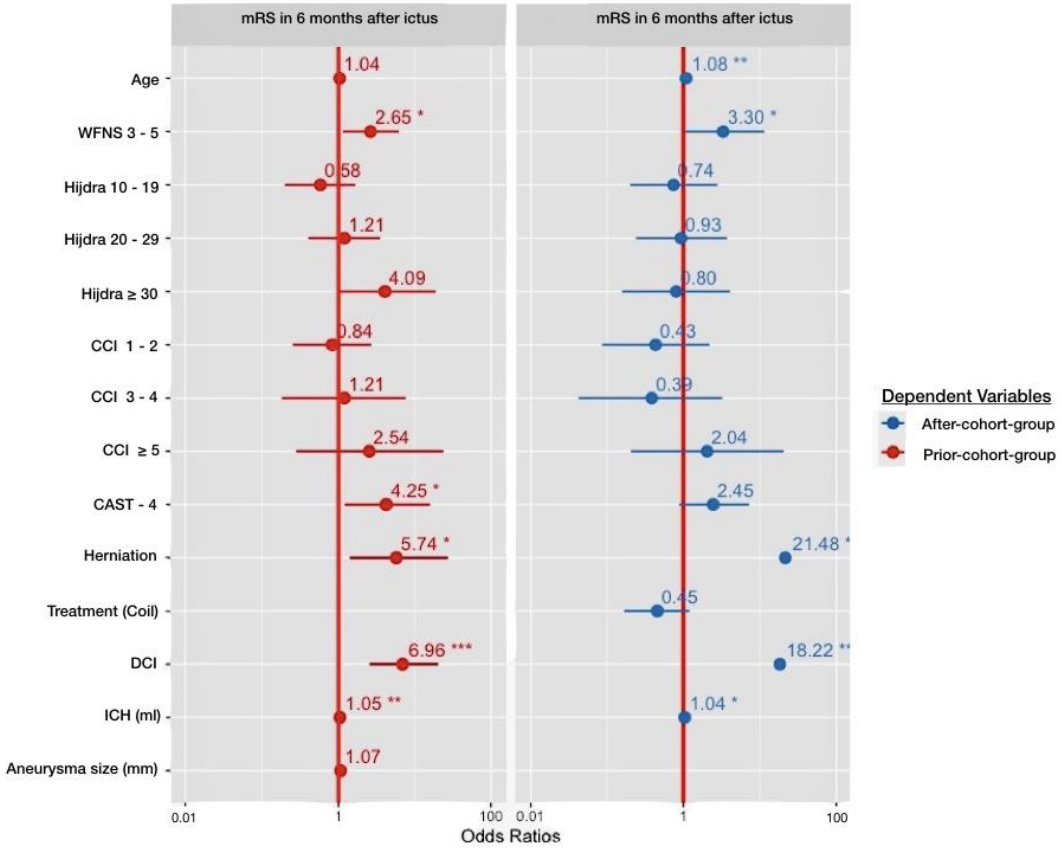
Results

Worse neurological outcomes occurred in the BEFORE population with 41.45 % (BEFORE) vs. 30.77 % (AFTER) unfavorable outcome (mRS >3) six months after aSAH, HR: 1.59 (95% CI 1.08 - 2.34, p=0.01). Admission WFNS grade, comorbidities (CCI), herniation signs, concomitant intracerebral hemorrhage, and the development of delayed cerebral infarction were strongly associated with poor outcome in both study groups. Intraventricular and cisternal blood load and, particularly, a cast fourth ventricle represented strong prognosticators of poor neurological outcome in the BEFORE cohort. This effect was lost after implementation of cisternal lavage (AFTER cohort).

Conclusion

Cisternal and ventricular blood load - in particular: a cast fourth ventricle - represent important prognosticators in patients with aSAH. They are, however, amenable to modification by blood clearing therapies.

Fig. 1


mRS in 6 months after ictus
mRS in 6 months after ictus
Age
WFNS 3 - 5
Hijdra 10 - 19
Hijdra 20 - 29
Hijdra ≥ 30
CCI 1 - 2
CCI 3 - 4
CCI ≥ 5
CAST - 4
Herniation
Treatment (Coil)
DCI
ICH (ml)
Aneurysma size (mm)
1.04
2.65 *
0.58
1.21
4.09
0.84
1.21
2.54
4.25 *
5.74 *
6.96 ***
1.05 **
1.07
1.08 **
3.30 *
0.74
0.93
0.80
0.43
0.39
2.04
2.45
21.48 *
0.45
18.22 **
1.04 *
0.01
1
100
0.01
1
100
Odds Ratios
Dependent Variables
After-cohort-group
Prior-cohort-group

Neurovaskuläre Zentren III/*Neurovascular centres III*

V154

Analyse des zeitlichen Verlaufs des Volumens der Arteria cerebri media in Patienten mit Subarachnoidalblutung
Natural volume time course of the middle cerebral artery in patients with aneurysmal subarachnoid haemorrhage

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Objective

Posthemorrhagic erebral vasospasm is one of the major contributors to delayed cerebral ischemia (DCI) which frequently causes neurological deterioration in SAH patients. A major target during intensive care treatment is monitoring of vasospasm with transcranial Doppler sonography (TCD), CT-angiography (CT-A) or digital subtraction angiography (DSA). Previous studies defined volume thresholds below which impaired perfusion is unlikely. Up to now no volumetric data on time course of the middle cerebral artery (MCA) volume during the initial phase after subarachnoid hemorrhage are available hence we set out to investigate this element.

Methods

We retrospectively identified patients admitted with aneurysmal SAH to our neurosurgical department with or without clinically DCI during therapy. Patients were routinely monitored by serial TCD. Volumetric vessel parameters of MCA segments were analyzed from CTA using a standardized protocol with Amira® software. Volumetric parameters were classified according predefined time points to illustrate the volume course in patients with and without DCI for the first 21 days after ictus.

Results

We identified 20 patients with the diagnosis of aneurymal SAH and serial assessment with CTA as well as TCD. Four patients developed DCI. 67 CT-A (DCI n=25, no DCI n=42) got completely analyzed. MCA volume at ictus was 8.334 ± 2.957 (no DCI) vs. 9.372 ± 1.761 (DCI) µl/mm and during day 1-3 9.535 ± 3.047 (no DCI) vs. 4.551 ± 0.993 (DCI) µl/mm. During day 4-10 and day 11-21 MCA volume was 7.778 ± 2.495 (no DCI) vs. 7.013 ± 1.956 (DCI) µl/mm and 7.122 ± 3.596 (no DCI) vs. 7.735 ± 2.608 (DCI) µl/mm. Statistically significant difference for MCA volume among patients with and without DCI was seen during day 1-3 ($p<0.05$).

Conclusion

To the best of our knowledge this study for the first time presents a neuroradiological time course of MCA volume in patients with aneurysmal SAH. Vessel volumes decrease over the first 21 days after ictus in all patients which indicates a general higher vessel tonus after SAH. During day 1 and 3 MCA volume was statistically significantly lower in the DCI cohort indicating a highly relevance of the initial days after ictus for developing DCI. These findings were concordant with corresponding TCD data documenting increased flow velocities during this time period in patients with developing DCI.

V155

Oxidativer Stress verursacht ein schlechteres neurologisches Outcome nach einer intrazerebralen Blutung
Oxidative stress is associated with poor neurological outcome after intracerebral haemorrhage

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Objective

Spontaneous intracerebral hemorrhage(ICH) is the most severe kind of stroke. Beside the primary brain injury by mass effect, secondary brain injury induced by several factors like inflammation or oxidative stress(OS) determines patients" outcome. An imbalance of oxidative and antioxidative processes results in OS. The aim of this study was to analyze the impact of OS on functional outcome of ICH patients.

Methods

19 consecutive patients receiving an external ventricular drain with an ICH>30ml were included(7 females, 12 males, 64.05±10.99 years). 29 patients(15 females, 14 males, 57.52±15.28 years) with diverse pathologies not associated with oxidative stress, served as controls. Blood and CSF samples were obtained for assessment of OS markers (superoxide dismutase(SOD), glutathione peroxidase(GPx), glutathione-sulfhydryl(GSH), total antioxidant status(TAS) and malondialdehyde(MDA)). The values were analyzed by colorimetry, HPLC or ELISA. Clinical and outcome data were evaluated by modified Rankin scale(mRS) at 6 weeks and 6 months and neurocognition (assessed by MOCA) was correlated to the OS markers and ICH volumes.

Results

Mean ICH volume was 63.3±57.4cm3. Mean TAS differed significantly in serum samples of patients (80.3±20.43mmol/l, *p=0.005*) and controls (40.0±31.4mmol/l, *p=0.005*) at day 1. At the same time point, free(61.34±30.60mg/l) and total(69.57±25.82mg/l) GSH levels were significant higher in controls compared to ICH group(42.86±8.15mg/l; 55.5±7.59mg/l; p<0.0001). The mean total GPx concentration was significantly reduced after ICH(54.04±28.7mg/l compared to 69.6±25.8mg/l; *p=0.03*). CSF TAS levels were reduced significantly after ICH(178.4±20.8) compared to controls(221.0±87.4mmol/l; *p=0.001*). While TAS was higher in serum, it was reduced in CSF after ICH. ICH volume and mean TAS level in CSF(*p=0.2)* and in serum(*p=0.039*) correlated significantly. In CSF MDA(*p=0.01*) and SOD(*p=0.03*) showed a significant correlation to the volume of ICH.Decreased mean GPX in serum was associated with a higher mRS at week 6(*p=0.04*). In CSF SOD(*p=0,04*) and reduced mean MDA levels correlated significantly with a higher mRS at 6 months(*p=0.05*).

Conclusion

In this study we found a clear association of ICH with a reduced antioxidative capacity in CSF and serum. Larger ICH volume showed higher OS levels, while latter correlated significantly with an unfavorable outcome. This might be one key factor in the pathophysiologic cascade of secondary brain injury.

V156

Optimierung des A. cerebri media Perforations-Modells für die Induktion einer Subarachnoidalblutung bei der Maus erlaubt Langzeit-Studien

Optimisation of the MCA perforation model for the induction of subarachnoid haemorrhage in mice allows long-term studies

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Objective

Middle cerebral artery (MCA) filament perforation is a standard technique to model aneurysmatic subarachnoid hemorrhage (SAH). To quantify hemorrhage induction and distinguish SAH from focal cerebral ischemia (i.e. MCA occlusion without perforation), intracranial pressure (ICP) and cerebral blood flow (CBF) monitoring are mandatory. For this, an ICP sensor needs to be placed intraparenchymally/ epidurally while CBF is measured over the ipsilateral (iCBF) or contralateral (cCBF) MCA territory. Due to its size, which for technical reasons cannot be further miniaturized an ICP sensor induces some inevitable brain tissue injury and may thus significantly alter long-term SAH pathology. We therefore assessed whether also bilateral CBF measurements may be suitable to detect SAH in mice thereby allowing long-term experiments.

Methods

Tissue damage caused by probe placement was assessed in C57Bl/6 mice (n=3) by T2 weighted MRI scans performed 7 and 14d after ICP-probe placement. To assess whether correct SAH induction can be monitored by CBF measurements alone, MCA perforation or sham surgery (n=7) was performed in C57BL/6 mice under bilateral CBF measurement by laser doppler flowmetry with (n=25) or without (n=9) additional epidural ICP measurement. We then determined maximum ICP, minimum CBF, hemorrhage volume at the skull base, and assessed histological brain damage in all groups.

Results

T2-imaging in mice after ICP probe placement showed edema formation and persistant cortical damage after 7 (14.7 ±11.7mm^3) and 14 days (11.8 ±1.4mm^3); p=0.6. Bilateral CBF and ICP measurements revealed a temporal correlation of ICP maximum and cCBF minimum: ICP vs. cCBF: r=0,5, p=0,01; ICP vs. iCBF r=0,7, p < 0,01. ICP and cCBF showed also a correlation of absolute extreme values: r=0,5, p=0,02. ICP clot volume and histopathological damage were comparable in both groups.

Conclusion

Although ICP measurement is the most reliable parameter for detecting SAH induction by MCA perforation, it is critical in the context of long-term experiments as it induces a progressive tissue lesion which may confound results. Bilateral CBF measurements correlate with ICP findings and allow ascertaining correct MCA perforation/ SAH induction. We therefore conclude that monitoring by bilateral CBF measurement alone is safe and effective for long-term experiments using the MCA perforation model in mice.

Neuroonkologie IV/*Neurooncology IV*

V157

Entwicklung eines neuartigen humanisierten *ex-vivo* Hirnschnittmodells zur Untersuchung von Glioblastomen und gliom-assoziierten Mikroglia

Implementation of a novel humanised ex-vivo brain slice model to study glioblastoma and glioma-associated microglia

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Objective

Glioblastoma multiforme is a highly malignant brain tumor. Resection followed by radio-chemotherapy leads to an overall survival of only 15 months. Up to 40% of the tumor mass consist of tumor-associated microglia and macrophages (TAMs). These cells were shown to promote tumor growth and invasiveness in many murine glioma models. The interaction between TAMs and tumor cells is crucial for tumor progression and includes several known pathways. Still, murine glioma models only partially mirror the human tumor microenvironment. Several known genes, which are highly upregulated in human glioma and TAMs are only expressed in human tissue and not in mice. To further investigate some of these genes, we aimed at establishing a humanized ex-vivo brain slice model, in which human TAMs and human glioma cells can be studied in a standardized manner.

Methods

We used 250 µm thick murine brain slices, which were depleted of intrinsic microglia by applying clodoronated liposomes. Next, we inoculated human glioma cells (originating from the cell lines U87, U251MG, LN229 and several patient derived cells lines) with or without human microglia derived from induced pluripotent stem cells (iPSCs). Slices were cultivated for 7 to 14 days. We then performed a detailed analysis of microglia morphology (sphericity, cell body volume, process length and branching pattern) and tumor volume.

Results

Clodronation efficacy was high, depending on duration of treatment and length of cultivation. iPSCs and tumor cells integrated into the slice very well. The presence of tumor cells led to an increased sphericity of iPSC-dervied microglia and to an increased cell body volume. Tumor volume was significantly larger when iPSC-derived microglia were present. This was found in various glioma cells lines and also in patient derived cells.

Conclusion

The newly established humanized ex-vivo brain slice system was shown to be feasible. The method successfully allows to study the interaction between human TAMs and tumor cells. Microglia foster tumor growth not only in murine glioma models, but also in a human paradigm. The humanized ex-vivo brain slice model therefore is the optimal basis to study the role human-specific genes in TAM-glioma interaction.

Neuroonkologie IV/*Neurooncology IV*

V158

Phasenbasierte optimierte Auswertung und Visualisierung zur Darstellung funktioneller Hirnareale während neurochirurgischer Eingriffe

Optimised evaluation approach for intraoperative optical imaging data using a fourier-based analysis with phase angle evaluation

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Objective

Intraoperative Optical Imaging (IOI) is a marker free and non-invasive imaging technique that can be utilized for visualization of metabolic changes within the cerebral cortex. During neurosurgical interventions, we use the method in clinical routine to visualize specific functional brain areas in their spatial extent. Here, we are presenting a novel analysis and visualization approach, that allows a more detailed look on the cortical metabolism within the activated areas, and therefore a refined assessment of the activations following different stimulation types.

Methods

Measurements of 22 patients (11 female, 11 male, median age 57.5 years) that underwent surgical resection of lesions were retrospectively evaluated with the new analysis approach. Different stimulation types were applied in the patients - sensory (electrical, median nerve, 15 patients), visual (flash light goggles, 3 patients), tactile (surgical rubber, 3 patients), and speech stimulation (awake surgery, 3 patients), resulting in 24 datasets. Two-dimensional maps of cortical activity, that are representing the location, spatial extent, as well as now the type and direction of metabolic change, were computed for each patient. We compared the maps, that are either based on changes in regional cerebral blood volume or changes in oxygenation, between the different groups.

Results

The results reveal that the new methodology can provide valuable additional information during the surgical procedure. We found significant differences in the nature of activations for the different stimulation types. On the primary sensory cortex, tactile stimulation evoked cerebral blood volume increases whereas electrical median nerve stimulation led in all patients to blood volume decreases, which might be an indication for neuronal deactivation following processing of noxious stimuli. The evaluation of speech activations revealed areas with increased metabolism, closely located to areas with decreased metabolism, whereas mainly the areas with decreased metabolism correlate with essential language areas identified latter during surgery by Electrical Stimulation Mapping (ESM).

Conclusion

The new evaluation and visualization approach reveals promising new insights into the nature of the underlying physiological processes of activated functional areas. This increases the reliability of IOI and may enable the use of the method in additional surgical fields of application in which the use was up to now limited, e.g. during language mapping.

V159

Gestörte Phasensynchronisierung bei motorisch-evozierten Potentialen von Hirntumorpatienten
Phase asynchrony of motor evoked potentials in brain tumour patients

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Objective

Motor-evoked potentials (MEPs) after navigated transcranial magnetic stimulation (nTMS) are mirroring the status of the complete human motor system, far beyond corticospinal integrity. Classic time domain features of MEPs (e.g. peak-to-peak amplitudes and onset latencies) exert a high inter-subject and intra-subject variability. Frequency domain analysis might help to resolve or quantify disease-related MEP changes, e.g. in brain tumor patients. The aim of the present study was to describe the time-frequency representation of MEPs in brain tumor patients, its relation to clinical and imaging findings and the differences to healthy subject.

Methods

This prospective study enrolled 12 healthy subjects and 29 consecutive brain tumor patients (with and without an apparent paresis) who underwent a nTMS mapping. Resulting MEPs were evaluated in the time series domain (i.e., amplitudes and latencies). After transformation to the frequency domain using a Morlet wavelet approach, event-related spectral perturbation (ERSP) and inter-trial coherence (ITC) were calculated and compared to results of the diffusion tensor imaging (DTI).

Results

MEPs were projecting to a frequency band between 30 and 300 Hz with a local maximum around 100 Hz for both healthy subjects and patients. Despite no significant differences in the standard time series characteristics, there was ERSP reduction for higher frequencies (>100 Hz) in patients in contrast to healthy subjects. This deceleration of the MEPs was mirrored in an increase of the inter-peak MEP latencies. Patients with an apparent paresis showed an additional disturbance in ITC in these frequencies. There was no correlation between the CST integrity (as measured by DTI) and the MEP parameters.

Conclusion

The present study demonstrates how time-frequency analysis could provide additional information about the MEP and the status of the corticospinal system in brain tumor patients. This first evaluation indicates that brain tumors might affect cortical physiology and the responsiveness of the cortex to TMS resulting in a temporal dispersion of the corticospinal transmission.

Neuroonkologie IV/*Neurooncology IV*

V160

Postoperative Riech- und Geschmacksbeeinträchtigung in Patienten operiert an Neoplasien im Verlauf der trigeminalen Bahn

Postoperative olfaction and gustatory impairment in patients operated on neoplasia affecting the trigeminal pathway

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Objective

Trigeminal and olfactory synergisms are crucial for a competent perception of smell and taste. Therefore, our intention was to demonstrate the impairment of olfaction and taste in patients operated on acoustic neurinoma, meningioma and other neoplasia affecting the anatomical course of trigeminal nerve.

Methods

The postoperative study comprised 49 patients with acoustic neurinoma (n=24), meningioma (n=19), trigeminal neurinoma (n=5) and one mature teratoma. 29 women and 20 men were included into study. The control group was composed of 36 healthy subjects. Comprehensive assessment of olfactory and gustatory function was conducted with the "Sniffin' Sticks" test kit and a chemosensory quasi-threshold test (taste strips). Prior to that, broad clinical examination of patients and control group was carried out.

Results

In comparison to patients with acoustic neurinomas, patients with meningiomas (posterior and middle fossa) and patients with trigeminus neurinomas have significantly lower function for smell and taste (odor threshold: p=0.017; odor discrimination: p<0.001; TDI score: p=.003). In contrast, patients with acoustic neuromas have significantly lower taste function at the affected side (taste strips at affected side: p=0.002; no significant difference for the healthy side: p=0.76). However, the 3 groups were not significantly different in terms of sensitivity towards trigeminal stimuli (CO2). The sense of smell in patients operated on tumor affecting N.V. is decreased compared to controls (odor threshold: p=0.049; odor identification: p<0.001; TDI score: p=.001).

Conclusion

Benign neoplasia can impair and hinder the integrity of trigeminal and olfactory pathways and thereby interfere their alliance that is crucial for preserving proficient olfaction and gustatory competence.

Neuroonkologie IV/*Neurooncology IV*

V161

Prädiktoren der gesundheitsbezogenen Lebensqualität nach der Resektion von Meningeomen WHO-Grad I
Predictors of health-related quality of life after WHO grade I meningioma surgery

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Objective

Intracranial meningioma WHO grade I is considered a benign disease with long-term disease control after extensive surgery. However, the psychooncological burden of these patients is still poorly defined. Here, we sought to analyse health-related quality of life (QoL) after meningioma resection.

Methods

We performed a retrospective cross-sectional analysis of health-related QoL in our institutional cohort of patients with surgery as the first intervention for intracranial meningioma. Standardized self-assessment questionnaires (HADS-D, EORTC-QLQ-C30) were sent out by mail after written informed content. Results were correlated with demographic, tumour- and treatment-related factors by univariate und multivariate linear regression and were compared to normative data derived from the general German population. Time-dependent effects of QoL data were assessed by Spearman correlation.

Results

Out of 653 patients addressed, 327 patients with intracranial meningioma WHO grade I returned the questionnaires. 81% were female, median age at diagnosis was 56 years and skull base and other tumour locations were evenly distributed (53% vs. 47%). Extent of resection was Simpson grade 1-3 in 86% and 4% underwent postoperative radiotherapy. Recurrence occurred in 17% after a median follow-up of 38 months. Health related QoL was assessed at a median interval of 31 months after last intervention. 34% and 24% of patients were screened positive on the anxiety and depression subscales of HADS-D as opposed to 21% and 24% of the general population. Compared to normative data, patients reported impaired QoL based on all function and symptom scales of EORTC-QLQ-C30. Noteworthy, both HADS-D and QLQ-C30 scores improved significantly in a time-dependent manner and levelled with the general population 5 years after last intervention. For the majority of QLQ-C30 subscales, female sex, residual disease (Simpson grade 4-5) and tumour recurrence were identified as independent predictors of impaired QoL.

Conclusion

Despite the supposedly benign nature of this disease, QoL of meningioma WHO grade I patients was impaired compared to the general population but improved significantly with increasing distance from the last intervention, indicating that the need for psychooncological intervention is highest in the first years after index surgery. Independent predictive factors of impaired QoL identified in this cohort can only in part be modified by tumour treatment.

Neuroonkologie IV/*Neurooncology IV*

V162

Beschleunigte Rehabilitation motorischer Defizite nach supratentorialer Tumorresektion mittels repetitive navigierte transkranielle Magnetstimulation (rnTMS) – Interim Analyse

Repetitive navigated transcranial magnetic stimulation (rnTMS) to facilitate recovery of motor deficits after supratentorial tumour resection – interim analysis

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Objective

Surgical resection of motor eloquent tumors poses the risk of causing postoperative motor deficits which leads to significantly reduced quality of life in these patients. Thus, development of treatment strategies to facilitate postoperative rehabilitation of motor deficits is crucial. The present study aims to investigate the effect of repetitive navigated transcranial magnetic stimulation (rnTMS) on motor function after supratentorial tumor resection by normalizing the interhemispheric excitability. Specifically, we hypothesize that rnTMS therapy will facilitate rehabilitation, leading to improvements in investigated outcomes early on.

Methods

19 patients (age 51 ± 13 years, range 30-67 years, 10 females) with supratentorial tumors and new postoperative motor deficits in upper limbs were recruited immediately postoperatively for this randomized, double-blinded, controlled clinical trial. Patients received rnTMS treatment (1Hz, 110% RMT, 15 minutes, daily for seven days) or sham stimulation to the motor cortex contralateral to the injury followed by 30 minutes of physiotherapy. Motor function was assessed using the Fugl-Meyer score at the beginning and end of rnTMS therapy as well as one month and three months after the end of rnTMS. Secondary endpoints included additional assessments of motor and neurological function as well as quality of life.

Results

The results presented here constitute an interim analysis of the clinical trial. Compared to the sham group, median Fugl-Meyer scores were higher in the active rnTMS group at the end of therapy and the one-month follow-up (day 7: 40.0 vs. 19.5, p = 0.083; month 1: 56.5 vs. 9.0, p = 0.050). Similarly, patients in the active arm presented with a better motor status of distal (day 7: 3.5 vs. 0.0, p = 0.053; month 1: 5.0 vs. 0.0, p = 0.036) and proximal muscles of the upper extremities (day 7: 3.5 vs. 1.0, p = 0.054; month 1: 4.5 vs. 3.0, p = 0.039) as well as higher finger tapping scores (day 7: 41.5 vs. 0.0, p = 0.028; month 1: 47.0 vs. 0.0, p = 0.026) compared to sham. There were no significant differences between both groups in any of the other measures or timepoints.

Conclusion

RnTMS therapy is a promising treatment tool for postoperative upper limb motor deficits, specifically improving early rehabilitation. In consequence, a faster recovery period potentially shortens the time to adjuvant tumor therapy, reduces the emotional burden on the patient and lowers socioeconomic costs.

Neuroonkologie IV/*Neurooncology IV*

V163

Einfluss auf die Depletion von Mikrogliazellen in organotypischen Hirnschnittkulturen
Environmental effect on microglial cell depletion in organotypic brain slice cultures

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Objective

Microglia are immunocompetent cells of the central nervous system (CNS). Uncovering the role of microglia under pathologic conditions is of high importance. Chlodronate Disodium is commonly used to deplete microglia in the neural microenvironment; however, it is still unclear whether the treatment induces damages to other brain cells. Here, we have characterized the effect of microglia depletion in human ex-vivo cultures using imaging and sequencing modalities.

Methods

Non-neoplastic human neocortical tissue obtained as entry cortex during GBM surgery was sectioned and cultured for up to 10 days. A microglia depletion model was created by supplementing the medium with 11 mM clodronate-di-sodium for 72 hours. The depleted sections were cultured for an additional 7 days to characterize microglia regeneration post depletion. Finally, primary glioblastoma cell lines were inoculated into both control and depleted sections to study the role of microglia in glioblastoma proliferation.

Results

Our data shows that 72 hours of clodronate treatment is necessary for the depletion of microglia in 300 µm thick human organotypic sections. We demonstrate that depletion leads to no significant reduction in neuronal cells but results in an increase in number of astrocytes over the culture period. RNA-sequencing revealed increased enrichment of astrocytic gene expression, however without a defined reactive signature. This increase of astrocytes was unique for human tissue and not observed in murine cortical tissue. Post depletion, no regeneration or repopulation of microglia was observed. Glioblastoma growth was significantly impaired in the absence of microglia. These data clearly indicates that microglia-glioblastoma interactions help promote tumor growth and migration by maintaining astrocytic functions in addition to clearing debris within the tumor microenvironment.

Conclusion

Our data showed that clodronate-di-sodium salt sufficiently deplete microglia but also lead to increased number of astrocytes which has to be taken into consideration for further use of this method. The important role of microglia for tumour growth was confirmed by our data.

Digitale und KI-basierte Anwendungen III/*Digital and AI-based implementations III*

V164

Machine learning als Prognoseinstrument für aneurysmatische Subarachnoidalblutungen
Machine learning as a prognostic tool for aneurysmatic subarachnoid haemorrhages

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Objective

Prognostication of functional outcome, drainage dependency and occurrence of delayed cerebral ischemia (DCI) has notoriously been a challenge in Neurosurgery. The development of machine learning algorithms in recent years has seen a revolution in the field of data analysis, with its application reaching medicine. We aimed to develop a tool to prognosticate (1) the long-term functional outcome, (2) the risk of drainage dependency at release/transfer and (3) the risk of occurrence of DCI.

Methods

A prospectively constituted database of patients treated for aneurysmal haemorrhage in our ICU between December 2015 and May 2020 was retrospectively consulted. The relevant variables and parameters for the used models were selected according to the existing literature and after a correlation analysis on the entire database itself. The analysis was performed on Jupyter lab using Python 3.0. Several machine learning models were then tested and, for each model, the accuracy, AUROC, specificity and sensitivity, as well as the NPV, PPV and the Matthew correlation coefficient, were calculated on a randomized validation dataset (consisting of 20% of the overall dataset). The chosen model was then improved using fine parameter tuning until optimal results were obtained. The endpoints were functional outcome at last follow up (dichotomized modified Rankin Scale), drainage dependency (need for a ventriculo-peritoneal shunt between the bleeding and last follow up, or need for an external ventricular drainage at release/transfer) and DCI (appearance of new infarct areas after exclusion of procedure-related infarction).

Results

Data was retrieved for 116 patients between 2015 and 2020.

For the functional outcome at last follow up, the best accuracy was found using the SVC algorithm. The Matthew correlation coefficient was 0.495, NPV0.94, PPP0.5, Sensitivity 0.67, specificity 0.89 and the accuracy was 85.7%.

For the drainage dependency, the best accuracy was found with the Linear Discriminant Algorithm. The Matthew correlation coefficient was 0.614, NPV0.92, PPP0.67, Sensitivity 0.8, specificity 0.85 and the accuracy was 83.3.7%.

For the occurrence of DCI, the best accuracy was found using the Naïves Bayes Gaussian algorithm. The Matthew correlation coefficient was 0.555, NPV 1.0, PPP 0.5, Sensitivity 1.0, specificity 0.62 and the accuracy was 72.2%.

Conclusion

Machine learning may offer itself as a valid prognostic tool in the management of aneurysmatic subarachnoid bleeding.

Digitale und KI-basierte Anwendungen III/*Digital and AI-based implementations III*

V165

Einsatz von maschinellem Lernverfahren zur Analyse der intraoperativ visuell evozierten Potentiale während Schädelbasisoperationen

Machine learning as applied to intraoperative monitoring of the visual evoked potentials during surgery near the anterior visual pathway

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Objective

Surgical interventions aimed at removing tumors involving the sellar and parasellar region are a common occurrence in the neurosurgical practice. Despite well established methods to monitor the function of the visual pathway, a clear understanding of the electrical potential changes during surgery and their objective postoperative consequences on the visual field are lacking.

Methods

Visual evoked potentials (VEP) were measured in 12 patients (24 eyes, median age=55, range=28-71, female=7, male=5) with sellar and parasellar tumors during microsurgical transcranial or endoscopic transnasal transsphenoidal approaches using LED pads (Inomed, Emerdingen, Germany) placed over closed eyelids and occipital needle electrodes placed subcutaneously according to the international EEG 10-20 system (O1, O2 as well as Oz and Fz). Changes in the visual field where quantified for each patient eye as percent change of the mean visual field defect (MD, arithmetic mean of sensitivity loss) using the formula (MDpreoperative - MDpostoperative)/MDpreoperative. For each set of visual evoked potentials recorded during surgery we applied a dimensionality reduction algorithm (principal components analysis) to identify the direction of largest variance in the set and subsequently separated the data into clusters using a simple unsupervised machine learning algorithm (k means).

Results

We obtained reproducible VEP waveforms in 75% of the cases (18/24 eyes) during surgery. Of the six eyes where VEP could not be recorded, two had a severe preoperative deficit whereas the other four could be ascribed to technical difficulties. Changes of visual evoked potentials are defined as patient recordings with > 1 cluster (66%, 10/18 eyes). A sanity check was performed in that the individual recordings assigned to clusters where inspected and the clustering rejected if noise clusters where found (10%, 2/18 eyes). We found that the machine learning algorithm reported changes in the recorded visual evoked potential more often than trained human observers (55% of cases as opposed to 20% of cases). Furthermore, detected changes of the VEP strongly associate to improved postoperative mean visual field defects (p=0.006, independent samples Mann-Withney test).

Conclusion

Unsupervised machine learning does better than human observers in identifying changes of the intraoperative visual evoked potentials that have a positive predictive value regarding clinical visual outcomes for surgeries near the anterior visual pathway.

Digitale und KI-basierte Anwendungen III/*Digital and AI-based implementations III*

V166

Auf maschinellem Lernen basierte Vorhersage des motorischen Status mit Traktometrie des Kortikospinaltrakts
Machine learning based prediction of motor status using corticospinal tract tractometry

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Objective

Reconstruction of white matter tract profiles and quantifying diffusion measures along them based on tractography have been widely used to study local microstructural changes caused by tumor effects (e.g edema or infiltration). This study sought to investigate how the changes in different dMRI-based metrics could be associated with and predictive of motor status in patients with brain tumors in motor area using machine-learning based analysis.

Methods

Constrained spherical deconvolution (CSD) based probabilistic tractography was performed for corticospinal tract (5000 streamlines) on 116 motor area glioma II°-IV° patients (43 females, 73 males, average age=48.24, SD=16.47, age range 20-78) with affected preoperative motor status as 1 (MRC grade <5, n=45) and unaffected one as 0 (MRC grade 5, n=71). Along tract profile was generated in individual space per hemisphere (healthy and pathologic) for DTI-based different diffusion measures (FA, ADC, RD and AD) and fixel-based apparent fiber density metric (FD). These features correspond to tract profile statistics (mean, std, kurtosis and skewness) per each measure for both hemispheres. A machine learning model based on SVM using linear kernel was trained on tractometry-extracted features, gender, age and tumor type and further evaluated with leave-one-out cross-validation to predict motor status.

Results

The best model performance was achieved with features extracted from FD, FA, RD, AD and ADC measures reaching up to accuracy 74.13% (specificity 73.23% and sensitivity 75.5%). Additionally, our model was trained with i) FD, FA, ADC and ii) FD, FA, RD, AD set of features separately, and showed the accuracy level of 66.37% (specificity 67.6% and sensitivity 64.44%) and 74.13% (specificity 74.64% and sensitivity 73.33), respectively. It has been shown that demographic features can be derived from WM structure. However, such features and tumor type didn"t improve the performance of the model as the information has already existed in WM structure and even tended to bias the results (accuracy 70.68, Specificity 73.23% and sensitivity 66.6%).

Conclusion

Detailed analysis of corticospinal tract characteristics applying tractometry-extracted features and a novel machine-learning based model allows to associate motor status and individual white matter integrity with high accuracy, potentially improving surgical planning in the future.

Digitale und KI-basierte Anwendungen III/*Digital and AI-based implementations III*

V167

Neuro-OP-Teammanager – progressive Web App zur Optimierung der Assistenten*innen-Ausbildung und deren Einsatz im OP

Neuro-OR-teammanager – data-driven surgical planning to optimise the resident's education and commitment in the OR

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Objective

Digital applications play an increasing role in clinical practice and everyday life. Young residents, considered to be digital natives, are very open-minded in this regard, since they grew up during the age of digitization. Hence, aim of this project was to develop a progressive Web App (PWA) that simplifies the surgical planning and allocates each resident adapted to her or his current state of skills.

Methods

In collaboration with digital experts we designed a PWA that includes different features like current state of skills (divided into different categories), number and type of surgeries done or assisted. Furthermore, an armamentarium of different surgical standard operation procedures will be available for young residents that should guide them through operative procedures. The PWA will be easily used as a smartphone-app during daily routine.

Results

So far, we have designed a mock-up including different features. Final aim is, that the surgeon in charge of the surgical planning, has access to each resident's account in order to allocate them to his or her current state of skills. The PWA should allow a postoperative evaluation of the current skills (assumed that the resident gives his or her positive consent). Up to date, legal aspects dealing with the protection of data privacy sill have to be finalized. In the future, the PWA might play a role for analytics and artificial intelligence.

Conclusion

The PWA will simplify the surgical planning and should optimize the resident's education and commitment, since each resident will take part in surgical procedures that fits his or her current state of skills. Furthermore, the application provides new staff members with current standard operating procedures, that are easily available in the operating room. Several further applications of the PWA in the future are conceivable.

Digitale und KI-basierte Anwendungen III/*Digital and AI-based implementations III*

V168

Patientenspezifische Computersimulation der Lendenwirbelsäule zur Evaluation verschiedener Dekompressionstechniken bei degenerativer Spondylolisthesis

Patient specific computer simulation of the lumbar spine for the comparison of different decompression methods in cases of degenerative spondylolisthesis

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Objective

Over the last years there is an ongoing debate if patients with degenerative spondylolisthesis and stenosis should receive decompression alone or additional fusion. Instability criteria from functional X-rays is a diagnostic tool mainly used to decide if additional fusion is needed. However it has been shown that this static imaging underestimates instability and does not take into account the dynamically complex behavior of the spine (1). Dynamic assessment methods could improve the understanding of individual spinal movement patterns and patient outcome.

Methods

A biomechanical computer simulation model able to be adapted to the spine of individual patients was created. Vertebra geometry from CT data and ligaments with parameters from literature were included. Next the model was fitted to neutral and inclination poses derived from X-ray functional images. The intermediate steps then were interpolated by simulation. The model was tested to retrospectively assess 9 patients that underwent lumbar decompression (+/- fusion) in our institution from January 1st 2017 to July 30 2018. Inclusion criteria were single level spinal stenosis with additional ventral displacement of the vertebral bodies. Exclusion criteria were instability, previous surgery, fractures or multilevel stenosis. The mean patient age was 69.7 years. For each patient an individual model was created followed by simulation of an inclination movement that was used as a baseline. Next interlaminar fenestration (ILF) and laminectomy (LAM) were performed for each model and the same inclination movement was simulated again to compare the destabilizing effects.

Results

Ventral sliding after LAM compared to ILF changed significantly. It increased from 2%, to 6.5% (ILF vs. LAM). The rotation angles showed a significant increase in the LAM group compared to ILF indicating this technique to be more destabilizing.

Conclusion

The simulation model showed that decompression surgery increased the instability of a spinal segment. The effect was stronger in more invasive decompression techniques (LAM vs. ILF). This fact, already well known, could now also be quantified. In future applications a preoperative simulation may help to better predict the destabilizing effect and to decide if e.g. additional fusion is needed.

1. Dombrowski ME, et al. dynamic imaging of degenerative spondylolisthesis reveals mid-range dynamic lumbar instability not evident on static clinical radiographs. European spine journal 2018;27(4):752-62.

Digitale und KI-basierte Anwendungen III/*Digital and AI-based implementations III*

V169

Supervidierte Machine-learning Ansätze zur Diagnostik der spontanen intrakraniellen Hypotension
Supervised machine learning approaches applied in the diagnostic workup of spontaneous intracranial hypotension

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Objective

Spontaneous intracranial hypotension (SIH) is a condition characterized by spinal cerebrospinal fluid (CSF) leakage. As opening pressure on spinal tab is normal in 2/3 of patients, further investigations have identified the resistance to CSF outflow (R_{CSF}) on lumbar infusion testing as a more sensitive parameter. Most recently R_{CSF} has been shown to depend on symptom duration. In order to improve the diagnostic yield of lumbar infusion testing we applied classical machine-learning (ML) approaches.

Methods

A total of 182 patients underwent lumbar infusion testing as part of a strict diagnostic protocol to identify spinal CSF leakage as the underlying pathology of orthostatic headache. The training set consisted of 122 patients" pressure curves. The final evaluation set contained 60 patients" pressure curves. The feature categories with 1016 features in total were extracted based on spectral analysis and pressure curve morphologies. We followed an approach with classical supervised ML algorithms. Performance metrics were accuracy, sensitivity, specificity and F1 scores.

Results

The R_{CSF} with a threshold of 5 mmHg/(ml/min) reached only 60% accuracy and 0.51 F1-score for detecting a spinal CSF leak on the final evaluation set, the ML algorithms reached accuracies up to 75% by maintaining F1-scores up to 0.7. The correct diagnosis of a leak rather depends on a set of different feature categories (mainly spectral analysis applications) than on one single CSF parameter. The time from symptom onset until diagnosis did not show to have a major impact using ML approaches.

Conclusion

Analysis of pressure curves can be automated. This may be crucial in diagnosis of complex conditions such as SIH. ML approaches outperformed the conventional lumbar infusion test analysis.

Intraoperatives Monitoring und Navigation/*Intraoperative monitoring and navigation*

V170

Entwicklung eines digitalen Datenmanagement-Tools für das intraoperative Neuromonitoring
Implementation of a digital data management tool for intraoperative neuromonitoring

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Objective

During intraoperative neurophysiological monitoring (IOM), data are captured together with clinical events. Classically, IOM is documented paper based. This leads to redundant data, which increases the susceptibility to errors and makes it difficult to query the data. The goal of this project was to increase data management by digitizing the whole documentation workflow.

Methods

Using systems analysis methods, covering data flow modeling, process and variant analysis, we developed a concept for digitized IOM data management. The concept was realized as a web application, called IOM-Manager, which was implemented with the MEVN technology stack.

As data input option for the IOM documentation, we used a web form with dropdown menus for selecting event descriptions from a restricted number of possibilities. Thus, the event catalog was developed in an iterative way, by manually reviewing the latest 100 paper protocols searching for recurring entries. Then standard expressions were defined, which were assessed to refine the catalog.

Results

A software application to record IOM data (IOM-Manager) has been developed as a prototype to support recording of events on a timeline and to store measurements in a common database. A protocol entry catalog was developed, which divides predefined clinical events into 25 subcategories for neurophysiological measurements, surgical steps, anesthesia changes and an others. The dropdown lists allowed that an event is stored with a time stamp corresponding to the signal curves and thus enabled rapid data entry for each clinical event.

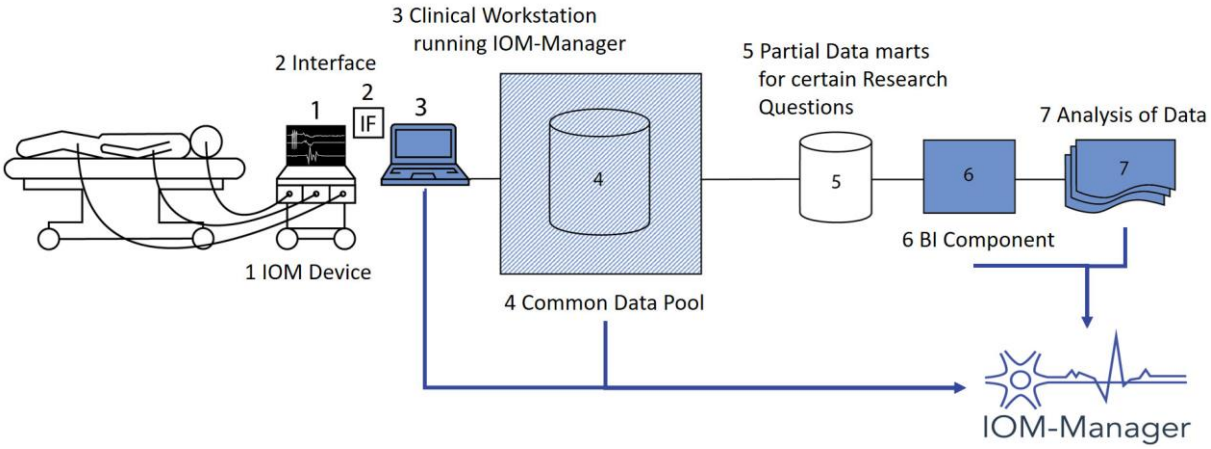
In a user survey the IOM-Manger achieved a score of 94.5 out of 100 points in the SUS score (System Usability Scale), which corresponds to a very good usability rating.

Figure 1: Concept for digitized IOM.

Conclusion

The IOM-Manager may replace the previous paper based IOM protocols. Systematic documentation of IOM events is essential for efficient analyses of events-outcome relations. A future ontology will facilitate benchmarking among centers, multicenter studies and big data registries.

Fig. 1


3 Clinical Workstation
running IOM-Manager
2 Interface
1
2
IF
3
5 Partial Data marts
for certain Research
Questions
7 Analysis of Data
4
5
6
7
6 BI Component
1 IOM Device
4 Common Data Pool
IOM-Manager

Intraoperatives Monitoring und Navigation/*Intraoperative monitoring and navigation*

V171

Die intraoperative Computertomographie (iCT) verursacht ein Vielfaches der Strahlenbelastung im Vergleich zum Fluoroskopie-basierten 3D Scan

Intraoperative computed tomography (iCT) produces a multiple of the radiation exposure compared to a fluoroscopy-based 3D scan

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[2]Department of Stereotactic and Functional Neurosurgery, Department of Stereotactic and Functional Neurosurgery, Freiburg, Germany
[3]Fraunhofer Institute for Laser Technology ILT, Aachen, Germany
[4]Helmholtz Zentrum München, German Research Center for Environmental Health, Individual Monitoring Service, München, Germany
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Objective

Intraoperative 3D image data acquisition is being increasingly used, in particular for spinal 3D navigation. The personnel usually leave the operating room during 3D image data acquisition, but the patient is exposed to the associated radiation. This experimental dosemetric study compares the patient's radiation exposure by intraoperative computed tomography (iCT) and 3D C-arms when generating spinal 3D image data sets.

Methods

This experimental study investigates the radiation exposure during spinal 3D imaging by an iCT (BodyTom®, NeuroLogica, Samsung) on an anthropomorphic Alderson phantom. Five 3D image data sets each of the cervical and lumbar spine were obtained. The average radiation dose was determined at defined locations using eye lens and film dosemeters (eye lens, thyroid gland, female and male gonads). In a second step, these data were descriptively compared with previously identically conducted and published examinations using a state-of-the-art 3D C-arm (Ziehm Vision RFD 3D, Ziehm Imaging).

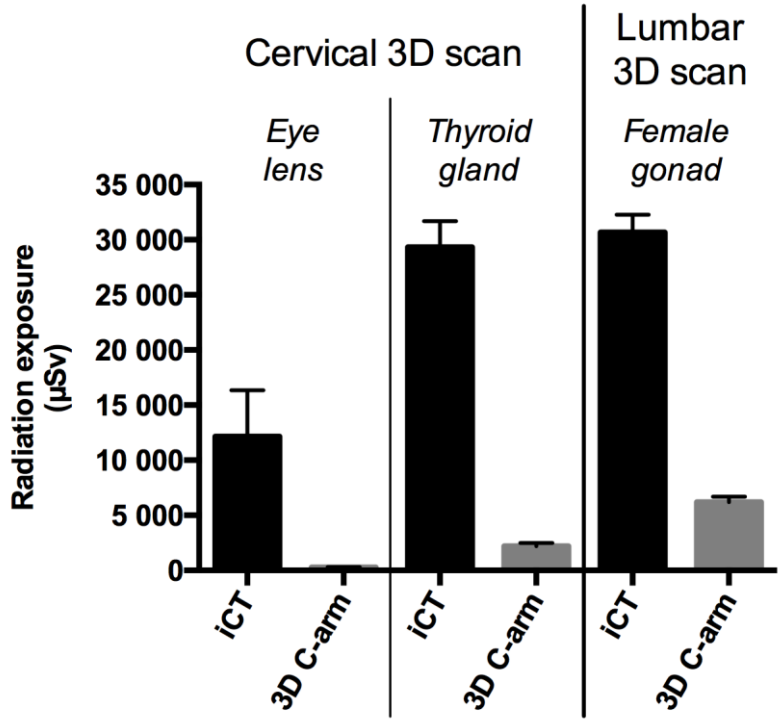
Results

At all dosemeter locations, higher radiation exposures were measured using the iCT compared to our previously reported 3D C-arm data (Figure 1). A cervical 3D scan caused a radiation dose of 12,155 vs. 287 µSv at the eye lens and 29,338 vs. 2173 µSv at the thyroid gland (iCT vs. 3D C-arm). A lumbar 3D scan caused a radiation dose of 30,677 vs. 6196 µSv at the female gonad and 396 vs. 67 µSv at the male gonad (iCT vs. 3D C-arm). Up to 13.5-fold higher radiation doses were measured using iCT compared to a fluoroscopy-based 3D scan using a 3D C-arm (at the thyroid gland during cervical 3D scans).

Conclusion

The radiation exposure of the patient during the acquisition of an intraoperative 3D image data set of the spine can be multiple times higher when using iCT compared to a fluoroscopy-based 3D scan. When using intraoperative imaging, this fact should be taken into account and weighed up together with other characteristics of the respective imaging device such as image quality, handling and costs.

Fig. 1


Cervical 3D scan
Lumbar 3D scan
Eye lens
Thyroid gland
Female gonad
Radiation exposure (µSv)
35 000
30 000
25 000
20 000
15 000
10 000
5 000
0
iCT
3D C-arm
iCT
3D C-arm
iCT
3D C-arm

Intraoperatives Monitoring und Navigation/*Intraoperative monitoring and navigation*

V172

Monopolares und bipolares Mapping außerhalb eines Standard Set UPs für intraoperatives Neuromonitoring während Operationen bei wachen und schlafenden Patienten
Monopolar and bipolar brain mapping during awake and asleep surgery beyond standard IONM settings

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Objective

Patients with eloquently located cerebral lesions require surgery using intraoperative motor or speech mapping with monopolar or bipolar stimulation.50-60Hz stimulation with an Ojeman stimulator can mainly be performed by the surgeon independently, whereas monopolar stimulation requires additional trained personnel for handling of the intraoperative monitoring (IONM) system.Here,we report our experiences using a device that can be operated by the surgeon independently for both intraoperative techniques.

Methods

For monopolar and bipolar cortical/subcortical stimulation two preset programmes were available and intraoperatively used.One enabling EMG real-time tracking of 8 muscles for monopolar mapping and a second programme for 60 Hz stimulation. Motor mapping was performed using a standard monopolar probe connected to the device.EMG signals were screened in real-time on the device monitor.For 60 Hz stimulation a standard bipolar stimulation probe was connected through a second port.Preoperative application of subdermal EMG needles as well as intraoperative handling of the device were performed by the surgeons independently.Postoperatively, evaluation of autonomous handling and feasibility of the device for chosen test parameters was conducted..

Results

From 04/19-10/20, 106 patients with eloquently located cerebral lesions underwent surgery using the device.In 95% monopolar and in 45% of the cases bipolar mapping was performed. Regarding setup and sufficiency for cortical/subcortical mapping the device was evaluated as independently usable for motor and language mapping in 96 patients (90%). Complete resection was achieved in 67%, functional limit throughout resection was reached in 27% of the patients. 6 patients postoperatively suffered from a new neurological deficit. Follow-Up showed persistent deficit in 2 patients at 3-6 month follow-up (2%).

Conclusion

The device was evaluated as sufficient in 90 % concerning monopolar and bipolar mapping, set-up and handling was sufficient in all patients. However, missing SSEP monitoring was seen as a limitation in some cases and led to exclusion of patients with expected neurovascular conflicts. Concerning grade of resection and neurological outcome results were comparable to IONM procedures using standard devices. In our cohort surgeons were able to perform motor and speech mapping adequately and safely by independent use of the device.

Intraoperatives Monitoring und Navigation/*Intraoperative monitoring and navigation*

V173

Erste Erfahrungen mit monopolarem Mapping in Notfalloperationen mit einem allein vom Operateur bedienten Gerät

Monopolar brain mapping in emergency situations using a device handled autonomously by the surgeon – first experiences

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Objective

Intraoperative neuromonitoring (IONM) including direct cortical/subcortical monopolar stimulation is widely used for elective resection of eloquent located cerebral lesions in order to increase safety and extent of resection. Due to the demand of special trained external personnel, sophisticated technical setup and time limitations, standard IONM is usually not taken for emergency situations. We here report the use of a device for monopolar brain mapping that can be quickly operated by the surgeon autonomously in emergency situations.

Methods

We here report three patients with residual neurologic function, in whom emergency surgery on eloquently located lesions (2 tumours, 1 intracerebral bleeding) was performed. To preserve residual motor function monopolar motor mapping using C2Xplore was performed. For monopolar cortical/subcortical stimulation a standard monopolar probe was connected to the device enabling EMG real-time tracking of 8 muscles. EMG signals were screened in real-time on the device monitor. Preoperative set up as well as intraoperative handling of the device were performed by the surgeons independently.

Results

In all patients cortical M1 mapping was performed (thresholds 4, 14 and 5mA). Subcortically the corticospinal tract (CTS) could be identified with 0.3, 2 and 5mA. Because of the eloquent tumor location and positive mapping, complete resection could not be achieved (residual tumor volume <2ml and 4.2ml). All patients fully recovered postoperatively with no new neurological deficits.

Conclusion

We could demonstrate feasibility of monopolar stimulation in patients undergoing emergency surgeries using a device autonomously operated by the surgeon. Due to fast set up and non-demanding handling monopolar stimulation could be used during emergency surgery under preservation of neurological function in all cases.

Intraoperatives Monitoring und Navigation/*Intraoperative monitoring and navigation*

V174

Präoperative navigierte TMS-DTI-basierte Traktographie der Sehbahn – ein Konzeptnachweis
Preoperative navigated TMS-DTI-based tracking of the optic radiation – a proof of concept

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Objective

The frequency of visual field deficits (VFD) after surgery in proximity to the optic radiation (OR) is high. Depending on its severity, VFD can cause a decrease in quality of life by affecting normal daily activities. Since localization of the OR can be challenging due to interindividual anatomical variation and severe tumor displacement or infiltration, we present a method for navigated TMS diffusion tensor imaging-based (TMS-DTI-based) OR tracking.

Methods

Twelve patients undergoing resective tumor or epilepsy surgery in proximity to the OR between June and November 2020, who underwent preoperative DTI sequences and occipital TMS, were enrolled in this study. In all 24 hemispheres, tractography of the OR was performed both anatomy-based (according to current literature) and TMS-based (seeding from positive TMS foci). Consecutively, OR tracts of the operated hemisphere were superimposed on the resection cavity and correlated to postoperative perimetry.

Results

TMS induced perception of phosphenes in 83% of patients (n=10), including patients with moderate preoperative VFD (n=6). Both patients in whom TMS was not able to induce perception of phosphenes showed severe preoperative VFD. We observed significant differences in course of the anatomy-based compared to the TMS-based OR, with the latter showing a more medial and caudal course in 9 out of 10 cases. In all 7 hemispheres with lesions in close proximity (<1 cm) to the OR, TMS-based OR mapped fibers more accurately and closer to the lesion than anatomy-based OR. Two of 5 patients had new VFD in postoperative perimetry. Superimposing of the OR on postoperative MRI in both patients demonstrated TMS-based OR fibers and not anatomy-based OR fibers within the resection cavity (Fig 1), supporting the accuracy of TMS-based tracking.

Conclusion

Here we show that TMS-DTI-based tracking of the OR is feasible. There was a clear difference between the course of TMS-based and anatomy-based OR. In this limited patient group, TMS-based OR seemed to be more accurate, especially in cases with lesions in close proximity to the OR and/or when there was a lot of associated edema. Integration of TMS-DTI-based visualization into preoperative workup can possibly help reducing VFD after resective surgery.

Fig. 1

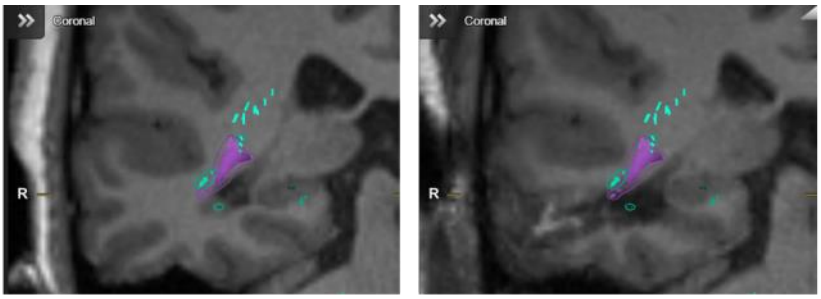

Fig 1: patient with a focal cortical dysplasia that showed a postoperative superior quadrantanopia. Pre- (left) and postoperative (right) coronal MRI, with projections of TMS-OR (green) and anatomy-based OR (purple).

Intraoperatives Monitoring und Navigation/*Intraoperative monitoring and navigation*

V175

Prognostischer Wert von transkraniellem MEP-Monitoring in minimalinvasiven osteoligamentären Dekompressionen bei zervikaler Spinalkanalstenose

Prognostic value of transcranial MEP-monitoring during minimally invasive dorsal decompression of cervical stenosis

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Objective

The value of intraoperative neuromonitoring during degenerative spine surgery is controversial. Data on transcranial motor evoked potentials (MEP) during dorsal decompression of the cervical spine are limited. The aim of this study was to determine the prognostic value of MEP based on changes in threshold level during dorsal decompression for cervical spondylotic myelopathy.

Methods

This is a prospective study, subsequently including patients who were operated for cervical spondylotic myelopathy at our institution, between June 2018 and October 2020. A minimally invasive dorsal decompression of the spinal canal through unilateral partial/hemilaminectomy using a cross-over technique was the standard procedure for all patients. For intraoperative monitoring, transcranial electrical stimulation using the combination C3-C4 was applied. MEP were recorded from the upper extremities and threshold levels were determined for each of the representative muscles of the relative cervical nerve root departing the spinal canal at/below the level of the decompression. The percentual change in threshold level was evaluated for each muscle and the differences (DTL) between start and end of the decompression were analyzed and their correlation with postoperative clinical outcome at discharge was investigated.

Results

We included 31 patients in this study. Surgical decompression was performed at 3 levels or more in 20 patients, at 2 levels in 10 patients and at one level in one. Intraoperative MEP improved at least in one muscle in 26 patients (1-8 muscles, median 4 muscles). In 21 patients, at least one of the presenting symptoms improved postoperatively. The remaining patients reported either no improvement (n=9) or a transient worsening of their symptoms (n=1). Average threshold level decreased in 23 patients, remained unchanged in one and increased in 7 patients. An independent t-test showed a significant difference when comparing DTL between patients with clinical improvement (n=21) and those without (n=10) (-8.16% ±8.78% vs 0.38% ±6.80%, p=0.012). A decrease in average threshold level was significantly associated with a postoperative clinical improvement (OR 5-95%, 1.53-184.9, P=0.017).

Conclusion

This pilot study shows a significant correlation between intraoperative MEP improvement and early postoperative clinical recovery. A more detailed assessment of clinical status via standardized symptom scoring may provide stronger evidence as to the prognostic value of MEP in cervical spine surgery.

Seltene Erkrankungen II/*Rare diseases II*

V176

Hypothalamisches Hamartom – Ergebnisse nach Diskonnektion mittels stereotaktischer Radiofrequenzablation
Hypothalamic hamartoma – seizure outcome after disconnection with stereotactic radiofrequency thermocoagulation

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[2]Universitätsklinikum Freiburg, Neurochirurgische Klinik, Freiburg, Germany
[3]Universitätsklinikum Freiburg, Epilepsiezentrum, Freiburg, Germany
[4]Universitätsklinikum Freiburg, Klinik für Neuropädiatrie und Muskelerkrankungen, Freiburg, Germany
[5]Universitätsklinikum Freiburg, Neuroradiologische Klinik, Freiburg, Germany
[6]University of Calgary, Department of Paediatrics and Department of Neuroscience, Cumming School of Medicine, Calgary, Canada

Objective

To evaluate safety and efficacy of disconnection of epileptogenic hypothalamic hamartomas with stereotactic radiofrequency thermocoagulation (SRT).

Methods

Between 07/2015 and 11/2020 we treated 30 consecutive patients (9 female, 21 male) with epileptogenic hypothalamic hamartomas with 38 SRT procedures. Patients with a follow up > 12 months after last intervention (n=18, 12 Delalande II, 3 Delalande III, 3 Delalande IV) were analyzed regarding seizure outcome and adverse events. All patients (6 female, 12 male, age 2-55, median 10, 11 children, 7 adults) underwent (at least 72h) video-EEG prior to treatment. A neuropsychologist evaluated pre- and postoperative intellectual and behavioral condition. 7 patients had previously undergone other treatments with no lasting improvement (2 open surgery, 5 stereotactic brachytherapy). Seizure types were: gelasitc (14), focal aware (6), focal non-aware (12), focal to bilateral tonic clonic (5) with a median epilepsy duration of 8.8 years (1-48).We carried out 1 procedure in 11, 2 procedures in 5 and 3 procedures in 1 case. Between 1 to 5 trajectories (median 3) with a total of 1 to 17 (median 6) coagulation targets were used per procedure (75°C, 60 seconds per target). Intraoperative stereotactic fluoroscopy was used to confirm the electrode position for each trajectory.

Results

At follow-up (12-50 months, median 23 months) seizure outcomes were: Engel Class 1: 77.7%, Engel Class 2: 5.6%, Engel Class 3: 11.1%, Engel Class 4: 5.6%). Freedom from gelastic seizures was achieved in 64.3% and freedom from non-gelastic seizures in 64.7% of affected patients. Emotional facial paresis occurred in 6 patients (24%, 3 transient, 3 permanent) and Horner syndrome in 1 patient (4%). 3 patients had a transient new neurological deficit (2 motor deficits, 1 vertical gaze palsy), all of them resolved completely until first follow-up. Postoperative neuropsychological performance was unchanged or improved in 16/18 patients.

Conclusion

This minimally invasive approach appears to be a safe and effective alternative to surgery or radiation in patients with hypothalamic hamartomas.

Fig. 1

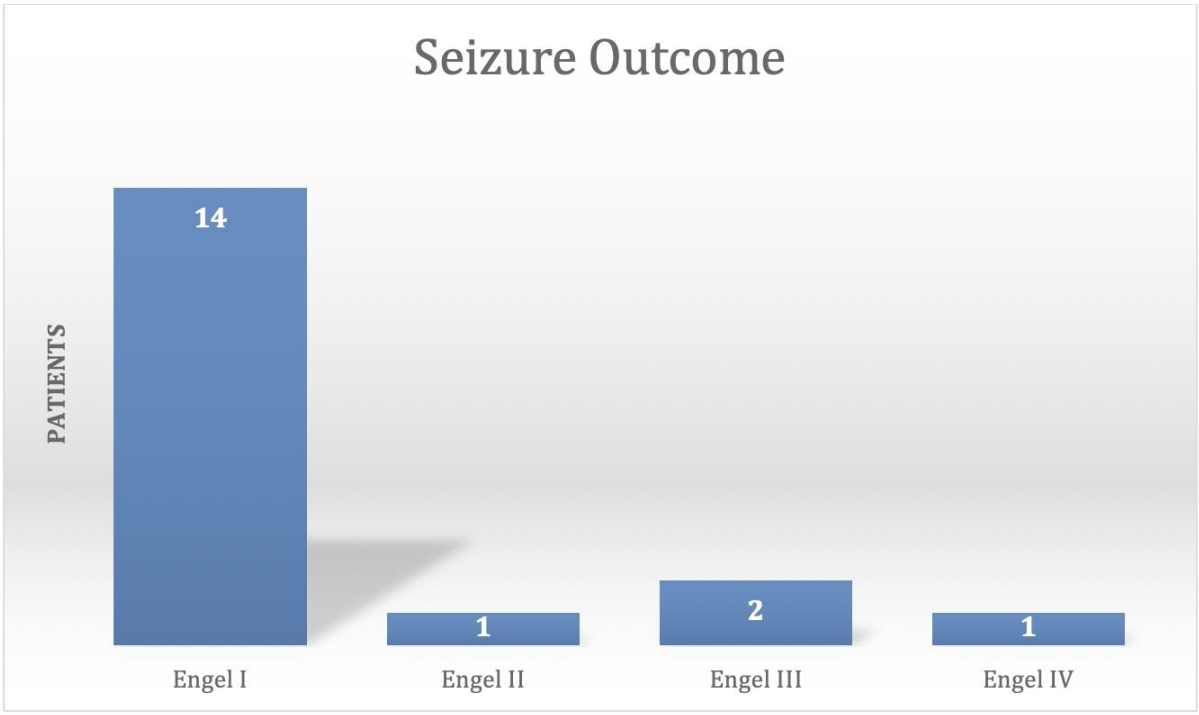
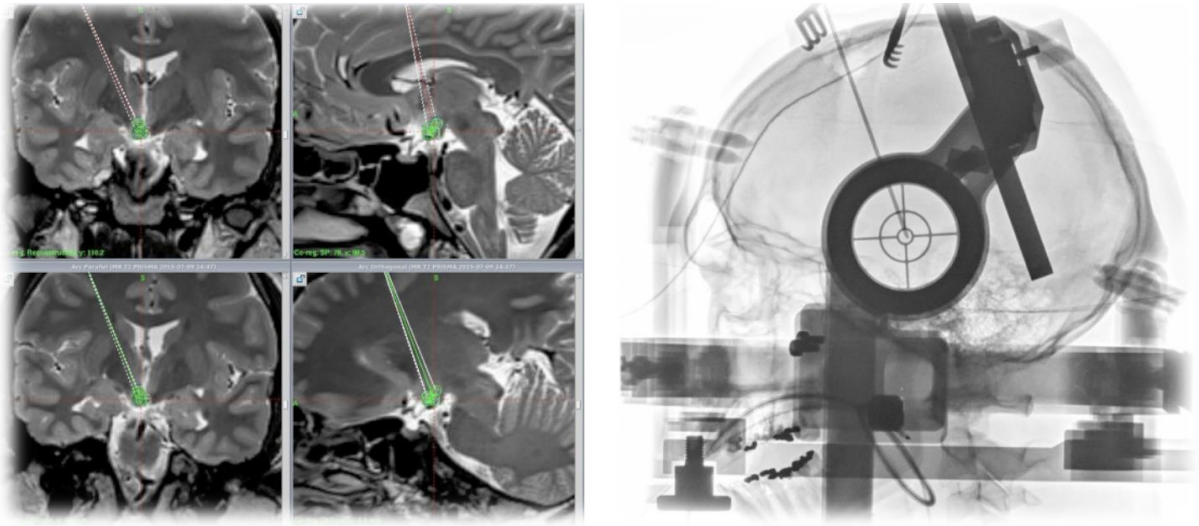

Seizure Outcome
PATIENTS
14
1
2
1
Engel I
Engel II
Engel III
Engel IV

Fig. 2



Seltene Erkrankungen II/*Rare diseases II*

V177

Mikrochirurgische infratentoriell-supracerebelläre Resektion von Pinealiszysten ohne Hydrozephalus – Indikation und klinisches Ergebnis – monozentrische Erfahrung

Infratentorial supracerebellar pineal cyst resection in the absence of ventriculomegaly – indication and clinical outcome – a single-centre experience

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[2]Universität Kairo, Klinik für Neurochirurgie, Kairo, Egypt
[3]Ruprecht-Karls-Universität Heidelberg, Klinik für Neurochirurgie, Heidelberg, Germany

Objective

The majority of pineal cysts are found incidentally on MR imaging. Secondary hydrocephalus and Parinaud-syndrome are well-described indications for an operation. However, the indication for surgery of pineal cysts without ventriculomegaly is still under debate. Pineal cysts may cause symptoms (e.g. headache, dizziness, vomiting, visual disturbances, sleep problems) without showing dilation of the ventricles. To further clarify the role of surgery in pineal cysts without ventriculomegaly, we prospectively analysed our patient cohort.

Methods

We collected all patients with a pineal cyst in the absence of enlarged ventricles treated surgically between 2003 and 2020. All patients were operated via an microsurgical infratentorial supracerebellar approach. Symptoms, cyst size, extent of resection, radiographic and clinical follow-up were analyzed pre- and postoperatively within a mean follow-up period of 21.6 months (Range: 1-134 month).

Results

74 patients underwent surgery for a pineal cyst. An absence of enlarged ventricles could be documented in 64 patients (53 female, 11 male, mean age 27.7 yrs (±12 yrs), range 4-59 yrs). Presenting symptoms included headache (62/64), visual disturbances (16/64), dizziness (29/64), sleep disturbances (12/64). The mean cyst size was 15.17 mm (range 7-27 mm). Complete cyst resection was achieved in 61/64 patients. 61 of 64 (95%) patients improved after operation with good or even excellent results according to the Chicago Chiari Outcome Scale (CCOS ≥ 12), with complete or partial resolution of the leading symptoms.

Conclusion

Surgical resection of pineal cysts may be an indication even in the absence of ventriculomegaly. The postoperative resolution of quality-of-life impairing symptoms in our series demonstrates a good indication for pineal cyst resection. Preoperatively, other causes of the leading symptoms have to be excluded. Intermittent occlusion of the aqueduct or compression of the internal cerebral veins may cause increased intracranial pressure leading to intermittent symptoms.

Seltene Erkrankungen II/*Rare diseases II*

V178

Lumbale Infusionstests bei spontaner intrakranieller Hypotension vor und nach mikrochirurgischer Versorgung eines Duralecks – eine internationale konsekutive Kohortenstudie

Lumbar infusion testing in spontaneous intracranial hypotension before and after microsurgery of spinal CSF leaks – an international consecutive cohort study

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Objective

Spontaneous intracranial hypotension is an under-recognized diseases caused by spinal CSF leakage. Diagnostic approaches include dynamic CSF studies by lumbar infusion testing. Specific alterations in lumbar infusion testing have been found in patients with SIH. The aim of this study was to compare lumbar infusion test parameters pre- and post-microsurgical closure of a spinal CSF leak in SIH.

Methods

The analysis included all patients with a proven spinal CSF leak who presented to the authors" institutions between 2018 and 2020. All patients who underwent lumbar infusion testing prior to and after microsurgical closure of a CSF leak were included. A strict stepwise diagnostic protocol was applied including cranial and spinal MRI imaging and dynamic myelography to localize the spinal CSF leak. Postoperatively, patients received spinal MR imaging to exclude spinal extrathecal fluid collection. Lumbar infusion testing yielded resistance to CSF outflow (R_{CSF}), lumbar pressure at baseline and plateau ($ICP_{baseline}$/$ICP_{plateau}$), pulse amplitude at baseline and plateau ($ICP_{baseline}$/$ICP_{plateau}$), pressure-volume-index (PVI) and the elastance coefficient.

Results

Eight patients were included in the analysis. Orthostatic headaches were the main symptom in all patients preoperatively. At postoperative re-admission orthostatic symptoms had entirely vanished. Symptoms at re-admission included diffuse headaches (n=7), nausea (n=3) and papilloedema (n=1). MR imaging did not show extrathecal fluid collection in seven patients, one patient did not receive MR imaging. Comparing post to pre-surgical lumbar infusion testing parameters mean R_{CSF} increased from 6.98 mmHg/(ml/min) to 13.60 mmHg/(ml/min), mean $ICP_{baseline}$ increased from 4.54 mmHg to 16.37 mmHg, $ICP_{plateau}$ increased from 19.31 mmHg to 31.16 mmHg, $AMP_{baseline}$ increased from 0.22 mmHg to 0.31 mmHg, $AMP_{plateau}$ increased from 1.15 mmHg to 2.51 mmHg and the elastance coefficient increased from 0.10 ml^{-1} to 0.22 ml^{-1}. PVI decreased from 55.40 ml to 12.53 ml.

Conclusion

Microsurgical closure of a spinal CSF leak changed lumbar infusion testing parameters towards a normalization. Findings of single parameters were comparable to healthy individuals. Lumbar infusion testing may offer a diagnostic tool to exclude persisting spinal CSF leakage in postoperative patients without the need of radiation exposur

V179

Minimal-invasive Chirurgie als Behandlung spinaler Liquorlecks bei Patienten mit spontaner intrakranieller Hypotension

Minimally invasive surgery for spinal CSF-leaks in spontaneous intracranial hypotension

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Objective

Spinal cerebrospinal fluid (CSF)-leaks cause spontaneous intracranial hypotension (SIH). Surgical closure of spinal CSF-leaks is the treatment of choice after conservative therapy and blood patching have failed. The objective of the study was to detail the safety and feasibility of minimally invasive microsurgical sealing of spinal dural CSF-leaks using tubular retractors.

Methods

Since April 2019 we included all consecutive patients with SIH undergoing surgery for a spinal CSF-leak. Dynamic myelography studies were used to localize the leak. Surgery was performed under general anesthesia in the prone position via a 2.5 cm dorsal midline incision using 18-20 mm tubular retractors. After microsurgical unilateral hemilaminotomy ventral leaks were sealed via a transdural route while cutting the dentate ligament. Intraoperative neuromonitoring was used for ventral leaks in the first 16 cases. The primary outcome was the successful achievement of minimally invasive dura sealing; secondary outcome was the occurrence of complications.

Results

45 patients, mean age 48.4 years (SD 13.5), 30 female and 15 male patients, with the diagnosis of SIH and Superficial Siderosis have been included. We diagnosed 29 ventral leaks, 14 dorsal/lateral leaks, 1 CSF-venous fistulas. In all but one patients (98%) the leak could be approached, identified and closed via the tubular retractor. In 1 (2%) patient the leak was missed due to misinterpretation of imaging studies. Microspurs were removed or drilled and leaks were either closed by suturing (6-0) or by sandwich patch using a fibrin sealant patch (TachoSil).

Imaging signs of SIH (brain or spine MR) improved in all cases. Despite surgical closure of the leak, clinical outcome was mixed, all patients improved to some extent, but a significant number of patients was still symptomatic and needed prolonged recovery. There were no permanent neurological deficits. There was one reoperation for wound healing and one for dorsal suture deficiency.

Conclusion

Minimally invasive surgery using tubular retractors of 18-20mm diameter can be safely and effectively performed for closure of spinal dural CSF-leaks in specialized centers.

Seltene Erkrankungen II/*Rare diseases II*

V180

Einfluss modifizierbarer kardiovaskulärer Risikofaktoren auf das Blutungsrisiko bei Patienten mit familiären kavernösen Malformationen

Modifiable cardiovascular risk factors and haemorrhage risk in patients with familial cavernous malformation

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Objective

This study aims to assess the influence of modifiable cardiovascular risk factors on hemorrhage risk in patients with familial cavernous malformations (CMs).

Methods

From a register of 1345 CM patients (2003-2020), subjects with familial CMs and complete MRI data were included. We evaluated presence of intracerebral hemorrhage (ICH) as mode of presentation, occurrence of ICH during follow-up and risk factors arterial hypertension, diabetes mellitus, hyperlipidemia, nicotine abuse, and obesity (BMI>30kg/m²). Impact of risk factors on ICH at presentation was calculated using univariate and multivariate logistic regression with age- and sex-adjustment. We performed Kaplan Meier and Cox regression to analyze cumulative 5-year-risk for (re-)bleeding.

Results

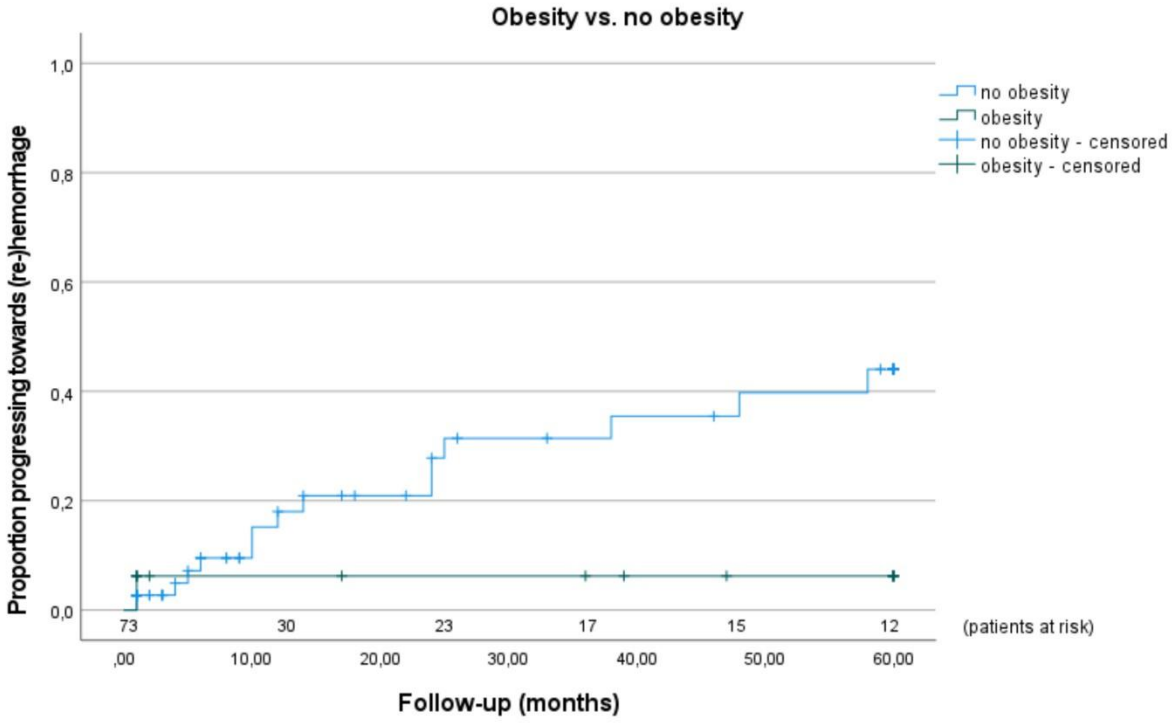
We included 229 patients with familial CMs. In our cohort, 56.8% were female, 51.6% presented with ICH as mode of presentation, 27.3% suffered from cavernoma related epilepsy, and 30.1% were asymptomatic. Lesion were located supratentorial (78.1%), in the brain stem (12.1%), cerebellar (4.5%), and spinal (4.0%), risk factor distribution was comparable with the normal population: hypertension (27.0%), diabetes (7.4%), hyperlipidemia (12.2%), nicotine abuse (23.1%), and obesity (17.8%). Thirty percent underwent surgical treatment, 10.8% suffered from (re-)bleeding during the 5-year follow-up period (cumulative 5-year risk 20%).

The univariate logistic regression and multivariate adjusted logistic regression did not show significant relationships between all risk factors and ICH as mode of presentation. Cox regression did not identify predictors for occurrence of (re-)hemorrhage. The Kaplan-Meier regression (see Figure 1) and log rank test showed a tendency towards a lower hemorrhage risk in patients with obesity in the longitudinal outcome without reaching statistical significance (χ^2=2.899, p=0.089), neither did the other risk factors reach statistical significance: hypertension (χ^2=0.462, p=0.497), diabetes (χ^2=0.267, p=0.605), hyperlipidemia (χ^2=0.001, p=0.972), and nicotine abuse (χ^2=0.035, p=0.852).

Conclusion

In contrast to patients with sporadic cavernous malformations, obese patients with familial CMs showed a trend towards less hemorrhagic events during a 5-year follow-up period in our cohort.

Fig. 1


Obesity vs. no obesity
Proportion progressing towards (re-)hemorrhage
1,0
0,8
0,6
0,4
0,2
0,0
no obesity
obesity
no obesity - censored
obesity - censored
73
30
23
17
15
12
(patients at risk)
,00
10,00
20,00
30,00
40,00
50,00
60,00
Follow-up (months)

Seltene Erkrankungen II/*Rare diseases II*

V181

Spinale maligne Gliome – ein monozentrischer Erfahrungsbericht über zehn Jahre
Spinal high-grade gliomas – a ten-year single-centre experience

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Objective

Spinal high-grade gliomas (sHGG) are a rare entity with poor prognosis. They are typically treated similar to cranial gliomas with surgical (partial) resection and radio-chemotherapy. However, the role of different molecular tumor profiles still remains unclear. We, therefore, aimed to assess the clinical courses of patients with sHGG at our institution in the recent decade with a focus on molecular tumor histology.

Methods

All consecutive patients with sHGG (WHO grad III or IV), treated at a single center between 2007 and 2017 were retrospectively reviewed. Only patients with available histopathological classification were included. Clinical, imaging and histopathological data were retrieved from the patients" hospital records and tumor specific surgical as well as adjuvant treatments were noted. Functional outcome (McCormick Grade, KPI) was assessed at discharge and at follow-up visits. Overall survival (OS) was calculated.

Results

Six sHGG patients (five male, one female; age 49.3±19.7 years) were included in this analysis. All tumors were located in the thoracic spinal cord, most often lead to hypesthesia and paresis as the first symptoms and 66% showed contrast enhancement on MR-imaging. In all patients, surgical treatment consisted of a tumor biopsy or partial tumor resection. Histopathological classification revealed two WHO grade III sHGGs and four sHGGs with WHO grade IV. All tumors were negative for an IDH R132 mutation and 50% presented a H3.3 K27M- mutation. Of the three H3.3 K27M wildtype patients, two showed a methylation in the MGMT-promoter region. At discharge, a median McCormick grad of 3.2 (2-4) and a mean KPI of 58±18.3% were observed. All patients were treated with adjuvant radiotherapy 37.8±13.4 days after surgery and 50% of the patients received adjuvant chemotherapy (Temozolomid simultaneously to radiation, Bevazizumab (two patients) in the course). At 3-months follow-up, the median McCormick grade had decreased to 3.7 (3-4) and the KPI showed worsening to 43.3±8.16% as well. The mean OS of the sHGG patients was five months (1-13 months).

Conclusion

Treatment of sHGGs consists of partial surgical resection, followed by adjuvant radiotherapy and chemotherapy. The molecular genetic profiles of those rare tumors are still partially undetermined, but H3.3 K27M mutations seem to be relatively common. Prognosis is still very poor with a mean OS of less than six months and worsening of neurological symptoms during the course of disease.

Seltene Erkrankungen II/*Rare diseases II*

V182

Langzeit telemetrische Hirndruckmessung für Diagnose und Therapie der idiopatischen intrakraniellen Hypertension

Long-term telemetric intracranial pressure monitoring for diagnosis and therapy optimisation of idiopathic intracranial hypertension

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Objective

Idiopathic intracranial hypertension (IIH) is a disease which is difficult to diagnose and moreover difficult to treat. We developed a strategy for long-term telemonitoring of intracranial pressure (ICP), by incorporation of the NEUROVENT®-P-tel System, for improved diagnosis and consequent therapy of this disease.

Methods

20 patients with suspected IIH who were treated in our hospital from August 2014 to October 2020 (16 females, 4 males, median age 36,6 years), were assigned to one of two ICP monitoring settings, "Home-Telemonitoring" (n=12) and "Home-Monitoring" (n=8). The ICP data were analysed and used conjointly with the clinical picture for establishment of IIH diagnosis, and telemonitoring was resumed for therapy optimisation of confirmed cases.

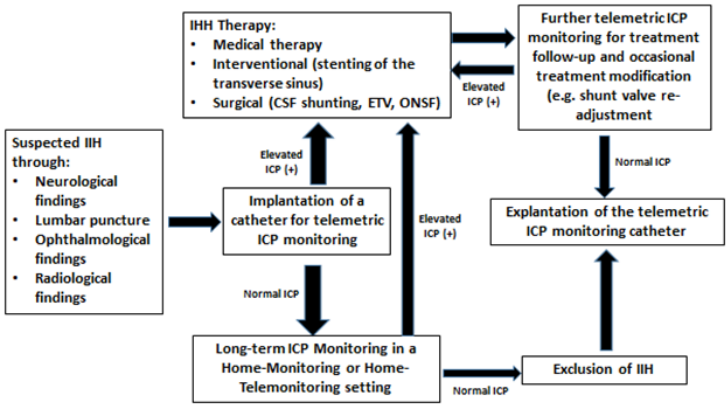
Results

The diagnosis of IIH was confirmed in 18 of the 20 patients. Various surgical/interventional treatments were applied to the confirmed cases, including ventriculoperitoneal (VP) shunting (n=15), stenting of the transvers venous sinus (n=1), endoscopic third ventriculostomy (ETV) (n=1), and ETV in combination with endoscopic laser-based coagulation of the choroid Plexus (n=1). Optimal shunt-valve adjustment was achieved with an average valve opening pressure of 6,3 ± 2,17 cmH2O for differential valves, and of 29,8 ± 3,94 cmH2O for gravitational valves. The Home-Telemonitoring setting reduced consequent outpatient visits, compared to the Home-Monitoring setting, with an average of 3,1 visits and 4,3 visits, respectively. No complications were reported.

Conclusion

This strategy of long-term telemetric ICP monitoring was safe and efficient in the management of IIH, with improved patient outcome, especially in complicated cases. The data suggest an initial adjustment of dual-valve VP-shunts of 30 and 6 cmH2O, for gravitational and differential valves, respectively.

Fig. 1


IHH Therapy:
• Medical therapy
• Interventional (stenting of the transverse sinus)
• Surgical (CSF shunting, ETV, ONSF)
Further telemetric ICP monitoring for treatment follow-up and occasional treatment modification (e.g. shunt valve re-adjustment
Elevated ICP (+)
Suspected IIH through:
• Neurological findings
• Lumbar puncture
• Ophthalmological findings
• Radiological findings
Elevated ICP (+)
Implantation of a catheter for telemetric ICP monitoring
Elevated ICP (+)
Normal ICP
Explantation of the telemetric ICP monitoring catheter
Normal ICP
Long-term ICP Monitoring in a Home-Monitoring or Home-Telemonitoring setting
Exclusion of IIH
Normal ICP

P121

Die Expression des zytotoxischen T-Lymphozyten-assoziierten Antigen 4 (CTLA4) ist in malignen Gliomen hochreguliert

The expression of cytotoxic T-lymphocyte-associated antigen 4 (CTLA4) is upregulated in high grade gliomas

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Objective

Cancer treatment with immune checkpoint inhibitors led to increased patient survival. Cytotoxic T-lymphocyte-associated antigen 4 (CTLA4), an immune checkpoint expressed on T-cells, already showed promising results in ongoing clinical studies with melanoma and non-small cell lung cancer. Although the TCGA database exhibited an upregulation of CTLA4 in glioblastomas first studies could not indicate increased survival. In this study, we aimed to analyze the expression of CTLA4 in gliomas.

Methods

Tumor was obtained during neurosurgery and directly frozen in liquid nitrogen. Protein was extracted using RIPA lysis buffer and measured with Western Blot. Therefore, seven subgroups were classified: control tissue, grade II, grade III, secondary glioblastoma (sGBM) and primary glioblastoma (pGBM) with or without temozolomide (TMZ) treatment. CTLA4 was detected with a primary CTLA4 antibody and visualized with a peroxidase-conjugated secondary antibody. Results were normalized by ß Actin. Immunofluorescence was performed with cryo slices, stained with a primary CTLA4 antibody and a Cy3-conjugated secondary antibody. Nuclei were stained with DAPI. Statistical analysis was done with Kruskal-Wallis and Mann-Whitney- U test.

Results

Western Blot showed a strong heterogenic expression rate within each subgroup. However, a significant reduced expression of the immune checkpoint inhibitor in low grade astrocytoma"s (grade II) compared to control tissue (low grade 0.052 ± 0.016 vs. control 0.358 ± 0.381; p=0.0121) and high grade (grade III + sGBM ± TMZ) (low grade 0.052 ± 0.016 vs. high grade 0.395 ± 0.401; p=0.0092) was measured. Results could be confirmed with immunostaining. Recurrence of primary glioblastoma led to a decreased expression of CTLA4 (pGBM 0.46 ± 0.39 vs. pGBM with TMZ 0.129 ± 0.11) but did not make a significant difference for secondary glioblastoma. Likewise primary compared to secondary glioblastoma, who were without distinction (p=0.0831).

Conclusion

Grade II has a significant lower CTLA 4 expression then high grade gliomas and recurrence decreases the expression in primary glioblastomas. Furthermore, the strong heterogenic expression we found in each subgroup could make glioma treatment with immune checkpoint inhibitors much more complex compared to other solid tumors.

P122

Thioredoxin verleiht eine intrinsische Resistenz zu Zytostatika in humanen Gliomen
Thioredoxin confers intrinsic resistance to cytostatic drugs in human glioma cells

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Objective

Thioredoxin (Trx) is a 12 kDa ubiquitous protein of 104 amino acids with reducing activity. Trx is involved in cellular redox homeostasis, maintaining the balance between reactive oxygen species generation and elimination. Trx overexpression is known to be a cause of chemotherapy resistance in various tumor entities. However, Trx effects on resistance are complex and depend strictly on tissue type.

Methods

In the present study, we analyzed the impact of the Trx system on intrinsic chemoresistance of human glioblastoma multiforme (GBM) cells to cytostatic drugs. Resistance of GBM cell lines and primary cells to drugs and signaling inhibitors was assessed by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assays. Impact of Trx inhibition on apoptosis was investigated by proteome profiling of a subset of proteins and annexin V apoptosis assays. Trx-interacting protein (TXNIP) was overexpressed by transfection and protein expression was determined by immunoblotting.

Results

Pharmacological inhibition of Trx by 1-methyl-2-imidazolyl-disulfide (PX-12) reduced viability of three GBM cell lines, induced expression of active caspase-3, and reduced phosphorylation of AKT-kinase and expression of β-catenin. Sensitivity to cisplatin could be restored by both PX-12 and recombinant expression of the upstream Trx inhibitor TXNIP, respectively. In addition, PX-12 also sensitized primary human GBM cells to temozolomide. Combined inhibition of Trx and the phosphatidylinositide 3-kinase (PI3K) pathway resulted in massive cell death.

Conclusion

AKT-kinase phosphorylation and β-catenin protein expression were substantially reduced under the action of the Trx blocker PX-12, which also suggests that the AKT-kinase pathway is closely interconnected with Trx. We conclude that the Trx system and the PI3K pathway act as a sequential cascade and could potentially present a new drug target.

P123

Gehemmte Expression von Ubiquitin C-Terminal Hydrolase L1 in Tumoren des zentralen Nervensystems
Ubiquitin C-terminal hydrolase L1 is downregulated in tumours of the central nervous system

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Objective

Ubiquitin C-terminal hydrolase L1 (UCHL1) is a neuron specific deubiquitinating enzyme. It hydrolyses small polypeptides from Ubiquitin, a small molecule regulating protein degradation by the Ubiquitin Proteasom System. Mutations in UCHL1 are associated with neurodegenerative diseases caused by protein accumulation. In tumours, UCHL1 has been controversially discussed. While its expression is increased in several cancer types like adenocarcinoma or breast cancer it is downregulated in melanoma and colorectal cancer. In meningiomas decreased UCHL1 expression is corelated with malignancy and promotor methylation. Paediatric glioma cell lines showed an elevated expression. Since there is not much known about UCHL1 in brain tumours, we aimed to analyse UCHL1 expression and promoter methylation in tumours of the central nervous system.

Methods

Tumour was obtained during neurosurgery and shock frozen in liquid nitrogen. Regarding WHO classification, meningioma grade I, II and III and glioma grade II and III, secondary- (sGBM) and primary glioblastoma (pGBM) before and after recurrence were grouped. Transcription rate was measured via real-time PCR. Amplification products were detected with SYBR Green and results normalized by ß-Actin. Protein expression was determined with Western Blot. UCHL1 was detected with a primary UCHL1 antibody and visualized with a HRP-conjugated secondary antibody. Samples were measured in triplets. Statistical analysis was done with Kruskal-Wallis and Mann-Whitney- U for non-parametric and one way ANOVA and Tukey"s test for normally distributed data. For immunofluorescence staining cryo slices were stained with a primary UCHL1 and a Cy3-conjugated secondary antibody. Nuclei were stained with DAPI.

Results

Transcription of UCHL1 is significantly decreased in meningioma (7.64±5.67 vs. 0.98±0.91, $p<0.0001$) and glioma (7.64±5.67 vs. 1.06±0.68, $p=0.0004$) compared to peritumoral tissue. Western Blot confirmed PCR results with a downregulation in meningioma (1.97±0.49 vs. 0.19±0.22, $p<0.0001$) and glioma (1.35±0.12 vs. 0.49±0.35, $p<0.0001$) compared to control tissue. Results could be confirmed with immunostaining.

Conclusion

UCHL1 is significantly downregulated in meningioma and glioma compared to peritumoral tissue. Since the protein expression is brain specific, UCHL1 could be a possible therapeutic target for treatment of tumours of the central nervous system.

P124

Transnasale endoskopische Versorgung von Clivuspathologien – eine konsekutive Fallserie von 51 Patienten und Vorstellung einer neuen Ausdehnungsklassifikation

Transnasal endoscopic surgery of clival pathologies – a case series of 51 patients and introduction of a new extent classification

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Objective

Clival pathologies present challenging entities regarding their treatment options. Due to their close proximity to critical neurovascular structures, the operative goal of gross total resection is rendered more difficult with a high risk of neurological deficits.

Methods

We performed a retrospective cohort study of all consecutive patients treated through a transnasal endoscopic approach between 2009 and 2020. Clival tumors were classified depending on their extension (CE1-4), and tumor extension, preoperative clinical status, surgery duration and preoperative radiotherapy were considered prognostic factors.

Results

In total, 68 transnasal endoscopic surgeries were performed in 51 patients over a time period of 12 years. Most lesions were clival chordomas, 66.7% of the lesions did not reach the brainstem (classified extent CE1 and CE2). Cranial nerve impairment was present in 56.9% of the patients, 60% remained clinically stable after surgery, 60% of the patients with cranial nerve palsy improved after surgical treatment. Interrater reliability for tumor extension classification showed a perfect agreement (Cohen"s Kappa= 0.807).

Conclusion

Clival pathologies exhibit heterogenous characteristics. Depending on tumor extension, the patient should be advised regarding his postoperative outcome and the probability of single- vs. multi-staged approaches.

P125

Gezielte Glioblastomtherapie und -PET-Bildgebung mit einem neuen Peptid spezifisch für eine deglykosylierte Isoform von Brevican

Targeting glioblastoma using a novel peptide specific to a deglycosylated isoform of brevican

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[4]Universität Zürich, Chemie, Zürich, Germany
[5]BWH / Harvard Medical School, Radiology, Boston, MA, United States
[6]University of Western Ontario, Chemistry, London, United Kingdom
[7]Erasmus MC, Neurosurgery, Rotterdam, Netherlands
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[9]State University of New York UMU, Neuroscience and Physiology, Syracuse, NY, United States

Objective

Glioblastoma (GBM) is the most common and deadliest form of brain tumor and treatment options available today have limited success. Brevican (Bcan), a central nervous system (CNS)-specific extracellular matrix protein, is upregulated in high-grade glioma cells, including GBM. A Bcan isoform lacking most glycosylation, dg-Bcan, is found only in GBM tissues and therefore represents a viable target for tumor specific targeted therapy.Our objective was to explore dg-Bcan as a molecular target for GBM by identifying a dg-Bcan specific peptide.

Methods

A microfluidic chip for magnetic-activated sorting was used to screen a one bead one compound (OBOC) library containing a vast number of different D-peptides (theoretical diversity more than > 10^16 different unique peptides). Candidate peptides were then screened *in vitro* for affinity and specificity to dg-Bcan as well as cell uptake in patient derived GBM cells. The most promising candidate (BTP-7) was further evaluated *in vivo*, radiolabeled with ^{18}F and used as a PET imaging agent in a GBM orthotopic xenograft mouse model. The potential of BTP-7 based targeted therapy was evaluated by functionalizing BTP-7 with camptothecin and testing its efficacy in vitro and in vivo.

Results

BTP-7 binds to dg-Bcan with high affinity and specificity (KD= 0.26 µM). BTP-7 is preferentially internalized by dg-Bcan-expressing patient derived glioma cells and can cross the blood-brain barrier (BBB) *in vitro* and in mice. Radiolabeled ^{18}F-BTP-7 enabled PET imaging of orthotopic xenograft tumors in mice (n = 3/3). Conjugation of BTP-7 to camptothecin via a cleavable linker led to significantly increased DNA damage in intracranial GBM-6 tumors ($p < 0.0001$) and prolonged survival in tumor-bearing mice in comparison to vehicle and a scrambled control compound (Scr) (median survival in days = 73 (BTP-7) vs. 67 (Scr) vs. 46 (vehicle), $p < 0.01$ / $p < 0.001$); n = 7 mice per group).

Conclusion

dg-Bcan is an attractive molecular target for GBM, and BTP-7 represents a promising lead candidate for further development into novel imaging agents and targeted therapeutics.

P126

Dreidimensionale Rekonstruktion der individuellen Gehirnanatomie bei Patienten mit Glioblastom
Threedimensional reconstruction of individual brain anatomy in patients with glioblastoma

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Objective

Considering the current literature on the examination of functional magnetic resonance imaging of brain tumors, it is noticeable that Statistical Parametric Mapping 12 (SPM12) dominates as an evaluation tool. Overall, there are only few studies using the FreeSurfer software to analyze data from patients with cranial tumors, as this often leads to flawed reconstructions of the brain anatomy. In this study, we want to present and evaluate a pre-processing approach that supports such reconstruction with a minimum of subjective influence on the data.

Methods

Here, we analyzed structural MRI data from 30 patients with a glioblastoma as these patients showed most flawed cortical reconstructions in previous attempts due to huge areas of edema and contrast enhancement. The tumor is first segmented using an automated software and replaced by healthy tissue of the contralateral hemisphere using enantiomorphic normalization. The resulting processed anatomical image was the basis for the three-dimensional anatomical reconstruction in FreeSurfer. These reconstructions were subsequently used to perform a first level functional analysis which was compared to the results obtained with SPM12.

Results

After establishing the pre-processing protocol presented, these patient brains showed significantly fewer errors when performing the described steps before running the reconstruction compared to the application of standard FreeSurfer protocols. More than 90% of cases were even reconstructed without errors. Comparisons with functional results obtained using the SPM12 showed similar activation patterns in both methods.

Conclusion

The pre-processing protocol established here allows the three-dimensional reconstruction of the individual brain anatomy of patients with brain tumors which radiologically even show the most inhomogeneous form of brain tumor. Therefore, it can be used as a basis for further analyses of patients data and it might even be possible to integrate this protocol in clinical setups of presurgical functional imaging.

P127

Der Tunel Assay bestätigt den durch Methadon induzierten Zelltod in Glioblastomzelllinien und normalen Astrozyten

Tunel labelling assay confirmed induced cell death by methadone in glioblastoma cells and normal astrocytes

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Objective

Glioblastoma (GBM) is the most frequent primary brain tumor in the adulthood and carries a dismal prognosis. Recently, it has been shown, that D,L-methadone induced apoptosis in GBM cell lines detected by annexin V FACS analysis. To confirm and to assess the executive state of apoptotic cell death with another method, we applied TUEL labelling assay.

Methods

We utilized three different established rat GBM cell lines (9L, F98, S635) and a normal rat astrocytes as a primary culture from Fisher 344 rats. All cell lines were exposed to 5 concentrations of D,L-methadone (0.3, 1.0, 15, 30, 45 µg/ml) alone or in addition to TMZ (100 µM). After 6 days cells were harvested and apoptosis was detected by annexin V FACS analysis and fragmentated DNA was detected by TUNEL labelling assay to confirm apoptosis.

Results

All tested cell lines express of the µ-opioid receptor was similarly; in particular, there was no difference between the GBM cells compared to normal astrocytes. Apoptosis, detected by annexin V FACS, is induced in all cell lines by D,L-methadone alone beginning at 15µg/ml and in addition to TMZ with 0.3µg/ml (9L), respectively with 15µg/ml D,L-methadone (F98, S635, 9L). The tunnel assay showed cell death with defragmented DNA in all cell lines, conforming apoptosis detected by annexin V FACS analysis. The TUNEL labelling experiments confirmed the data of apoptosis. In comparison to GBM cell lines, the astrocytes react refractory against D,L-methadone alone, confirmed in apoptosis and TUNEL labelling assay.

Conclusion

TUNEL labelling experiments confirmed the findings of annexiv V FACS, indicating the induction of apoptotic cell death in higher concentrations of methadone (> 15 mg/ml), with the astrocytes showing the lowest susceptibility.

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Variable Expressionen der CD44-Isoformen in humanen Meningiomen
Variable expressions of CD44 isoforms in human meningiomas

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Objective

Tumor stem cells (CSCs) are considered tumor inducing. However, they also suggest that they play an essential role in chemoresistance, malignancy and recurrence. The clear identification of the CSCs is difficult and done mostly via specific marker proteins. One of these is CD44. This surface molecule acts as an interaction partner for various macromolecules of the extracellular matrix (ECM). By alternative splicing exist besides a stable form of CD44 (CD44s) also 10 variable (CD44v1-v10) via which these have a variety of tumor cell properties control (proliferation, adhesion, migration, invasion). The aim of this study was to investigate which of the CD44 isoforms are specifically expressed in human meningiomas and which of them increase with rising WHO grade.

Methods

RNA were isolated from 78 specimens of individual patients (WHO °I: n=43, WHO °II: n=32, WHO °III: n=3) and analysed by quantitative polymerase chain reaction (qPCR). The transcription of the stable form of CD44 (CD44s) as well as the variable isoforms CD44v1 until CD44v10 were analysed using delta Ct method to determine the expression level.

Results

It was found that there were strong variations in the detectability of the expression of the individual isoforms in human meningiomas. The only isoform that could be detected in all samples was *CD44v6*, whereas *CD44v1* could not be detected in any of the samples tested. All other isoforms were detectable in least 35% of samples. The analysis of the expression levels of the isoforms *CD44v6* and *CD44v4* showed an increase with increasing WHO grade. For the isoforms *CD44s* and *CD44v10* a decrease in expression levels was detected.

Conclusion

The data show that the *CD44s* and *CD44v10* expression described for tumor progression in malignant tumor entities is detectable in low-grade meningiomas. However, for the malignant course additionally an increased expression of CD44v6 and CD44v4 seems to be specific for high grade tumors.

P129

Vario-gesteuerte Biopsie vs. stereotaktische Rahmenbiopsie – eine Single-Center-Experience
Vario-guided biopsy vs. stereotactic frame biopsy – a single-centre experience

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Objective

Stereotactic needle biopsy is a common procedure in neurosurgery for deep-seated or multiple brain lesions. The objective of this study was to compare skin-to-skin, duration of anesthesia, negative biopsy rates an number of complications in a frame-based vs. a frameless setup.

Methods

We analyzed all frame based (i.e. Leksell Stereotactic System) and frameless (i.e. Vario-guided) biopsies performed at the Department of Neurosurgery in the University-Hospital of Bonn during 01/18 and 08/2020. Assessment of operative times used the local operating room database whereas radiology database and histological results were used to evaluate bleeding complications and negative biopsy rates. After testing values for Gaussian distribution using Shapiro-Wikl normality tests, we tested for significance using Mann-Whitney testing.

Results

In total 109 biopsies (i.e. 40 vario-guided vs. 69 frame guides biopsies) were compared. Vario-guided biopsies showed significantly shorter duration of anesthesia (163 min median with IQR 138-194 min vs. 193 min median with IQR 167 – 215 min; p= 0.0009). We saw no difference in skin to skin time (28 min median with IQR 20-38 vs 30 min median with IQR 25-39; p= 0.1352) and no difference in complications such as bleeding or infection (2 of 40 vs. 4 of 69; p=0.7133). We found a slight higher false-negative biopsy rate in frameless than in frame guided biopsies (3 vs 1; p= 0.1347).

Conclusion

Vario guided biopsies showed significant shorter time under anesthesia and did not show any difference in complication rate compared to frame guided biopsy. Frameless biopsy could therefore be used as an time-saving alternative patients with large cerebral lesions.

P130

Vergleich von Ultraschall (US) und MRT ONSD – klinisch ergänzende Anwendung beider Verfahren in der Pädiatrischen Neurochirurgie

Comparison of ultrasound (US) and MRI ONSD – clinical complementary application of both techniques in paediatric neurosurgery

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Objective

Trans-orbital ultrasonographic measurement of the optic nerve sheath diameter (ONSD) is a sensitive, non-invasive and radiation-free technique to reliably identify potentially increased intracranial pressure (ICP) or, in case of a longitudinal assessment, changes of ICP over time. The spatial resolution of ultrasound is much higher than that of MRI, thus ultrasound assessment is the gold standard of ONSD measurement. In uncooperative infants and small children awake determination of ONSD might be difficult or impossible. Thin slice T2-weighted MRI of the orbit, visualizing the optic nerve sheath, can serve as an alternative method to assess ONSD. MRI measurements have also their importance as previous values for comparison to a recent ultrasound assessment. This study thus investigates the accuracy and reliability of MRI versus ultrasound ONSD assessment in pediatric patients in neurosurgery.

Methods

The presented prospective study investigates 150 patients (age range 0 to 18 years) diagnosed with tumor (n=40), hydrocephalus (n=42), and other intracranial pathologies (n=68). Bilateral ONSD was quantified by ultrasound in a standardized way, i.e. 3 mm behind the optical nerve papilla using an 11MHz linear array transducer. This was compared to simultaneously (usually within 24 hours) assessed ONSD on T2-weighted MRI of the orbit.

Results

Overall mean values for ONSD were 5.8 ± 0.88 and 5.7 ± 0.89 mm for ultrasound and MRI, respectively. There was a strong positive correlation between ONSD measured on MRI compared to ultrasound ($r= 0.976$, $p< 0.01$). Bland and Altman analysis of the two methods showed a mean bias of 0.078 mm with limits of agreement of -0.3 and 0.5 mm. 95% of the values were within the limits of agreement. A repeated measures correlation (rrm) in 9 patients showed an excellent value (rrm= 0.94, $p<0.01$) as well.

Conclusion

MRI-based determination of ONSD can serve as a reliable alternative if ultrasound assessment of ONSD is not possible for various reasons. The difference of US and MRI ONSD is low and insignificant, thus both values can complement each other in the daily routine diagnostic setup.

P131

Neurologische Entwicklung der Kinder mit Hydrocephalus in Malawi
Neurodevelopmental outcome in children with hydrocephalus in Malawi

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Objective

Pediatric hydrocephalus are one of main factors responsible for high pediatric morbidity, mortality and functional disability in low-income countries. The overview of neurodevelopmental outcomes in these regions is very limited. The aim of this pilot investigation was to evaluate neurodevelopmental delay and poor functioning in a population of children with hydrocephalus in Malawi.

Methods

We conducted a prospective observational cohort study, at the tertiary neurosurgery clinic in Blantyre, Malawi in 2018, recruiting consecutive children with congenital and infantile hydrocephalus. We conducted demographic and health questionnaires of parents of children and have evaluated children"s functioning using the Liverpool Outcome Score and Eating and Drinking Ability Classification System. We also conducted full anthropometric assessment and directly assessed children using the Malawi Developmental Assessment Tool. .

Results

We evaluated 41 children, with a mean age of 22.6 months. Functional assessment showed the majority of children 92.7% (CI 80.1- 98.5, n=38) had severe sequelae from the hydrocephalus and were found to be dependent on their parents or caregivers. Only 27 children ((27/41) 65.9%, CI 49.4 - 80.0) had full or expected control of their bowel and bladder and 6 children ((6/41)14.6%, CI 5.6 - 29.2) had recent history of seizures. Over two thirds of the children ((29/41)70.7% CI 56.8 - 84.6) were stunted and almost half of the cohort were underweight ((18/41) 43.9% (CI 28.5 - 60.3). Almost half ((20/41) 48.8% CI 32.9 - 64.9) had developmental delay on the MDAT with 17/41(41.5%, CI 26.4 - 56.6) graded as severely delayed (-

Conclusion

Our data demonstrates a high proportion of children with hydrocephalus who suffers from functional difficulties, stunted growth and developmental delay, in Malawi. There is a need for further research with larger numbers of patients to understand factors contributing to these results and potentially new strategies which could improve the treatment strategies.

P132

Rahmenbasierte stereotaktisch geführte Implantation von zysto-ventrikulären Shunts zur Behandlung erworbener intrazerebraler Zysten

Frame-based stereotactic cysto-ventricular shunt implantation for treatment of acquired intracerebral cysts

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Objective

The treatment of symptomatic, progressive or recurrent acquired intracerebral cysts is challenging especially when localized in eloquent or deep-seated midline structures. Hereby, the frame-based stereotactic implantation of cysto-ventricular shunts offers a minimally invasive and highly precise technique. Here we evaluated the feasibility and efficacy of this technique in patients with acquired intracerebral cysts of different origins.

Methods

In this single center retrospective analysis, we included all patients with acquired intracerebral cysts who underwent frame-based stereotactically guided internal cysto-ventricular shunt implantation between 2012 and 2020. Patient data were analyzed in terms of clinical symptom control, unexpected side effects and radiological outcome concerning cyst volume reduction (3D volumetry).

Results

Thirty-five patients (f/m =18/17, median age 43 years, range 2-77 years) were identified. Median cyst volume before treatment was 11.6 cm3 (range 1.6-71.6 cm3) and mean follow-up was 21 months (range 0-82 months). At last follow-up, a mean reduction of cyst volume of 73.3% could be achieved. Initial symptoms improved or were completely regressive in 49% of cases (n=17) and remained stable in 40% (n=14). No permanent clinical deterioration after treatment was observed. Three patients required surgical catheter revision due to shunt obstruction or infection.

Conclusion

In our analysis, stereotactic internal cysto-ventricular shunting proves to be a safe and effective surgical method with excellent long-term control of cyst volume, clinical improvement and a lack of severe permanent side effects. Therefore, this technique offers an alternative to endoscopic or microsurgical approaches as a first-line treatment in patients with acquired intracerebral cysts of different entities.

P133

Nicht nur genetische Merkmale bestimmen Ergebnisvorhersage bei Patient*Innen mit Gliomen
Not only genetic factors of gliomas determine outcome

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Objective

The updated WHO classification stratifies diffuse or anaplastic gliomas with the extensive use of molecular features. Clinical trials for the treatment of those tumors were mostly done before the classification update, leading to a lack of knowledge in how to treat our patients. Therefore, we evaluated patients with gliomas, that were assessed according to the previous phenotypical WHO classification (before 2016). We compared the acquired genetic markers – IDH1, ATRX and EGFR – with the clinical outcome.

Methods

All consecutive patients with diffuse or anaplastic glioma WHO °II & III, operated at our institution between 2010 and 2019, were evaluated. IDH1, ATRX and EGFR IHC testing using FFPE tissue from the institutional biobank was performed, if these features had not already been assessed routinely. Clinical and follow-up data were gained from our neurooncological database.

Results

From 202 evaluated cases, IDH1 was not tested in 50, ATRX not in 78 and EGFR not in 63. From these, FFPE tissue was available and immunohistochemistry performed for 30 IDH1, 48 ATRX and 44 EGFR samples. In 16 (53%) IDH1 was mutated and in 14 (47%) wild-type, nuclear ATRX was expressed in 26 (54%) and lost in 24 (46%) cases, EGFR showed advanced expression in 24 (55%) cases, moderate in 11 (25%) and none in 9 cases (20%).

The decision for adjuvant treatment was not influenced by the molecular features that have been unknown at that time ($p>0.05$). In the group of known IDH1 gliomas it did affect the decision for CTX ($p=0.035$) or RTX ($p=0.031$) after surgery. This decision was not affected by ATRX or EGFR status of the tumor, even if it was known ($p>0.05$).

The fact that IDH1, ATRX or EGFR were known, did not influence the OS in our series (CoxReg, $p>0.05$ for each). In multivariate Cox-regression, only IDH1 (HR 2.1, $p=0.05$) affected the OS, but also WHO Grade (HR 9.0, $p<0.01$), preoperative tumor T1 CE volume (HR 1.03/cc, $p=0.02$), postoperative T1 CE tumor volume (HR 1.21/cc, $p<0.01$) as well as postoperative T2 volume of remnant tumor and perifocal oedema (HR 1.01/cc, $p<0.01$).

Conclusion

Genetic features of diffuse and anaplastic gliomas support but do not exclusively define the understanding of tumor behaviour. Other factors like WHO grade and determination of tumor volumes as well as contrast enhancement remain crucial.

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Hydrocephalus bei supratentoriellen Glioblastomen – Risikofaktoren, Indikationen und Outcome
Hydrocephalus in supratentorial glioblastoma – risk factors, indications and ouctome

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Objective

Glioblastoma is the most common adult primary CNS tumor and is marked by a challenging treatment. Modern treatment strategies have improved the overall prognosis however with a clinical course often scattered by treatment side effects and cognitive decline. Some patients present with clinical and radiological evidence of hydrocephalus either obstructive or communicating. The aim of our study was to investigate the incidence of hydrocephalus, risksfactors and treatment in a contemporary 10 years cohort of GBM patients

Methods

We performed a retrospective review of glioblastoma patients treated and operated at least one time at our institution (Department of Neurosurgery, Medical Center – University of Freiburg) from 2009 to 2019. We identified a subgroup of 46 patients presenting with glioblastoma accompanied by symptomatic hydrocephalus treated by ventriculo-peritioneal (VP) or ventriculo-atrial (VA) shunt. Demographics, clinical characteristics, radiological features were analyzed and descriptive statistics as well as Fisher exact tests were performed

Results

Of the 46 patients who underwent shunting, 42 (91.2 %) had a communicating hydrocephalus (CH), 4 (8.6%) an obstructive hydrocephalus (OH). In the subgroup of patients with CH opening of the ventricular system [Office1] during a previous surgery was present in 34 of 46 patients and identified as a risk factor (Fisher"s exact test $p<0.05$). There was also a trend toward location (frontal and temporal) and the volume of the tumor. Number of craniotomies before shunting was also considered as a risk factor (Fisher"s exact test $p<0.05$).

Hydrocephalus symptoms improved in 95%of the patients. Infection, over/under-drainage were the most common complications encountered requiring a shunt revision in thirteen patients of forty-six (28%).Thirteen patients needed a revision surgery, of whom five patients (10,9%) had an early complication (<30 days) and eight (17.5%) a late complication which needed arevision surgery. No peritoneal metastasis were found.

Conclusion

Ventricular system opening, number of craniotomies, and volume of the tumor were identified as risks factors for hydrocephalus in the context of a GBM. However, treatment of hydrocephalus in the context of a glioblastoma is challenging but improves symptoms in most of the patients and may therefore be considered even in palliative setting for relieve of symptoms.

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P135

Hemmung von Tumorangiogenese durch das Anti-Altertums-Eiweiß Klotho in Glioblastom
Inhibition of tumour angiogenesis by the anti-ageing protein Klotho in glioblastoma

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Objective

Klotho is a kidney-derived protein that has been shown to exert anti-tumor effects in a variety of malignancies. To date, the inhibition of tumor cell proliferation, the induction of apoptosis, the inhibition of tumor cells migration, and the induction of autophagy have been identified as the responsible mechanisms. It is unknown, however, whether Klotho can inhibit tumor angiogenesis. To assess whether Klotho inhibits tumor angiogenesis, we explored the effects of exogenous Klotho stimulation in glioblastoma (GBM) models, since GBM is amongst the most vascularized solid cancers.

Methods

We investigated the indirect, GBM cell-mediated, effects of exogenous Klotho stimulation in *in vitro* tube formation assays and in the *in ovo* chorioallantoic membrane (CAM) model (N = 11-14 eggs per group).

Results

We found that Klotho-treated GBM cell-conditioned medium (U251, U87 and GSC23 cells) significantly inhibited tube formation *in vitro*. Supernatants from Klotho-stimulated GBM cells (U87 and GSC23) reduced *in ovo* capillary vascularization by 45% and 36%, respectively, compared to PBS-stimulated control groups.

Conclusion

In short, we found that Klotho acts as an inhibitor of GBM-induced angiogenesis *in vitro* and *in ovo*. These data comprise the first indication that Klotho inhibits tumor angiogenesis. Furthermore, these data indicate that the potential for Klotho-based treatments merits further research.

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Intratumorale Heterogenität tumor-assoziierter Makrophagen im Glioblastoma multiforme
Intratumoral heterogeneity of tumour associated macrophages in glioblastoma multiforme

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Objective

Previous work of our group did assess the PSGL-1 expression on tumour associated macrophages (TAM) by FACS and Immunohistochemistry (IHC). The FACS and IHC results did not correlate with each other, but we noticed that the samples for both methods came from distinct regions in the tumour (sample for pathology and sample for research). The present study aimed to investigate the intratumoral heterogeneity of TAM in GBM with a special focus on PSGL-1 expression.

Methods

Tumour samples of n=11 GBM patients at initial diagnosis were gathered under neuronavigational guidance from up to 6 different defined regions per tumour of the contrast-enhancing tumour margin. Samples were snap-frozen immediately. Overall 12 antigens were investigated with their immunofluorescence staining utilizing the Operetta CLS high content imager followed by algorithm-driven quantification with the Harmony 4.9 analysis software. Overall expression intensity (Foldchange (FC): MFI to MFI of the negative control) was quantified. Also, the heterogeneity of expression *(Score = 0 − (1/(x<1)) × 100)* in between different regions of one tumour was quantified.

Results

As expected, GFAP as tumour cell marker showed up with the highest expression level across all patients and sample locations (mean FC 6.9, range from 2.1 to 19.9). A medium expression level (mean FC from 2 to 3.1) was shown for CCR7, CD204, Arg1, iNOS, CD163, CD206 and CSFR1. MHCII, CD16, CD68 and PSGL1 (mean FC = 1.2 to 1.5) were among the low abundant antigens. Interestingly, those low abundant antigens showed up with the highest score in the assessment of the intra-tumoral heterogeneity (Score 7.5 to 10). The lowest intra-tumoral heterogeneity has been seen in GFAP expression (Score 5.5).

Conclusion

The present study reveals a tremendous intratumoral heterogeneity of common surface expression marker of TAM in GBM. Especially low abundant antigens as PSGL-1 have a high intra-tumoral heterogeneity. That shows that immunological studies using one sample per tumour are rather limited in their significance.

P137

Die Lokalisation, nicht aber eine frühere Resektion beeinflusst das Auftreten von Strahlennekrosen bei radiochirurgisch therapierten Meningeomen

Location, but not previous resection influences the occurrence of radiation necrosis in meningiomas undergoing radiosurgery

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Objective

Radiosurgery is an interdisciplinary treatment concept for meningiomas with a similar postoperative outcome compared to surgical resection. Radiation necrosis is a possible complication, but there are still only few known risk factors for its occurrence. The aim of this study was to identify risk factors for radiation necrosis in patients with meningiomas after radiosurgery.

Methods

All patients with meningiomas treated with radiosurgery at the author"s institution between January 2004 and November 2020 were retrospectively included. The clinical, imaging and medication data were gained from patient records. The largest axial diameter of the tumors was measured using MRI scans in T1 weighted imaging. Patients with radiation necrosis and patients without radiation necrosis were compared.

Results

52 patients were included with a median age of 53 years (47-63). The mean tumor diameter was 18mm (±4.9mm) and the median isodose amounted to 14 Gy (14-16). 40.4% of the meningiomas were located at the skull base (SB), 59.6% were distributed over the rest of the cranium. The median overall dose of cortisone for prophylaxis of radiation necrosis was 120mg (72-120). 48.1% of patients had already undergone at least one surgical resection at the time of radiosurgery. 18 (34.6%) patients showed radiation necrosis at a median of 8 months (6-12), 7 (38.9%) of whom needed conservative treatment.

In this series a significant difference in radiation necrosis between SB meningiomas compared to those of other locations was found. SB meningiomas showed a significantly lower risk of radiation necrosis with an Odd"s Ratio (OR) of 0.241, $p<0.001$.

Interestingly, administered steroid dose did not correlate with the risk of radiation necrosis. Furthermore, no significant difference of radiation necrosis between previously operated and newly diagnosed meningiomas was found.

Conclusion

The risk of radiation necrosis for SB meningiomas appears to be low. For extended meningiomas of the skull base, combinations of a surgical approach and radiosurgery have already become increasingly important. Furthermore, no difference between previously resected tumors and tumors treated primarily with radiosurgery was found, which may underpin the use of radiosurgical treatment for patients with recurrent meningiomas.

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Molekulare und funktionelle Stabilität von Langzeit-Glioblastom-Sphäroidkulturen unterstützten ihre Nützlichkeit als reproduzierbare *In-vitro*-Modelle

Longitudinal molecular and functional stability of a glioblastoma spheroid cultures supports their utility as reproducible in vitro models

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Objective

Reproducible and clinically relevant *in vitro* drug testing of gliomas depends on appropriate cell models. Glioma stem-like cell-based 3D cultures emerged as an alternative to monolayer cell lines as 3D cultures may better represent tumor biology and hence also be more suitable for cancer drug testing. However, stability of molecular and biological properties as well as reproducibility of drug response of these models over time remains an issue.

Methods

We performed longitudinal cell passaging, molecular profiling and drug response testing of 7 glioma spheroid models under standardized procedures. Next generation gene panel sequencing, 850K DNA methylome analysis and RNA sequencing were performed on early and late passages of each model and the respective primary tumor tissues in three models. Molecular profiles were compared to drug response data obtained for 231 clinically approved drugs.

Results

The three cell models for which corresponding primary tumor tissue was available retained the original tumor mutational profiles but showed *in vitro* culture-related differences at the epigenetic and transcriptional levels. The comparison of the early and late passage cultures revealed that these models remained molecularly stable over time and allowed for reproducible results in *in vitro* drug testing. Gene expression pathway analysis revealed possible mechanism linked to *in vitro* sensitivity or resistance to specific drugs, indicating the potential of gene expression-based prediction of therapy sensitivity.

Conclusion

Glioblastoma spheroid cultures remain molecularly and functionally stable over time and thus represent versatile glioma cell models for reproducible biomedical research in neurooncology. Gene expression profiles in these models may predict *in vitro* drug response.

P139

Meclofenamat führt zu einer funktionellen und morphologischen Zerstörung der interzellulären Netzwerkarchitektur des Glioblastoms

Meclofenamate demolishes the network architecture and electrophysiological coupling of malignant gliomas

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Objective

Glioblastoma cells assemble to a syncytial communicating network based on tumor microtubes (TMs) as ultra-long membrane protrusions. The relationship between network architecture and transcriptional profile remains poorly investigated. Drugs that interfere within this syncytial connectivity such as meclofenamate (MFA) may be highly attractive for glioblastoma therapy.

Methods

In a human neocortical slice model using glioblastoma cell populations of different transcriptional signatures, three-dimensional tumor networks were reconstructed and TM-based intercellular connectivity was mapped on the base of two-photon imaging data. MFA was used to modulate morphological and functional connectivity; downstream effects of MFA treatment were investigated by RNA sequencing and fluorescence-activated cell sorting (FACS) analysis.

Results

TM-based network morphology strongly differed between the transcriptional cellular subtypes of glioblastoma and was dependent on axon guidance molecule expression. MFA revealed both a functional and morphological demolishment of glioblastoma network architectures which was reflected by a reduction of TM-mediated intercellular cytosolic traffic as well as a breakdown of TM length. RNA sequencing confirmed a downregulation of NCAM and axon guidance molecule signaling upon MFA treatment. Loss of glioblastoma communicating networks was accompanied by a failure in the upregulation of genes that are required for DNA repair in response to TMZ-treatment and culminated in profound treatment response to TMZ-mediated toxicity.

Conclusion

The capacity of TM formation reflects transcriptional cellular heterogeneity. MFA effectively demolishes functional and morphological TM-based syncytial network architectures. These findings might pave the way to a clinical implementation of MFA as a TM-targeted therapeutic approach.

P140

Metabolische Reprogrammierung im Glioblastom – intratumorale Verteilung von Laktat sowie den Monocarboxylattransportern 1 und 4 und ihre Zusammenhänge mit anderen tumorprogressionsrelevanten Prozessen

Metabolic reprogramming in glioblastoma – intratumoral distribution of lactate and the monocarboxylate transporters 1 and 4 and their relationships to other tumour progression-associated processes

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Objective

Glioblastoma multiforme (GBM) is the most common and most malignant brain tumor. Rapid growth, despite a lack of energy substrates, is one reason for its poor prognosis. To develop this aggressive property, tumor cells can undergo metabolic reprogramming (mr), leading to an oxygen-independent glycolysis. Thus, mr depicts a promising therapeutic target also in GBM. Proton-coupled monocarboxylate transporters (MCT) have been described in connection with the distribution or membrane passage of lactate produced by oxygen-independent glycolysis. MCT1 and MCT4, in particular, are overexpressed in GBM cells. Till date, only a few studies focus on their role and connection to other tumor progression related processes in GBM. Furthermore, only little is known concerning a possible connection between MCT expression and changes in multi voxel magnetic resonance spectroscopic imaging (MRSI), a method for assessing local metabolites noninvasively. Thus, the objective of this study was to gain more insights into the molecular mechanisms involved in mr in order to use this knowledge for an advancement of diagnostic, monitoring and therapy of GBM in the future.

Methods

We examined the distribution of lactate by MRSI and ELISA in GBM patients. In addition, we investigated the expression and cellular localization of MCT1, MCT4, and of several markers connected to tumor progression by quantitative PCR and immunofluorescence double-staining in human GBM *ex vivo* tissues.

Results

The highest lactate concentration was found at the center of the vital parts of the tumor. Whereas MCT1 (p: 0.025) showed a higher gene expression at the center of the tumor compared to the edge, glial acidic fibrillary protein (p:0.010), the epithelial to mesenchymal transition (EMT) marker ß-catenin (p: 0.039) and the stem-like cell markers krüppel-like factor4 (p: 0.035) and octamer-binding transcription factor4 (p: 0.026) showed an increased expression. Three main GBM groups could be distinguished according to their regional gene expression differences of the investigated genes. MCT1 and MCT4 were found on cells undergoing EMT and on tumor stem-like cells. GBM cells revealing an expression of cellular dormancy markers, showed positive staining for MCT4.

Conclusion

Our findings indicate the existence of individual differences in the regional distribution of MCT1 and MCT4 and suggest that both transporters have distinct connections to GBM progression processes, which could contribute to the drug resistance of MCT-inhibitors.

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P141

Multiomische Kartierung der räumlichen und zeitlichen Architektur identifizieren entkoppelte Abstammungslinien und reaktive Transkriptionszustände beim Glioblastom

Multiomic mapping of spatiotemporal architecture identified decoupled lineage and reactive transcriptional states in glioblastoma

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Objective

Glioblastomas (GBM) are highly malignant tumors of the central nervous system (CNS). Evidence suggests that these tumors display a large intra- and inter-patient heterogeneity, hallmarked by subclonal diversity and dynamic adaptation within developmental hierarchies. However, the source for dynamic reorganization of cellular states within their spatial context remains elusive. Here we integrate spatial transcriptomics and matrix assisted laser desorption/ionization (MALDI) imaging to acquire a high-dimensional map of transcriptional/metabolomic interactions.

Methods

We performed spatial transcriptomics using Visium technology. The dataset consists of 10µm sections from 24 donors (tumor n=18, non-neoplastic n=6), placed on a glass slide with 5000 targeted capture areas (6x6mm). Each capture area contains oligo-dt nucleoids with unique barcodes coding for their spatial coordinates. After permeabilization mRNA binds to the oligo-dt and are then extracted for library preparation. Additionally, consecutive slices were also used to perform matrix assisted laser desorption/ionization (MALDI), with a spatial resolution of 50µm. We established a R-based software package for integrative analysis of our data (SPATA, github.com/heilandd/SPATA-Lab).

Results

We mapped over 90k spatially resolved transcriptomes from 22 malignant and non-neoplastic human tissue samples and were able to reconstruct exclusive as well as shared transcriptional programs with repetitive spatial patterns, in both malignant and non-neoplastic CNS tissue. We inferred that brain tumors differentiate along defined glial or neural developmental lineages and further adapt to inflammatory or metabolic stimuli. These findings were confirmed by a large overlap of both metabolomic and transcriptional programs, which were shared across the whole cohort. Analysis of copy number variations (CNV) revealed spatially coherent subclonal organization, associated with a reactive transcription program within regions of nutrient scarcity, which confirms that environmental stress leads to selection pressure.

Conclusion

Our data suggest that metabolic and immunological alterations of the microenvironment of tumors drive their heterogeneity. It still remains unclear to what extent the tumor itself is responsible for regulation of its own microenvironment.

P144

Serosa als *in vitro* 3D-Modell für Medikamententests zur Behandlung von Glioblastoma multiforme
Porcine serosa as in vitro 3D-model for testing glioblastoma drug treatment

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Objective

Suitability of Two-dimensional (2D) cell culture tumour models is limited in view of examining drugs for the treatment of glioblastomas (GBM). Three-dimensional (3D) cell culture models bridge the gap between 2D cell culture experiments and *in vivo* animal models. We developed such a 3D *in vitro* model based on a biological scaffold derived from decellularised porcine jejunum. This model allows to grow GBM cells inside a collagen matrix named SISser (small intestine submucosa and serosa), to form a 3D structure and to study the efficacy of chemotherapeutic agents. Here, we present first data on developing this GBM 3D model utilizing different GBM cell lines and tested its eligibility by assessing cytotoxic effects of cisplatin.

Methods

Porcine intestine was decellularised and mounted onto sterile cell crowns. The GBM cell lines U87 and GaMG were seeded onto the serosal side of the matrix SISser and cultured for at least 10 days. After that, the cells were treated for 48h with 5µM and 10µM cisplatin, respectively. The cell-containing SISser was fixed, paraffin-embedded and sectioned (3µm). DNA double-strand breaks (γH2AX) and glial fiber acidic protein (GFAP) were visualised by immunofluorescence staining. Images were evaluated by applying a specialised macro in ImageJ.

Results

We successfully established an *in vitro* 3D GBM cell culture model by growing human U87 and GaMG cells on a porcine serosa-containing matrix. The GBM cells displayed a 3D growth pattern after 10 days of culture. Adding 5µM and 10µM cisplatin to the culture led to a three- and fourfold increase of cells with DNA-double-strand breaks compared to the control, respectively, as shown by immunofluorescence staining of γH2AX.

Conclusion

Our proof-of-principle experiment revealed that the porcine matrix SISser is well suited as a 3D matrix to grow GBM cells 3-dimensionally for investigating new GBM-targeting chemotherapeutics. This GBM 3D cell culture model has the potential to serve as an alternative or supplement to animal experiments while avoiding the disadvantages of 2D cell culture.

P145

Zeitliche und räumliche Vielfältigkeit zellulärer Kommunikation erhöht die transkriptionelle Plastizität in Glioblastomen
Spatiotemporal diversity of cell communication in glioblastoma aid transcriptional plasticity

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Objective

Owing to recent advances in understanding of the active functional states exhibited within glioblastoma (GBM), intra-tumoral cellular signaling has moved into focus of neuro-oncological research. In our study, we aim to explore the spatial and temporal diversity of transcellular signaling and investigate the correlation to transcriptional dynamics, cell behavior and target molecules.

Methods

Electrophysiological mapping was performed by planar array-based microelectrodes, in addition to calcium imaging in both cell culture and human neocortical section based GBM models. Selective inhibition/activation of selected ion-channels was performed to identify the channels involved in the alteration of cytosolic ionic flux. Paired patch-clamp recordings within the GBM network were used to validate intercellular electrical signaling. Transcriptional dynamics and plasticity were examined by means of scRNA-sequencing with CRISPR based perturbation, spatial transcriptomics and deep long-read RNA-sequencing.

Results

Investigation of electrophysiological profiles of six different cell lines revealed highly variable baseline activity, significantly enriched in cell lines with astrocytic/mesenchymal transcriptional signature. Despite the different characteristics of transcellular communication, all cell-lines followed the rules of scale-free networks, which was confirmed in human neocortical section based GBM model. In the GBM model, a significantly increased level of baseline activity was shown for all cell lines. Cellular signaling was directly correlated to changes in the environment, like hypoxia or acidification. Using single-cell sequencing and proteomics, we identified Neurobeachin (NBEA) which plays a crucial role in synaptogenesis. CRISPR loss-of NBEA resulted in alterations in cellular morphology and decreased cellular connectivity. Electrical signaling was lost in cell culture and significantly reduced in the GBM model. Single-cell sequencing of perturbed tumor cells in the GBM model revealed a loss of neuronal lineages and significant reduction of cellular stress levels (mesenchymal signature).

Conclusion

Our findings highlight the role of electrical signaling in glioblastoma. Cellular stressors induce electrical signaling, leading to transcriptional adaptation suggesting that there exists a highly complex and powerful mechanism for fast dynamic cellular adaptation. The identification of key player, e.g. NBEA, will help to therapeutically target transcellular signaling.

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Spinale intradurale Tumore – epigenetische Aufarbeitung einer Fallserie
Spinal intradural tumours – epigenetic analysis of a case series

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Objective

DNA methylation-based classification of central nervous system (CNS) tumors using DNA methylation arrays (EPIC) is a new technique that allows precise tumor characterisation resulting in defining novel tumor entities and/or changing of diagnosis (reclassification) in around 10-15% of traditionally diagnosed CNS tumors. We present a case series of epigenetically analyzed spinal intradural tumors and highlight the role of EPIC-based classification for such tumors.

Methods

In the years 2018-2019 a total of 1792 operations, including 756 spinal procedures, were performed at our department. Among these, we identified a group of 13 patients with spinal intradural tumors. EPIC analysis was performed either by recommendation of the tumor board or the neuropathologists in charge. Primary data of EPIC methylation arrays were reanalyzed with the latest classifier version 11b4 as of 11/2020.

Results

Five out of 13 spinal cases metachronically disclosed cerebral tumors of a seemingly different entity as well; one case could not be classified first hand. EPIC data helped to identify two cases of primary spinal manifestation of diffuse midline glioma, K27M mutant, one intradural metastasis of a gliosarkoma, one case of intradural malignant meningioma metastasis and one case of an exceedingly rare spinal cord MN1 fusion associated tumor, compatible with an astroblastoma, MN1 altered. While in three cases the EPIC analysis was instrumental to bring forward a distinct diagnostic entity, in two cases the EPIC data helped to assign the respective metastatic lesions to its primary tumor source. Four of five patients died within the first year after diagnosis. EPIC analysis did not change the intended treatment (combined radio-chemotherapy/radiotherapy) or the time point of secondary treatment for the described five patients.

Conclusion

EPIC classification is a most precise and essential novel neuropathological diagnostic method. Here, we report of 13 intraspinal intradural tumor cases. In 5 of 13 cases an EPIC analysis was performed due to a nonconclusive diagnosis using conventional, non-molecular neuropathological methods. In 3 out of 13 cases EPIC analysis identified rare tumor entities with less than 300 published cases. Our data illustrates the necessity of EPIC analysis as an essential tool allowing to overcome traditional limitations of neuropathological diagnostics. Only applying precise diagnostic classification will allow to guarantee the adequate applicatoin of future therapeutic approaches.

P148

Operative Versorgung geriatrischer Patienten mit Hirnmetastasen
Surgical treatment of geriatric patients with brain metastases

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Objective

Due to the aging population and ongoing advances in cancer control, the pursuit of optimal management in geriatric patients with brain metastases is an increasing challenge, especially due to the scarce data available. We have therefore analyzed our institutional data with regard to factors influencing overall survival in geriatric patients with brain metastases.

Methods

Between 2013 and 2018, patients aged ≥ 65 years with surgically treated brain metastases were included in this retrospective analysis. In the search for preoperatively identifiable risk factors for poor overall survival (OS), in addition to the underlying cancer, the preoperative frailty of patients was analyzed using the modified Frailty Index (mFI).

Results

A total of 189 geriatric patients with surgically treated brain metastases were identified. Complete follow-up was available in 180 patients. Geriatric patients categorized as least-frail achieved a median OS of 18 months, while frailest patients achieved an OS of only 3 months ($p<0.0001$). Cox regression analysis detected "primary cancer site other than the breast" ($p=0.028$), "further intracranial metastases" ($p=0.001$), "infratentorial localization" ($p=0.011$), "preoperative CRP >5mg/dl" ($p=0.01$) and "frail patients (mFI ≥ 0.27)" ($p=0.003$) as predictors for poor survival in geriatric patients undergoing surgical treatment for brain metastases.

Conclusion

In this study, preoperatively detectable conditions are presented that lead to poor survival in geriatric patients with brain metastases requiring surgery. Particularly noteworthy is the impact of frailty in geriatric patients with brain metastases. The results of this study are intended to contribute to better counselling/support of affected geriatric patients and their families.

P149

Systemische Alterationen des CD4+ T-Helfer-Zell Phänotyps in Gliomen
Systemic alterations of the CD4+ T helper cell phenotype in glioma

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Objective

Cancer is a systemic disease. Due to the exceedingly rare occurrence of metastasis of cerebral glioma, systemic alterations have, however, not been considered to play a major role in disease progression of glioma. CD4+ T helper (TH) cells orchestrate the adaptive immune response in an antigen-specific, cytokine mediated manner. The aim of our study was to investigate how far cerebral glioma impacts the systemic CD4+ immune repertoire.

Methods

We performed a multi-color flow cytometry analysis of the peripheral blood CD4+ TH cell phenotype and cytokine production in 100 patients with IDHwt, 30 IDHmut and 16 IDHmut 1p19q co-deleted gliomas in comparison with age-matched healthy donors (HD). Data was analyzed using a Fortessa LSR and Diva software. Multiparameter analyses were performed using UMAP analyses and SpadeVizR trees. The study was approved by the local ethics committee (PV4904).

Results

We found a significant skewing of the peripheral immunophenotype in IDHwt glioma patients, showing a TH1 expansion and reduced numbers of T follicular helper cells (TFH), TH1* and mucosa associated invariant T (MAIT) cells ($p<0.001$), while TH2 and TH17 percentages remained stable compared to IDHmut and HD. Interestingly, although TH1 cells were dominant in IDHwt patients ($p<0.01$), intracellular cytokine staining showed a distinct reduction of IFNg and TNFa production after *in vitro* stimulation, while IL-4 was significantly increased compared to HD ($p<0.05$). No alterations between all groups were observed in IL-2, IL-10 or IL-17 production. Profiling of metabolic surface markers further revealed increased expression of GLUT1 on CD4+ T cells in IDHwt patients, indicating an activated CD4+ repertoire compared to HD.

Conclusion

Taken together, our results show a CD4+ TH cell type specific skewing of the peripheral immune repertoire in patients with IDHwt gliomas. Our data highlights the importance of considering malignant glioma as a disease with profound systemic effects fundamentally altering the immune repertoire in affected patients.

P150

Spezifischer Transfer eines TLR3-Agonisten zur Immuntherapie des Glioblastoma multiforme
Targeted delivery of a toll-like receptor 3 agonist for immunotherapy of glioblastoma multiforme

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Objective

Glioblastoma multiforme (GBM) represents the most common primary adult brain tumor. Despite surgical resection followed by radiotherapy and chemotherapy, these tumors ultimately recur. One promising strategy for the treatment of GBM is immunotherapy. Yet, several vaccination approaches as well as adoptive transfer of tumor-reactive lymphocytes revealed disappointing responses due to immunosuppressive mechanisms of GBM. Thus far, agonists for toll-like receptors (TLRs) appear promising to reprogram the immunosuppressive environment of GBM. Yet, systemic treatment with TLR agonists is limited due to off-target effects. We sought to develop a selective delivery system for TLR3 agonists for treatment of GBM. Therefore, we designed immunoconjugate-nanoparticles (IC-NPs) for targeting exclusively astrocytoma/GBM cells with surface expression of oncogenic EGFRvIII.

Methods

For assembly of EGFRvIII-specific IC-NPs mono-biotinylated scFv(MR1.1)-P-BAP was conjugated to (neutr)avidin and mono-biotinylated 50bp dsRNA (TLR3 agonist). The specific endosomal localization of anti-EGFRvIII-IC-NPs in murine EGFRvIII-positive cells was examined by confocal microscopy (CM). Endosomal activation of TLR3 and the consecutive release of proinflammatory cytokines, chemokines, and type 1 interferons was analyzed via cytokine-specific multiplex bead-based flow cytometry. The immunotherapeutic anti-tumor effects of EGFRvIII-specific IC-NPs were investigated employing the syngeneic immunocompetent SMA-560/VM-Dk mouse model.

Results

The receptor-specific endocytosis and endosomal localization of anti-EGFRvIII-IC-NPs in EGFRvIII-expressing murine anaplastic astrocytoma cells (SMAvIII) was confirmed by CM. Furthermore, upon anti-EGFRvIII-IC-NP treatment the release of type 1 interferons, chemokines, and proinflammatory cytokines in SMAvIII followed a dose-dependent manner. Serial intraperitoneal application of anti-EGFRvIII-IC-NP tumors led to significant regression of subcutaneous SMAvIII tumors, and prolonged overall survival compared to PBS-treated controls.

Conclusion

Our results demonstrate the feasibility of IC-NPs for targeted delivery of TLR3 agonists to murine astrocytoma. Furthermore the IC-NP-mediated induction of innate and adaptive immune responses holds promises to improve immunotherapy of GBM.

P151

Testung der feinmotorischen Fähigkeiten prä- und postoperativ bei Patienten mit Tumoren in supplementär-motorischen Arealen

Testing fine motor skills pre- and postoperatively in patients suffering from tumours in the supplementary motor area

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Objective

Supplementary motor area (SMA) syndrome is a common neurosurgical sequela, however the incidence and time frame of its occurrence have not yet been characterized in a structured manner. This study therefore examines targeted fine motor skills of these patients preoperatively, postoperatively and after 3 months.

Methods

13 patients (median age: 46.6 years, 62% males) suffering from a tumor (glioblastoma / astrozytoma / oligodendroglioma / metastasis) in the dorsal part of the superior frontal gyrus (10 right, 3 left) underwent preoperative, early postoperative and 3-month follow-up testing of the fine motor skills using the Jebsen-Taylor Hand Function Test (JHFT) consisting of 8 modalities for both upper extremities. Test completion times (TCTs) were recorded and compared between time points and sides.

Results

Preoperatively no patient suffered from impairment of motor strength. Postoperatively we detected paresis in 2 patients (BMRC 2/5) which remained clinically stable at 3-month follow-up. Except for page turning, every test from the JHFT showed highly statistically significant worsening and longer TCTs ($p < 0.05$) in the postoperative and 3-month follow-up examinations for the contralateral upper extremity. Excluding page turning, simulated feeding and the nine-hole peg test, we also detected highly statistically significant longer TCTs ($p < 0.05$) in the ipsilateral upper extremity. At 3 months following surgery an improvement of just writing (83.3% of all patients), page turning (50%) and simulated feeding (58.3%) could be detected in the contralateral upper extremity compared to postoperative state. In terms of the ipsilateral upper extremity only the writing function recovered after 3 months (53.8%). The other fine motor skills did not improve.

Conclusion

This study suggests persistent worsening of fine motor skills even 3 months after resection of tumors of the SMA region which indicates the necessity of targeted physical therapy for these patients.

P152

Die Kombinationstherapie von Tumor Treating Fields mit dem TERT-Inhibitor Eribulin zeigt synergistische antiproliferative Effekte an humanen Glioblastomzellen

The combination therapy of tumour treating fields with the TERT-inhibitor eribulin shows synergistic antiproliferative effects on human glioblastoma cells

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Objective

Treatment of glioblastoma (GBM) is challenging. Past milestones in the therapy were the addition of radiation therapy with temozolomide (TMZ), and the treatment with Tumor Treating Fields (TTFields) during TMZ maintenance. The aim of the study was to analyze, for the first time, the effects of the TERT-inhibitor eribulin in combination with TTFields on cell death and clonogenicity of human GBM.

Methods

Human GBM cells of the established cell lines U87, A172 and U251, as well as two patient-derived cell lines (447 and 455), were treated with eribulin, TTFields, or both modalities. After 72 hours of therapy, cell counts were measured. Additionally, clonogenic assays were performed. Cell death was analyzed using annexin V staining and fluorescence-activated cell scanning (FACS). The mean differences between cell counts, clonogenic fractions and FACS were evaluated.

Results

The mean surviving fractions over all cell lines (Figure 1) were 42.6±SD % for eribulin, 35.7±% for TTFields, and 15.2±SD% for the combination. The mean annexin positive fractions over all cell lines were 12.8±SD% (control), 30.1±SD% (eribulin), 35.3±% (TTFields), and 75.5±SD% (combination), respectively. The mean clonogenic fractions over all cell lines (Figure 2) were 19.1±SD% for eribulin and 33.6±SD% for TTFields. In the combination therapy, synergistic effects with a decreased mean of 3.2±SD% clonogenic fractions were observed.

Conclusion

Eribulin increases cell death and reduces clonogenicity in human GBM cells. Furthermore, for the combined treatment of TTFields and eribulin synergistic effects on cell proliferation were observed. Our data highlight the therapeutic potential of eribulin used in combination with TTFields and offer important insights for possible new effective GBM therapies.

Fig. 1

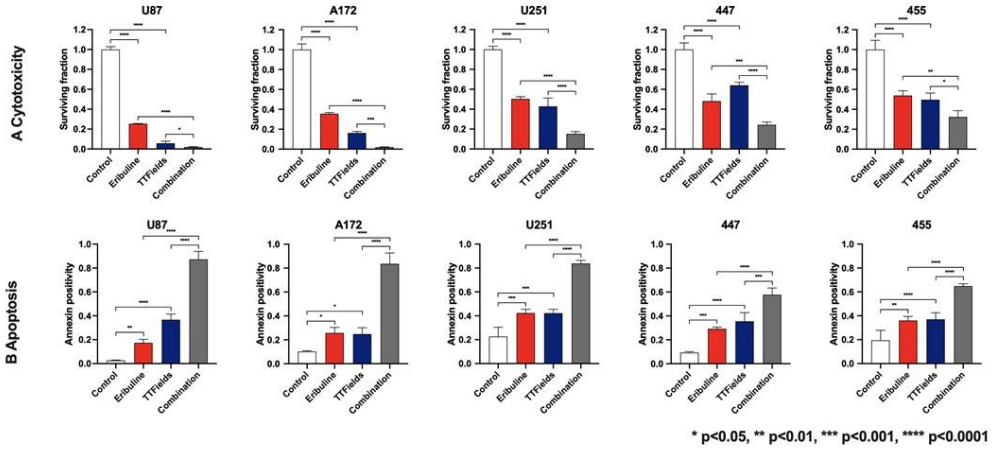

Figure 1: Mean surviving fractions (+SD) (A) and mean annexin-positive fractions (+SD) (B). Levels of significance are shown by stars as indicated.

Fig. 2

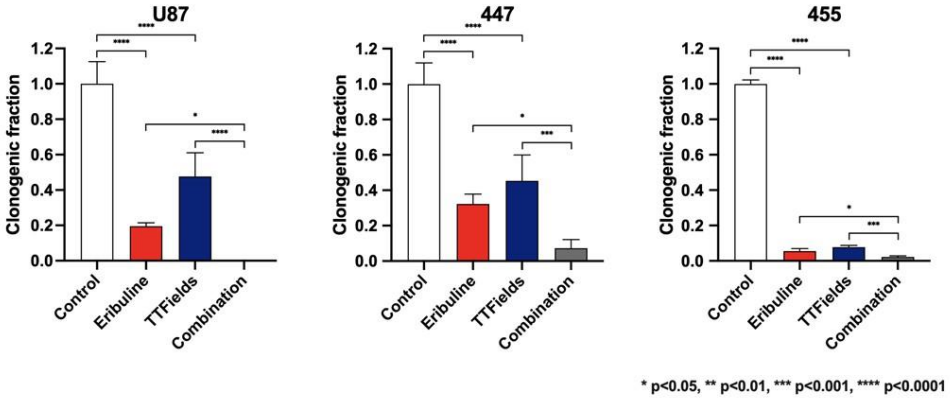

Figure 2: Mean clonogenic fractions (+SD).. Levels of significance are shown by stars as indicated.

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Behandlung rosetten-bildender glioneuraler Tumore (RGNT) der Pinealisloge
Treatment of pineal region rosette-forming glioneuronal tumours (RGNT)

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Objective

Rosette-forming glioneuronal tumour (RGNT) is an extremely rare entity described for the first time in the WHO classification in 2007. So far only single case reports of RGNT in the pineal region have been published and clear therapy concepts are pending.

Methods

The study group comprised all patients with the histopathological diagnosis of RGNT (WHO grade I) that underwent microsurgical tumour removal in the pineal region in our centre between 08/2018 and 11/2020. Surgical strategy, histological findings and clinical outcome are presented and the results are evaluated in comparison to published case reports.

Results

Four male patients with age under 50 years (range between 20 and 48 years) were included in this study. Two patients presented with chronic headache since several month and two patients presented with a generalised epileptic seizure. Cystic lesions adjacent to the pineal gland and the third ventricle were diagnosed in MRI and supra-cerebellar infratentorial gross total tumour resection was performed in three cases without permanent neurological deficits. One patient underwent subtotal tumour resection with deliberate tumour remnants bilaterally in the thalamus. This patient had no neurological deficit except a vertical gaze palsy which recovered three months after surgery. None of the patients underwent additional chemotherapy or radiotherapy.

Figure 1: Intraoperative view before (A) and after (B) supracerebellar, infratentorial tumor resection in semi-sitting position (T: tentorium; C: cerebellum; double dagger: 3rd ventricle white arrowhead: tumour)

Figure 2 A benign mixed tumor with neurocytic (synaptophysin staining, (A, B)) and astrocytic (GFAP(F) staining, olig2(C) staining) differentiation. HE staining (E) shows typical neurocytic rosettes and perivascular pseudorosettes. In the Ki67 (D) staining only very few proliferation-active cells can be recognized.

Conclusion

Resection of RGNT in the pineal region is feasible without permanent neurological deficits and should be the treatment of choice. No additional chemotherapy or radiotherapy is recommended if gross total resection can be achieved.

Fig. 1

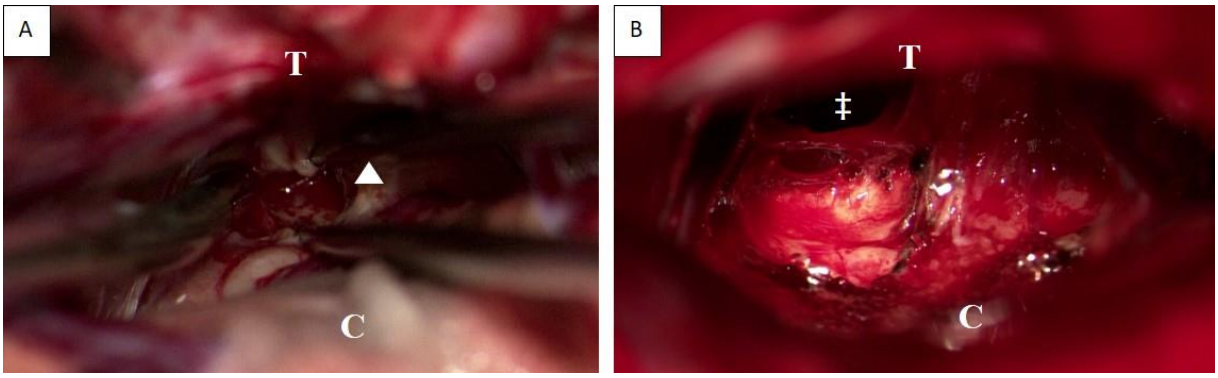
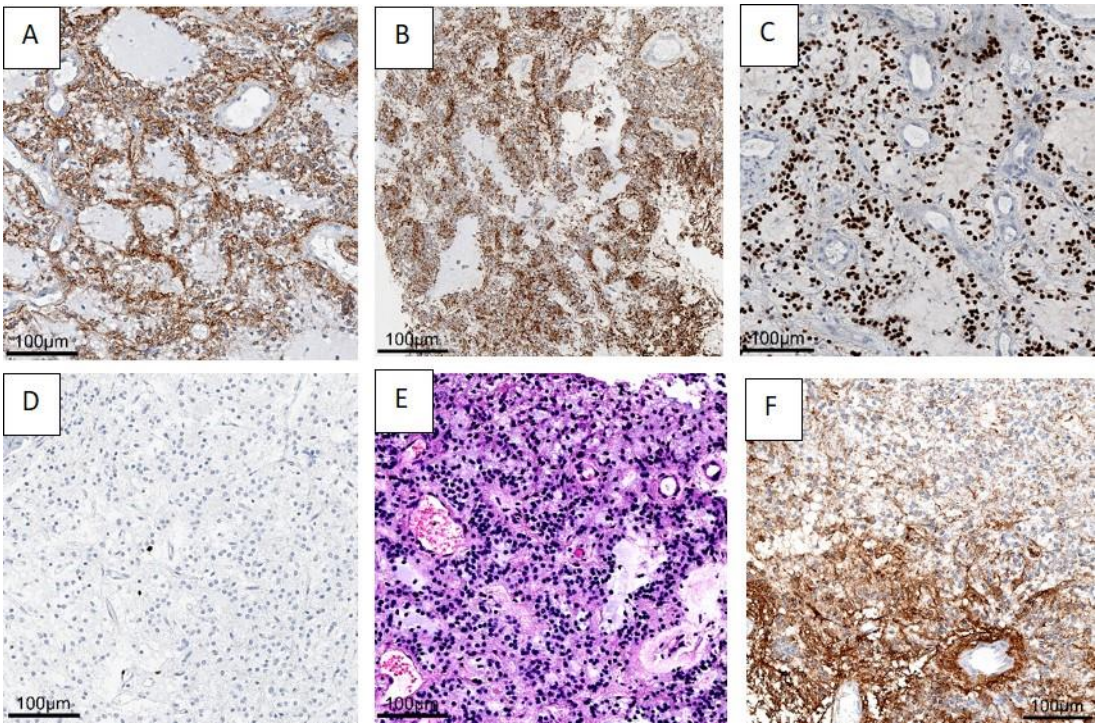


Fig. 2



P156

Die Korrelation zwischen Connexin-43 Expression und Mitoserate in häufigen ZNS Tumoren
The correlation between Connexin-43 expression and mitosis rate in common CNS tumours

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Objective

Connexin-43 (Cx43) is the crucial structural element in junctional cell-to-cell communication. It was shown, that its expression reversely correlates with glioma mitosis rate. The aim of this study was to identify the expression of Cx43 in other common CNS tumors – metastases, neurinomas and meningiomas – as well as to find a potential correlation with proliferation rate.

Methods

The IHC expression of Cx43 and MiB as mitosis marker was analysed in FFPE tissue from adult patients with different CNS metastases, meningiomas and neurinomas, that were randomly selected from our biobank. Neurinomas and meningiomas were evaluated together based on their comparable non-malignant behavior.

Results

17 metastases of different carcinomas, 7 meningiomas and 10 neurinomas were evaluated. MiB was expressed in a median of 10% of tumor cells (IqR 3 – 29), with a median of 28% (IqR 5 – 40) for metastases and 5% (IqR 1 – 11) for neurinomas and meningiomas. 7 (41%) metastases and 3 (18%) meningiomas/neurinomas showed no Cx43 expression, whereas 6 (35%) metastases and 5 (29%) meningiomas/neurinomas showed minor expression. In 4 (24%) metastases and 9 (53%) meningiomas/neurinomas, advanced expression of Cx43 could be demonstrated. The higher expression of Cx43 in meningiomas and neurinomas correlated with increased mitosis rate, $r = 0.53$ ($p = 0.034$). For metastases we could not identify a significant correlation between Cx43 and MiB.

Conclusion

The expression of Cx43 as junctional intercellular communication protein showed a significant correlation with the proliferation rate of primary intracranial tumors, but does not appear to play a role in intracranial metastases. Its role in primary intracranial CNS neoplasms is still largely unclear and mandates further investigation.

P157

Neuer Score zur Prädiktion des langfristigen Outcomes nach chirurgischer Behandlung chronischer Subduralhämatome – eine prospektive Studie

A new scoring system for prediction of long-term functional outcome after surgery for chronic subdural hematoma – a prospective study

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Objective

A recent study showed a frequent elevation of brain natriuretic peptide (BNP) serum levels in patients with symptomatic chronic subdural hematoma (cSDH). In this study, the prediction of the long-term functional outcome was assessed, and a new predictive score developed.

Methods

We prospectively included patients with symptomatic cSDH that were surgically treated in our department between November 2016 and December 2019. BNP serum levels and clinical condition on admission were recorded. The patients were followed up at 5-6 months after surgery using a simplified modified Rankin Scale (mRS) questionnaire in a standardized telephone interview. An unfavorable outcome was defined by a mRS> 3. Based on predictors of the long-term functional outcome, a predictive score was computed, and its accuracy was tested using the area under the curve (AUC) of the receiver operating characteristic analysis.

Results

Altogether, 119 patients were analyzed (median age: 76 years, range: 44-94 years). BNP on admission was elevated in 77 patients (64.7%). Only 101 patients (84.8%) were available for the follow-up phone interview. In the multivariate analysis, unfavorable outcome at follow-up could be predicted using BNP serum levels (p=0.034), patient"s age (p=0.036), motor deficit (p=0.013) and Glasgow coma scale score on admission (p=0.008). The computed "Functional Long-term Outcome Predictive score" (FLOP-score) revealed an excellent discriminative capacity for unfavorable outcome at follow-up compared to other scores, with an AUC of 0.86 (0.77 – 0.95).

Conclusion

The FLOP-score is an easy-to-use tool providing crucial clinical information that may guide neurosurgeons in decision-making and help to anticipate persistent functional impairment prior to surgery. To validate our promising data, an external validation of the proposed score is mandatory.

P158

Eine neue Technik für *in vivo* live Untersuchung der zellulären Bestandteile der neurovaskulären Einheit (NVU)
A novel technique for in vivo live cell imaging of the cellular components of the neurovascular unit (NVU)

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Objective

Treatment of ischemic stroke is limited to mechanical and pharmaceutical recanalization of the affected vessel. Cure of post ischemic tissue, aiming at conservation and rehabilitation of the NVU and functional recovery is non-existent in clinical context. Lack of understanding of molecular processes in these areas following hypoxia is in parts responsible for the shortage of possible treatments. We intended to use two-photon excitation microscopy (2PM) to illuminate the single components of the NVU in a post ischemic context *via* chronic cranial windows (CCW) *in vivo* and thereby aimed at enhancing the understanding of specific processes following ischemia in the brain.

Methods

We performed a distal middle cerebral artery occlusion as well as a fronto-lateral CCW implantation. For the window, we either used a glass plate or a silicone-based polydimethylsiloxane (PDMS) membrane. For imaging of vessels, either Cascade Blue® or FITC-Dextran was administered intravenously. For imaging of astrocytes, Sulforhodamine 101 (SR101) was applied intravenously, subpially or intracortically before the respective measurement time points, either *via* the PDMS membrane or a separate burrhole on the contralateral side. To complete imaging of the NVU, we examined transgenically modified Thy-1 mice, which expressed YFP-positive neurons (Thy-1-CreERT2/Efnb2 lox/lox). These mice further had possibility of an induced knockdown of the ephrinB2 signaling pathway. To add a fourth component, display of the dura was effectuated by the use of second harmonic generation (SHG).

Results

Cascade Blue® proved to be advantageous over FITC-Dextran in physiological circumstances, due to its differing light-spectrum compared to the YFP-expressing neurons. Yet, for the virtue of its minor molecularity, Cascade Blue® tended to extravasate more than the heavier FITC-Dextran, following breakdown of the NVU. We found the ideal method for imaging astrocytes intracortical injection two hours before 2PM. As we considered injection through the PDMS membrane to be traumatic to the investigative side, we continued performing burr holes on the contralateral side of the window, as we discovered the SR101 to spread globally across the brain. The transgenic mice expressed YFP-positive neurons for up to 28 days postoperatively.

Conclusion

Triple imaging of the single components of the NVU combined with SHG is a stable tool to image and examine delicate processes in the brain physiologically and post-stroke by means of 2 PM *in vivo*.

P160

Kollagenmarkierung zur Darstellung der strukturellen Stabilität von intrakraniellen Aneurysmen
Collagen labelling for visualisation of structural instability in intracranial aneurysms

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Objective

The main molecular constituent in the wall of intracranial aneurysms (IA) is collagen type I, which cannot be illustrated by existing imaging modalities. Ongoing wall remodelling in IA, especially molecular turnover with synthesis of immature/structural deficient collagen type I, seems to be associated with IA instability. At present the estimation of the individual IA instability, i.e. the rupture risk, remains challenging. Therefore, we developed a novel Positron Emission Tomography contrast agent to visualize immature/novel collagen in human IA as a possible indicator for instability.

Methods

IA samples derived from patients undergoing surgical IA repair, were used for radio- and immunolabelling as well as histological staining. Longitudinal cryosections of the IA including the dome and transition zone (between dome and neck) were performed. 12µm cryosections were incubated with the tracer 68Ga-NODAGA-Collagelin and visualised by autoradiography. 9µm cryosections were used for immunolabelling of collagen alpha 1 chain type I and visualized by confocal laser microscopy. 9µm cryosections were used for histological staining and visualised by light microscopy. Immature and mature collagen was differentiated by polarisation microscopy. Qualitative assessment was performed by two independent investigators.

Results

Between 6/2016 and 11/2019 25 IA samples (11 unruptured, 14 ruptured) from 25 IA patients (18 female, 6 male) with 57.4±9.9 years were included. Polarisation microscopy demonstrated regions of mature collagen, which were localised independent of the IA region (neck to dome), but regions of immature collagen were predominantly found in IA domes. Radiolabelling demonstrated increased uptake in IA regions with immature collagen and less uptake in regions with mature IA collagen. Figures 1 and 2 serve as illustrative examples for an unruptured and a ruptured IA.

Conclusion

Our novel collagen radiotracer seems to specifically label human IA regions with immature/structurally deficient collagen and could serve as a novel radiological indicator for molecular IA stability. To further facilitate clinical use, we will corroborate our current findings on collagen imaging *in vivo* after induction of IA in an animal model by autoradiography and PET.

Figure1: Unruptured IA

Figure2: Ruptured IA

Immuno- (A), radiolabelling (B), histological staining (C) and polarisation microscopy (D) of an unruptured (Figure1) and ruptured IA (Figure2). Regions with immature collagen are labelled (*).

Fig. 1

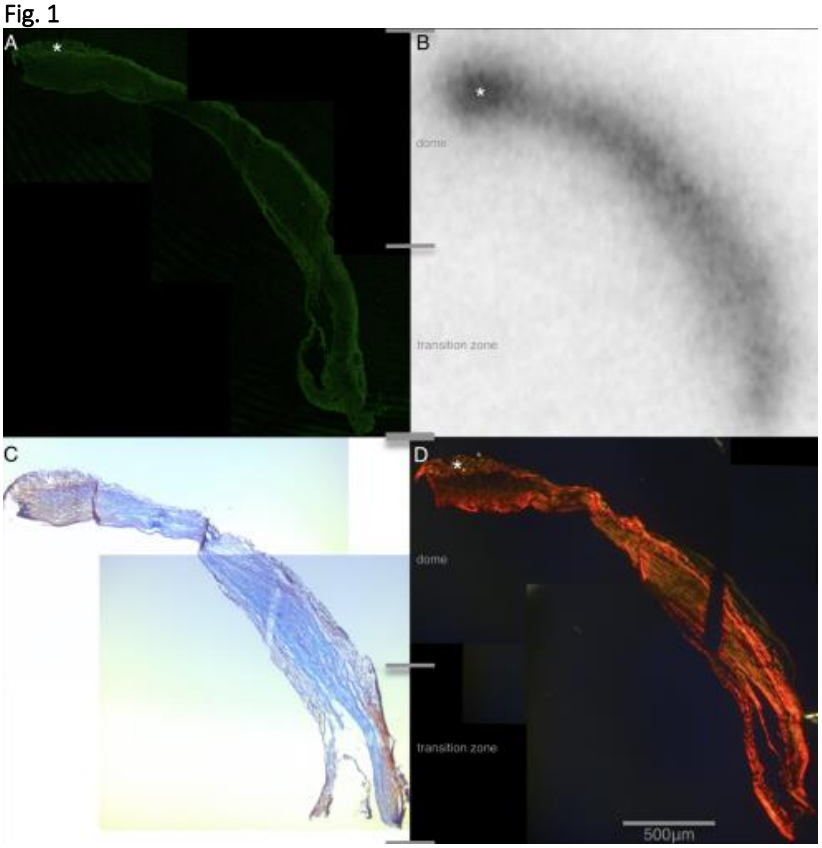
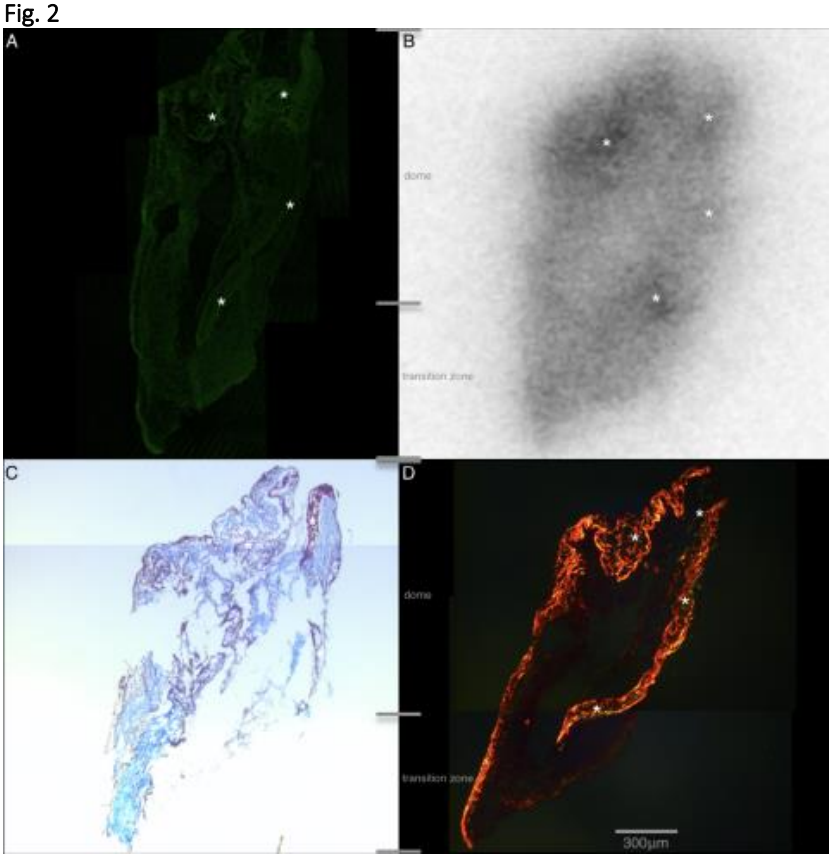


Fig. 2



P161

Inkompletter oder vollständiger Verschluss des Trägergefäßes – Effekt der Okklusionsstrategie auf die Komplettverschlussrate komplexer Aneurysmen

Complete or partial parent artery sacrifice – effect of vessel occlusion strategies on complete obliteration of complex aneurysms

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Objective

A small number of complex intracranial aneurysms is not amenable to direct clipping strategies or endovascular treatment. In these patients, parent artery sacrifice and bypass revascularization for aneurysm occlusion is an option. There are three strategies for parent artery sacrifice: trapping, with complete occlusion of the inflow and outflow segment, proximal occlusion of the inflow vessel and distal occlusion of the outflow vessel(s).This study aimed to compare these techniques with regard to aneurysm occlusion rates.

Methods

We reviewed our database for cerebral revascularization before parent artery sacrifice to treat cerebral aneurysms. We assessed aneurysm occlusion rates 3 and 12 months after surgery, outcome and postoperative aneurysm rupture

Results

121 patients underwent parent artery sacrifice for complex aneurysms. 30% of the parent arteries were trapped, 58% proximally, and 12% distally occluded. Postoperative DSA revealed an aneurysm occlusion rate of 100% after trapping. Proximal occlusion led to early complete aneurysm occlusion in 71% of the cases, 21% occluded during follow-up. Complete occlusion rate was 96%. Distal occlusion had an early aneurysm occlusion rate of 40%, 40% occluded during follow-up. Complete aneurysm occlusion rate was only 80%. All three techniques resulted in a volume reduction of more than 60% without a significant difference between the groups. The annual aneurysm rupture rate after distal parent artery sacrifice was 15%, there was no rupture after trapping or proximal parent artery sacrifice

Conclusion

Trapping and proximal parent artery sacrifice seem to be superior to distal parent artery sacrifice regarding occlusion rates and rupture rates.

P162

Korrelation von Aneurysmamorphologie mit dem Fischer-Grad, Vasospasmen, Hirninfarkten und klinischem Outcome in Patienten mit Subarachnoidalblutung

Correlation of aneurysm morphology with Fisher grade, vasospasm, cerebral infarction and clinical outcome in patients with subarachnoid haemorrhage

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Objective

Aneurysmal subarachnoid hemorrhage is associated with high morbidity and mortality. In particular, the extent of the initial bleeding, vasospasm and cerebral infarction decisively affect clinical outcome. The aim was to identify specific morphological aneurysm characteristics that could serve as predictive values for aSAH severity, disease-related complications and functional outcome.

Methods

This is a retrospective, single-center analysis of 453 aSAH patients. The morphometric analysis included aneurysm location, dome width, height, neck width, dome-to-neck ratio, aspect ratio, width-to-height ratio, vessel diameter, size ratio, and aneurysm shape. These characteristics were correlated with the following outcome measures using univariate and bivariate logistic regression analyses: World Federation of Neurosurgical Societies (WFNS) grade 4 and 5, Fisher grade 4, vasospasm, cerebral infarction and unfavorable functional outcome (6-month modified Rankin scale score > 2).

Results

The mean aneurysm size was 7.5 ± 3.6 mm and 15% were located at the posterior circulation. An irregular aneurysm shape was seen in 81%. In the multivariate analysis, a wider aneurysm neck was independently associated with Fisher 4 hemorrhage (OR: 1.1, 95%CI: 1.0 – 1.3, p=0.048). Aneurysm dome width (OR: 0.92, 95%CI: 0.86 – 0.97, p=0.005) and internal carotid artery location (OR: 2.1, 95%CI: 1.1 – 4.2, p=0.028) were predictive for the occurrence of vasospasm. None of the analyzed morphological features were independent predictors of functional outcome. Patient age (OR: 0.95, 95%CI: 0.93 – 0.96, p<0.001), WFNS score (OR: 4.8, 95%CI: 2.9 – 8.0, p<0.001), Fisher score (OR: 2.3, 95%CI: 1.4 – 3.7, p<0.001) and cerebral infarction (OR: 4.5, 95%CI: 2.7 – 7.8, p<0.001) were independently associated with unfavorable outcome at 6-month follow-up.

Conclusion

The results showed an independent correlation between aneurysm neck width and Fisher grade and between dome width and internal carotid artery location and vasospasm. However, none of the investigated morphological characteristics were independently associated with cerebral infarction and functional outcome and have thus a limited value as predictor for these outcome measures. In the near future, the occurrence of complications and clinical outcome may be more precisely predicted based on computed tomography angiography with the help of artificial intelligence.

P163

Verursacht körperliche Aktivität von Menschen mit ZNS-Kavernomen den Ausbruch der Krankheit?
Does physical activity undertaken by people with CNS cavernomas provoke the onset of the disease?

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Objective

Background: Theories that suggest that certain activities pose a risk to patients with cavernomas are not supported by clinical studies.

OBJECTIVE: To assess the relationship between the physical activity state in the last one hour and the onset of the first symptoms in people harboring cavernoma.

Methods

A monocentric retrospective conducted study in patients that were surgically treated between the years 2005 and 2019 in a tertiary hospital. 52 of 81 patients had been interviewed between January 2017 to January 2020. 34 patients included in the study. The authors evaluated the incidence of cavernoma following physical activity.

Results

The study included 20 females (58.9%) and 14 males (41.1%), the mean age at onset was 38.1 years (F: 39.4, M:36.5). The symptomatic cavernoma was 24 in supratentorial (70.6%), 4 in the cerebellum (11.8%), 4 in the brainstem (11.8%), one in the spinal cord (2.9%), and the last in the orbital region (2.9%).

Of the 34 subjects, 30 patients (88.2%) reported the onset of the disease followed a light activity or no active state, only 3 cases (8.8%) reported having engaged in a moderate activity during the hour before cavernoma onset, and the last under emotional stress.

Conclusion

We concluded that physical activity in the last hour likely does not evoke the onset of the disease in patients harboring CNS cavernomas, as the cavernous malformation is a passive capillary anomaly.

Fig. 1

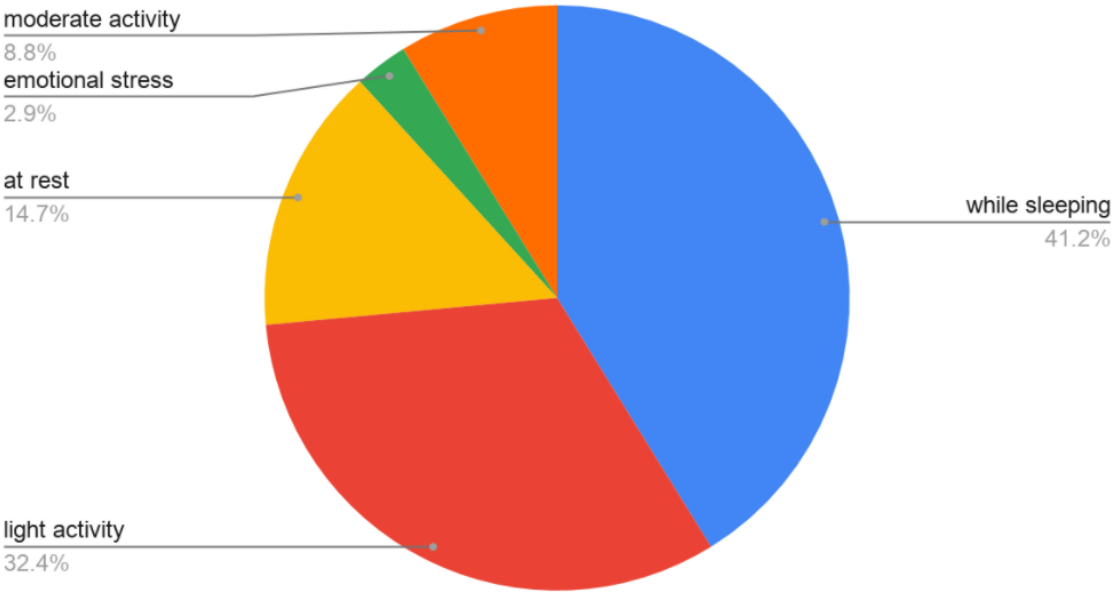

Figure 2. Pie Chart: demonstrating the number and percentages of cases according to physical activity state one hour prior to the onset of the first symptom from the cavernoma.

Fig. 2

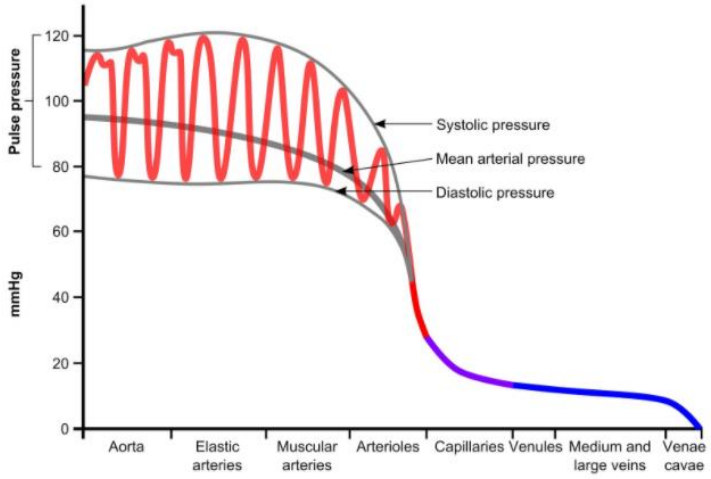

Fig. 3

The graph demonstrates the difference in blood pressure as it goes through the different blood vessels in the circulation.

It clearly shows that any change in the mean arterial pressure will have no effect on the capillary pressure and thus the cavernoma. [24] (modified with permission, (Lumen Learning and OpenStax))

P164

Erweiterte perivaskuläre Räume als Risikomarker für intracerebrale Blutungen bei DBS-Implantation – eine retrospektive Analyse

Enlarged perivascular spaces as a potential risk marker for intracerebral haemorrhage in DBS surgery – a retrospective investigation

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Objective

Intracerebral hemorrhage (ICH) poses a devastating complication of DBS surgery associated with high age and the use of microelectrodes. In preOP MRIs we encountered wide perivascular spaces (PVS) in cases with ICH during electrode implantation. PVS enlargement is associated with occurrence of spontaneous intracerebral hemorrhage (Raposo et al. 2019, Duperron et al. 2019) and may reflect a general vascular vulnerability. Here we aimed to explore the role of enlarged PVS as a risk indicator for ICH during DBS electrode implantation.

Methods

The data of 362 consecutive patients (01/2013-09/2020) were analyzed. Unsuitable MR images were excluded (movement artefacts, <3 Tesla, WMH of non-vascular origin e.g. multiple sclerosis, preexisting DBS, etc.), resulting in 270 MRIs. Prior to PVS burden quantification, 1mm isotropic T1 und T2 images were coregistered and T1 images segmented using SPM12"s segmentation algorithm in WM/GM/CSF. For normalization of the T2 contrast a smooth T2 CSF reference image was computed by 1) masking out the all signal non-CSF in the T2 image (using SPM"s CSF-T1 segmentation), and 2) extending the CSF signal to adjacent regions by a broad Gaussian smooth. The raw T2 is then divided by this reference image to obtain comparable contrasts. PVS burden was computed by the commonly used Frangi-filter for tubular structures (smin=0,4mm, smax=2,0mm, scale ratio=2, α=0,1, β=1, c=0,01) on the normalized T2 (Frangi et al. 1998). All responses in non-WM and in cerebellum, pons and medulla oblongata were excluded. Finally, PVS index was computed by a simple summation of all non-negative filter responses within white matter. A Mann-Whitney-U-Test across all 206 operations with microelectrodes (encompassing all cases with subcortical ICH) was calculated to analyze age and PVS-Index in cases with and without ICH.

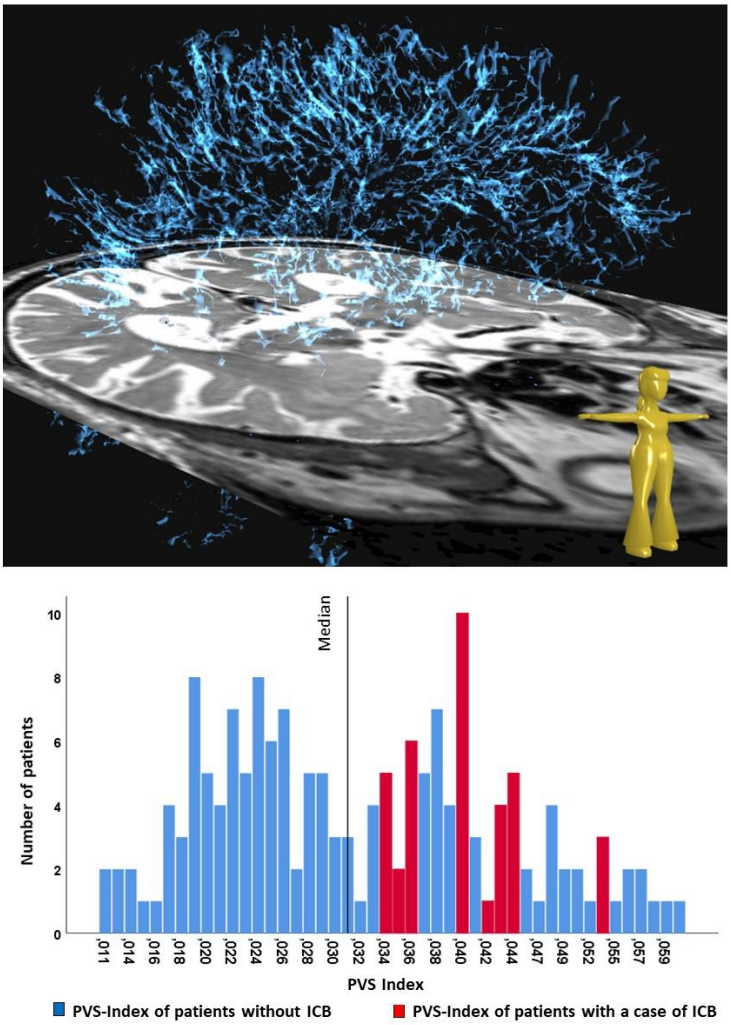
Results

10 cases of subcortical ICH occurred during implantation of 722 electrodes in 374 operations (2.7 %) in 362 patients. Relevant neurological deficits resolved in all but one of the affected patients. ICHs occurred more often in patients with PVS enlargement (p = .006, 2-sided) and higher age (p =.022, 2-sided).

Conclusion

Enlarged PVS may serve as an additional risk indicator for ICH in DBS surgery and help to mitigate invasivity (e.g. avoid microelectrodes) in patients at risk. The presented results are preliminary and further analyses are in preparation to address the sparse data bias (Greenland et al. 2016) due to low incidence of ICH.

Fig. 1



Upper Panel: Rendering of PVS in a patient with ICB during DBS-electrode-implantation (PVS-Index = 0.054). Lower Panel: Bar graph plotting the frequency of the PVS-Index across all patients with suitable MRI. PVS-Index values of 8 patients with ICB are marked red. MRI data of two patients with ICB were not suitable (MRI not feasible due to cochlea implant in one patient; multiple sclerosis in another patient)

P165

Flow Diverter-Devices als Behandlungsoption für komplexe (fusiforme) Aneurysmen der Ateria cerebelli superior (SCA) – Literaturübersicht und illustrativer Fall

Flow diverter devices as treatment option for complex (fusiform) superior cerebellar artery (SCA) aneurysms – review of literature and illustrative case

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Objective

Superior cerebellar artery (SCA) aneurysms are rare entity accounting for only 0.2% of all cerebral aneurysms, with only a small portion of these being fusiform aneurysms. Due to this rarity, there are few studies and reports that compare the different therapy options. Currently, surgical revascularization procedures using IC-IC or EC-IC bypass and distal clipping or trapping are the valid and rescue treatment modality for extremely rare unilateral distal fusiform superior cerebellar artery (SCA) aneurysms. Jet, in case of bilateral fusiform SCA aneurysms surgical therapy reaches its limit. Mini-FDDs have only recently become available for treating fusiform aneurysms of such small vessels. However, clinical experience with these devices is still lacking. Therefore, as part of treatment in the complex case of bilateral SCA aneurysms in our clinic, we examined the data on the use of flow diverters in SCA aneurysms.

Methods

We present an illustrative case of bilateral distal fusiform SCA aneurysms treated with endovascular implantation of two mini-FDDs. Furthermore, we performed a review of the literature using the electronic databases PubMed and Google Scholar to search for additional data in published studies and case reports of SCA aneurysms treated with FDDs.

Results

Overall, 7 studies and case reports presenting 8 patients in whom an SCA aneurysm was treated with endovascular FDD implantation, were found. In particular, complex aneurysms without any further treatment option were treated with FDDs jet, only 2 patients had fusiform aneurysms. Nevertheless, 78% of the patients showed no or little impairment (mRS = 0-2) on discharge. Except for the dislocation of the FDD in one case, only complications related to post-procedural dual platelet therapy occurred.

Conclusion

Endovascular therapy with implantation of FDDs in selected cases of distal SCA aneurysms is a valid treatment option. As in the present patient, reported cases in the literature demonstrated an overall good clinical outcome.

P166

Mikrovasospasmen in der Frühphase nach Subarachnoidalblutung entstehen unabhängig von Perizyten
Microvasospasm in the early phase after subarachnoid haemorrhage is independent of pericytes

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[3]Munich Cluster for System Neurology (SyNergy), München, Germany

Objective

The early phase after subarachnoid hemorrhage (SAH) is characterized by significant microcirculatory dysfunction. Microarteriolar constriction and spasms of the cerebral microcirculation (microvasospasm, MVS) have previously been demonstrated in patients as well as after experimental SAH and seem to contribute to microcirculatory deficits and, thus, posthemorrhagic brain damage. MVS pathophysiology has not yet been completely elucidated. Pericytes regulate cerebral perfusion as part of the neurovascular unit and have been described to cause capillary constriction after ischemic stroke; their role after SAH is unknown. We hypothesized that pericytes contribute to MVS after SAH. Therefore, we investigated their role in early microcirculatory dysfunction after experimental SAH using in-vivo 2-photon microscopy to directly assess the cerebral microcirculation.

Methods

In $NG2^+$ reporter mice, fluorescent perivascular cells (pericytes) were imaged and plasma was stained by Tetramethylrodamine. After baseline imaging of the pial and parenchymal cerebral microcirculation with 2-photon microscopy (2-PM), animals underwent SAH induction (MCA filament perforation model, n=10), or sham surgery (n=6). 3 hours after SAH induction, 2-PM imaging was repeated. Perivascular $NG2^+$ cells (pericytes) were then assessed with regard to the location of microarteriolar spasm formation/ constriction. In a second set of experiments, pericytes were immunohistochemically evaluated by PDGFR staining 3 and 24h after SAH (n=8 per time point) or sham surgery (n=5 per time point).

Results

No pericyte migration or loss was detected in the acute phase of SAH in cortex, hippocampus, or striatum at 3 or 24h after SAH (3h: cortex: SAH 26.9 ±8.9 $NG2^+/PDGFR^+$ cells per ROI, sham 24.5 ±9.9, p=0.7, hippocampus: p=0.4, striatum p=0.5; 24h: cortex: p=0.7, hippocampus: p=0.2, striatum p=0.4). Pericytes did not colocalize with the microarteriolar spasms or constriction (diameter at/ distal to pericyte: 100.2 ±8.2%/ 92.8 ±8.6% of proximal baseline, p=0.9 vs. proximal, p=0.1 vs. distal diameter).

Conclusion

Pericyte constriction does not contribute to the formation of microvascular contractions/ microvasospasm in the acute phase after SAH. The current results suggest that the microcirculatory dysfunction after SAH is not relevantly mediated by pericytes. The pathophysiology of early posthemorrhagic microcirculatory disturbances therefore seem to differ from changes observed after ischemic stroke.

P167

Prädiktoren des BNP-Anstiegs bei traumtischem akuten Subduralhämatom und seine Rolle in der Prädiktion der früh-postoperativen zerebralen Ischämie

Predictors of brain natriuretic peptide increase in traumatic acute subdural heamatoma and its role in the prediction of postoperative cerebral infarction

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Objective

The increase of plasma brain natriuretic peptide (BNP) concentrations on admission was demonstrated in patients with traumatic brain injury (TBI), but has been not yet addressed in traumatic acute subdural hematoma (aSDH). The aim of this study was to assess the relationship between plasma BNP levels and radiological findings in patients treated for traumatic aSDH.

Methods

Patients with unilateral traumatic aSDH that were admitted in our department between July 2017 and April 2020 were enrolled in the study. Plasma BNP level was measured at admission. Time between trauma and BNP sampling (TTS) was assessed. Admission radiographic variables included hematoma volume (Hem-Vol, using a computer-assisted volumetric analysis) , middle line shift, presence of intracerebral contusions, and brain edema (using SEBES). In the subgroup with aSDH surgery, radiographic evaluation was enhanced with postoperative cerebral infarction, new cerebral contusions and re-bleeding. BNP cutoff-value was assessed using the area under the curve of the receiver operating characteristic analysis.

Results

In total, 130 patients were included in the study (median age: 74.5 years). Surgical treatment was performed in 82.3% (n=107) cases, 14.6% (n=19) were conservatively treated, and only 3.1% (n=4) were not operated because of worse prognosis. Higher plasma BNP levels on admission were statistically significantly associated with longer TTS, higher Hem-Vol and lower SEBES. After adjusting for age and sex, multiple regression analysis showed that Hem-Vol (p=0.044) and advanced age (p=0.0005) were independent predictors of increased plasma BNP levels on admission. In contrast, lower plasma BNP levels were associated with postoperative early cerebral infarction (median: 3 days). Binomial logistic regression showed that preoperative plasma BNP level (cutoff <29.4, aOR=16.5, p=0.023) was an independent predictor of postoperative cerebral infarction when TTS=3-12h.

Conclusion

In patients with aSDH, BNP increase is related to aSDH volume and advanced age. Interestingly, there is a higher risk of postoperative cerebral infarction in aSDH individuals who showed low preoperative BNP values at 3-12h post-trauma.

P168

Präparation und Visualisierung des murinen Subarachnoidalraumes (SAR) für histologische und elektronenmikroskopische (EM) Analysen

Preparation and visualisation of murine subarachnoid space (SAS) for histological and electron microscopy (EM) analyses

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Objective

Histological analyses and EM visualization of local effects after subarachnoid hemorrhage (SAH) require a preservation of the anatomical structure of the SAS. However, systematical approaches for conserving SAS in animal models of SAH are scarce in the literature. Hence, we aimed at establishing a protocol to preserve and depict the SAS for further immunohistochemical and EM analyses.

Methods

Male C57Bl/6 mice were operated, and they received either sham operation (n=6) or filament-perforation surgery to induce SAH (n=6). Magnetic Resonance Imaging was performed 24 hours post-operatively to confirm the bleeding. For immunohistochemical analyses, mice were perfused with 4% PFA and the whole skull was harvested. After 12 days of dehydration with an ascending sequence of sucrose, skulls were embedded and carefully cut upside-down with the microtome (Fig. 1A). Confirmation of anatomical orientation was obtained using Haematoxylin and Eosin (H&E) stainings and immunofluorescence with DAPI, the arachnoid cell marker AKAP12 and endothelial marker cd31. For EM imaging of the SAS, mice were perfused with 2,5% glutaraldehyde, and whole skulls were harvested and a 5*5 mm cube with our region of interest (ROI) was carefully dissected. In the next steps, fixation, fine preparation and documentation of the ROI followed to facilitate orientation with high-magnification EM. After postfixation steps and dehydration of the tissue, samples were coated with gold-palladium as a final step before EM imaging (Fig. 1B).

Results

The anatomical structures of the SAS were well-preserved in IF staining and EM imaging. Immunohistochemical display of SAS allowed specific analyses of intra- and extracellular compartments in the SAS (Fig. 1C). EM imaging showed maintained subarachnoid ultrastructure in control and SAH animals (Fig. 1D). In SAH condition, we observed a remarked collection of RBCs (red blood cells) and affinity towards arachnoid granulations.

Conclusion

With this study, we offer a technically feasible and reproducible approach for preservation and illustration of the SAS for IF stainings and EM imaging. These techniques can be potentially utilized for localization-specific analyses to the SAS in SAH.

Fig. 1

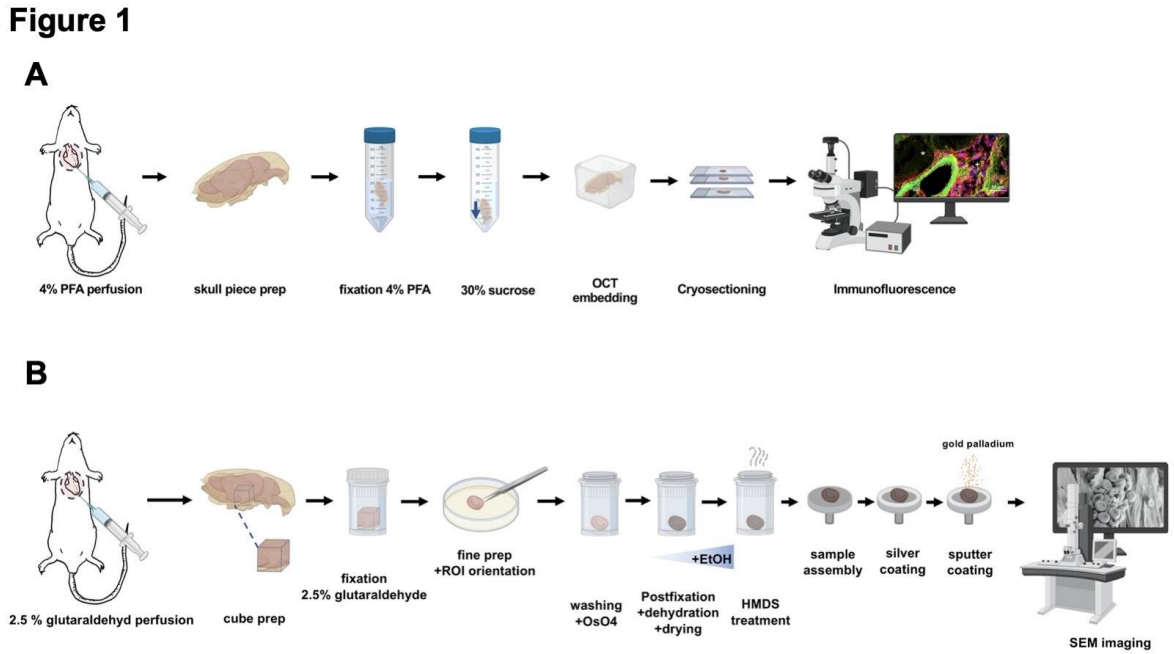
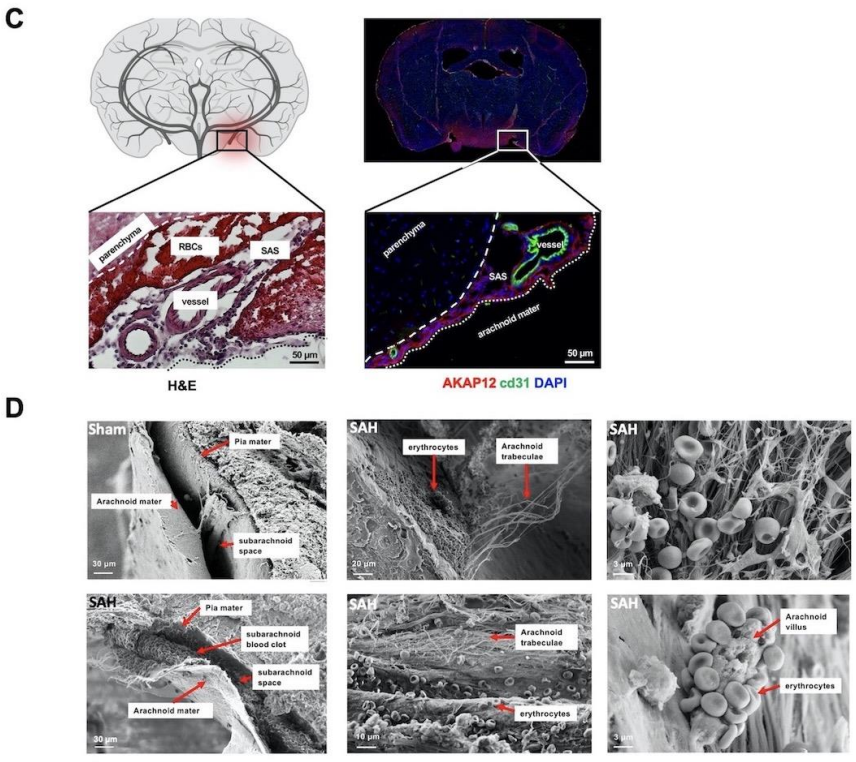


Figure 1
A
4% PFA perfusion
skull piece prep
fixation 4% PFA
30% sucrose
OCT embedding
Cryosectioning
Immunofluorescence
B
2.5 % glutaraldehyd perfusion
cube prep
fixation 2.5% glutaraldehyde
fine prep +ROI orientation
washing +OsO4
Postfixation +dehydration +drying
+EtOH
HMDS treatment
sample assembly
silver coating
gold palladium
sputter coating
SEM imaging

Fig. 2


C
parenchyma
RBCs
SAS
vessel
50 µm
H&E
parenchyma
vessel
SAS
arachnoid mater
50 µm
AKAP12 cd31 DAPI
D
Sham
Pia mater
Arachnoid mater
subarachnoid space
30 µm
SAH
erythrocytes
Arachnoid trabeculae
20 µm
SAH
3 µm
SAH
Pia mater
subarachnoid blood clot
subarachnoid space
Arachnoid mater
30 µm
SAH
Arachnoid trabeculae
erythrocytes
40 µm
SAH
Arachnoid villus
erythrocytes
3 µm

P169

Magnetresonanztomographie-basierte radiochirurgische Behandlung arteriovenöser Malformationen
Magnetic resonance imaging-based robotic radiosurgery of arteriovenous malformations

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Objective

CyberKnife offers purely MRI-based treatment planning without the need for stereotactically acquired DSA. The literature on CyberKnife treatment of cerebral AVMs is sparse. Here, a large series focusing on cerebral AVMs treated by the frameless CyberKnife stereotactic radiosurgery (SRS) system was analyzed.

Methods

In this retrospective study, 270 patients with cerebral AVMs treated by CyberKnife SRS between 2005 and 2019 were screened for inclusion. Patients below 18 years of age, or with follow-up periods < 3 months were excluded. Radiosurgical planning was purely MRI- and CT-based. Obliteration dynamics and clinical outcome were analyzed.

Results

215 patients were included (median age 40 ± 13 years, 49% female). 53% received SRS as first treatment; the remainder had prior surgery, embolization, SRS, or a combination. The majority of AVMs were classified as Spetzler-Martin grade I to III (55%). Hemorrhage before treatment occurred in 46%. The median radiation dose was 18 Gy and the median target volume was 2.4 cm^3. The most prevalent presenting symptom was headache (29%). New neurological deficits after SRS occurred in 5%. After SRS, 29 patients (14%) developed new seizures. Of all 59 (28%) patients manifesting symptomatic epilepsy before or after SRS, 36 were adequately controlled with medication. The yearly post-SRS hemorrhage incidence was 1.3%. In 152 patients who were followed-up for three years, 47% showed complete obliteration within this period. In univariate analysis, previous surgery (P = 0.028) and Spetzler-Martin grade (P = 0.007) were associated with increased chance of complete obliteration. Spetzler-Martin remained the only independent predictor of complete obliteration (P = 0.006) in multivariate analysis.

Conclusion

The obliteration rate in this cohort is consistent with data on Gamma Knife and LINAC-based SRS, where obliteration rates ranged between 30% and 58%. The rate of new neurological deficits in our cohort (5%) was comparable to a large meta-analysis on SRS treatment of cerebral AVMs with 8%.

Although data on radiosurgery of AVMs is available, this is one of the largest series, focusing exclusively on CyberKnife treatment. We showed that the frameless CyberKnife system compares favorably to frame-based systems in terms of safety and efficacy while providing higher patient comfort during treatment.

Schädelbasis, Radiochirurgie, Perspektiven/*Skull base, radiosurgery, perspectives*

P171

Radiochirurgie bei ventrikuläre Meningiomen
Radiosurgery for ventricular meningiomas

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Objective

meningiomas located in ventricular cavities are rare benign tumors which are dreaded for their surgically hardly accessible location.

Treatment options are radical microsurgery or radiosurgery as alternative treatment option by recurrence. We report on the efficacy of Gamma Knife radiosurgery (GKRS) for the treatment of intraventricular meningiomas.

Methods

From 15 participating centers under the auspices of the European Gamma Knife Society we performed a retrospective observational analysis of a cohort of 36 benign meningiomas treated with GKRS.

All were treated with Gamma Knife radiosurgery at least 5 years before assessment for this study. Clinical and imaging data were retrieved from each center and uniformly entered into a database by 1 author (A.S.)

Results

29 patients harbouring 36 meningiomas treated in fifteen institutions recruited were evaluated. The median age was 50 years old. The median tumour volume was 4.4 ccm. The median tumour margin dose to the 50 % isodose line was 15 Gy. The median cumulative imaging follow-up was 53 months. The detailed results from 31 meningiomas (86%) were available for analysis. The actuarial control rate was 100% at 5 years post GKRS. The permanent morbidity rate was12.9%.

Conclusion

GKRS is a safe and not invasive method of treatment of intraventricular meningiomas.

The data analyzed shows a high imaging tumor control and low morbidity rate even in the medium to long-term.

P172

Volumenveränderungen von Vestibularisschwannomen nach robotischer stereotaktischer Radiochirurgie
Volume changes of vestibular schwannoma after robotic stereotactic radiosurgery

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Objective

Different responses of volume can be observed after stereotactic radiosurgery (SRS) for vestibular schwannomas (VS) ranging from decrease, stability or increase of volume. The latter makes the differentiation between pseudoprogression and recurrence of VS after SRS difficult. Since only scarce data are available for robotic SRS with Cyberknife® we evaluated the course of volume changes during follow-up.

Methods

We included all patients with unilateral VS who underwent single fraction robotic SRS with a minimum follow-up of 24 months. Tumor volumes (TV) were measured on T1-weighted contrast enhanced images pre and post SRS every six months within the first year and then annually until last follow-up.

To classify different volume variations during follow-up volume changes of more or less than 10% of pre SRS TV were noted. A cox regression analysis was carried out to identify risk factors for changes in TV.

Results

Overall 63 patients with a median initial TV of 1.1 ml (0.1 – 8.6) matches the inclusion criteria. The median follow-up was 37 months (24-76). We observe different types of volume patterns: (1) partial response (62%, n=39), (2) stable disease (8%, n=5) and (3) a variable course of TV during follow-up encompassing increase followed by decrease (22%, n=14) or continuous increase followed by stable disease (8%, n=5). None of the patients requires further treatment.

Nor patient related parameters (tumor volume, age) neither radiation associated parameters (coverage, nCi, prescription dose, maximal dose) influenced the course of post SRS volume changes.

Conclusion

Volume regression after SRS for VS is observed in the majority of cases. However, there are cases of volume increase after SRS which require an extended observation period to differentiate between pseudoprogression and recurrence.

Schädelbasis, Radiochirurgie, Perspektiven/*Skull base, radiosurgery, perspectives*

P173

Stereotaktische Radiochirurgie für die Behandlung von komplett resektablen Meningeomen WHO I
Stereotactic radiosurgery for treating meningiomas WHO grade I eligible for complete resection

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Objective

For meningiomas, complete resection is recommended as first-line treatment following the EANO guidelines while stereotactic radiosurgery (SRS) is established for meningiomas of smaller size considered inoperable. If the patient´s medical condition or preference excludes surgery, SRS remains a treatment option. We evaluated the efficacy and safety of SRS in a cohort comprising these cases.

Methods

In this retrospective single-centre analysis we included patients receiving single fraction LINAC-based SRS for potentially resectable intracranial meningiomas. Treatment related adverse events as well as local and regional control rates were determined from follow-up imaging and estimated by the Kaplan-Meier method.

Results

We analyzed 188 patients with 218 meningiomas. The median radiological and clinical follow-up periods were 51.4 (6.2-289.6) and 55.8 (6.2-300.9) months, respectively. The median tumor volume was 4.2ml (0.1-22), and the mean marginal radiation dose was 13.0±3.1Gy, with reference to the 80.0±11.2% isodose level. Local recurrence was observed in one case (0.5%) after 239 months. The estimated 2-,5-,10-and 15-year regional recurrence rates were 1.5%, 3.0%, 6.6% and 6.6%, respectively. Early adverse events (

Conclusion

SRS is also a highly effective treatment for patients with meningiomas eligible for complete resection and provides reliable long-term local tumor control with low rates of mild morbidity.

Schädelbasis, Radiochirurgie, Perspektiven/*Skull base, radiosurgery, perspectives*

P174

Radiochirurgie bei rezidivierten oder residuellen Vestibularisschwannomen – eine volumetrische Analyse der Tumorverläufe

Radiosurgery for recurrent or residual vestibular schwannoma – volumetric evaluation of MRI follow-up and patterns of change in tumour volume

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Objective

Radiosurgery (RS) is a therapeutic option for recurrent or residual vestibular schwannoma (VS) after microsurgery or progression after initial RS. Tumors treated with RS show different patterns of tumor volume changes after treatment. We report on the volumetric analysis after RS for recurrent or residual VS.

Methods

All patients treated for recurrent or residual VS with at least two high-resolution MRI follow-up exams were analyzed. 2 patients with NF2 were excluded. Patient data, planning details and imaging were analyzed retrospectively. Volumetric analysis was performed on Iplan-Software (Brainlab, Munich). 4 patterns of tumor changes were defined as adapted from the literature: transient volume expansion, stable/regression, continuous enlargement and alternating enlargement/regression.

Results

26 patients (17 female, 9 male) treated from July 2013 to July 2019 were included in the analysis. Mean patient age was 60,7 years (range 31,6-78,8). 24 patients were previously treated with microsurgery, 2 patients had recurrence after RS. RS (mean margin dose 12 Gy, n=16) or multisession RS (mean margin dose 3x6 Gy, n=10) were performed at a mean time of 60,9 months after pretreatment (range 4,6 – 181,7 months). When performed after microsurgical resection, RS was applied upfront in only 2 cases, all other patients were treated upon tumor progression. Mean radiographic follow-up was 46,8 months (12,6-71,4). 117 data sets of follow-up MRI were evaluated. Transient enlargement was noted in 15 patients. 5 tumors showed sustained regression, 1 showed continuous progression. In 5 patients, volumetric analysis showed an atypical pattern with alternating regression and enlargement, with stabilization over time. Only one patient with continuous progression needed further intervention and was treated with microsurgery.

Conclusion

Recurrent or residual VS show different patterns of volume changes after RS that compare to those treated with primary RS. In our series, local control was favorable and the need for further intervention was low.

P175

Computertomographisch-navigierte, perkutane Ballonkompression bei Trigeminusneuralgie
Cone-beam CT-navigated percutaneous balloon compression for trigeminal neuralgia

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Objective

Percutaneous balloon compression (PBC) of the retrogasserian rootlets is an established procedure for the treatment of refractory trigeminal neuralgia (TN), capable of offering immediate and durable pain relief. Intraoperative CT-based navigation to assist with Fogarty catheter passage to the Gasserian ganglion via the foramen ovale has improved the accuracy and safety of this procedure in comparison with a landmark-based approach, with lower radiation exposure than traditional fluoroscopy. This study sought to determine the impact of anatomical and morphometric differences in the foramen ovale on operative parameters, cannulation success rate and the effectiveness of PBC.

Methods

Consecutive adult patients with typical or atypical TN treated with cone-beam CT-navigated (CBCT) PBC between April 2012 and August 2020 were identified from the departmental database. Demographic, clinical and operative parameters were extracted for each case, including duration of surgery, number of foramen ovale cannulation attempts, size of catheter used and total intraoperative radiation exposure. Preoperative CT imaging was reviewed to obtain two- and three-dimensional anatomical measurements pertaining to the foramen ovale for each patient (Fig. 1).

Results

30 patients (ages 31 to 90) received CBCT PBC during the study period. None of the foramen ovale morphometric parameters ascertained had a statistically significant effect on the number of attempts required to cannulate the foramen, the likelihood of ultimately successful cannulation or the intraoperative radiation exposure. However, surgical duration was reduced in cases with greater two-dimensional length and width of the foramen entry zone (p <0.05). There was no significant correlation between foramen morphometry on the affected side and patient age or sex. The foramen height on the affected side was a mean of 2 mm greater in women than in men (p <0.05).

Conclusion

This study determined anatomical parameters of the foramen ovale that are associated with a favourable intraoperative course in CBCT PBC. Specifically, a larger entry zone at the outer skull base is associated with a shorter operative duration.

Fig. 1

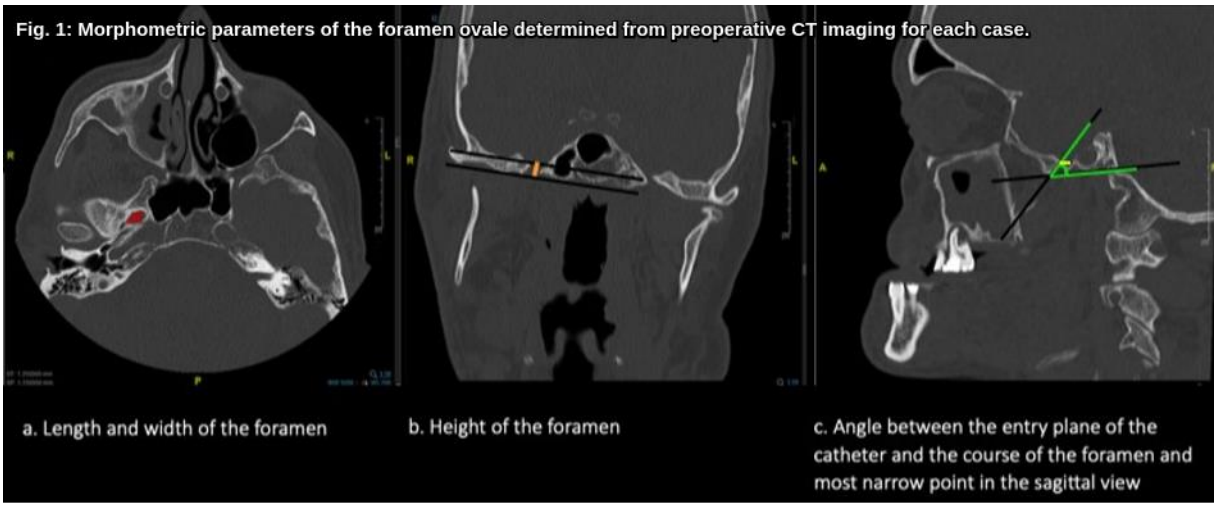
Fig. 1: Morphometric parameters of the foramen ovale determined from preoperative CT imaging for each case.
a. Length and width of the foramen
b. Height of the foramen
c. Angle between the entry plane of the catheter and the course of the foramen and most narrow point in the sagittal view

P176

Einfluss von 5-ALA auf den Meningiome-Resektionsgrad
Impact of 5-ALA in meningioma resection grading

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Objective

Recurrence after meningioma surgery may occur even after complete tumor resection (Simpson grade I). One possible cause may be the presence of remnant tumor cells that were left behind and not identified using microscope`s white light. Almost all meningiomas are aminolevulinic acid (5-ALA) positive. Fluorescence-guided resection of these tumors may discover small tumor remnants in some cases. The objectives of this study are to evaluate the possible advantages of using 5-ALA during meningioma surgery, reconsider the total resection concept and propose an adaptation of the Simpson Grading System.

Methods

Thirty two patients (36 tumors) with intracranial meningiomas in different locations were operated on using 5-ALA administered per os. At the end of the surgery, when total resection was supposed under microscope"s white light, final inspection was carried out using the fluorescence filter. Special attention was paid to remnant 5-ALA positive tissue and these were resected when found. Tumors as well as remnant 5-ALA positive tissue were submitted to histological and immunohistochemical studies. Surgical videos and magnetic resonance imaging were analysed.

Results

All 36 tumors were found to be 5-ALA positive, but there was a difference in the glowing intensity. Inspection of the surgical field, dura and the bone flap was performed. Remnant 5-ALA positive tissue was identified invading the arachnoid plane or over the brain in 22% of the cases after total resection was assumed using the microscope"s regular white light. Positive 5-ALA tissue could be completely removed in all cases. Histological analysis of the remnant 5-ALA positive tissue that was further resected demonstrated the presence of tumor cells.

Conclusion

The use of 5-ALA for meningioma surgeries may improve the chances of total tumor resection. Inspection of the surgical field, dura and the bone flap using 5-ALA should be encouraged. An adaptation of the Simpson Grading System is proposed, so that results in meningioma resection using 5-ALA can be evaluated and compared between different centres.

P177

Operative Behandlung rein intraorbitaler Läsionen – operative Techniken und neuro-ophthalmologisches Outcome
Operative treatment of pure intraorbital lesions – surgical techniques and neuro-ophthalmological outcome

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Objective

Resection of pure intraorbital tumors is challenging due to immediate vicinity to the optic apparatus. We report our experience with different intraorbital tumors and discuss classic approaches and obstacles.

Methods

A retrospective chart review at a tertiary neurosurgical center of patients who underwent surgery for intraorbital tumors between 06/2007 – 01/20 was performed.

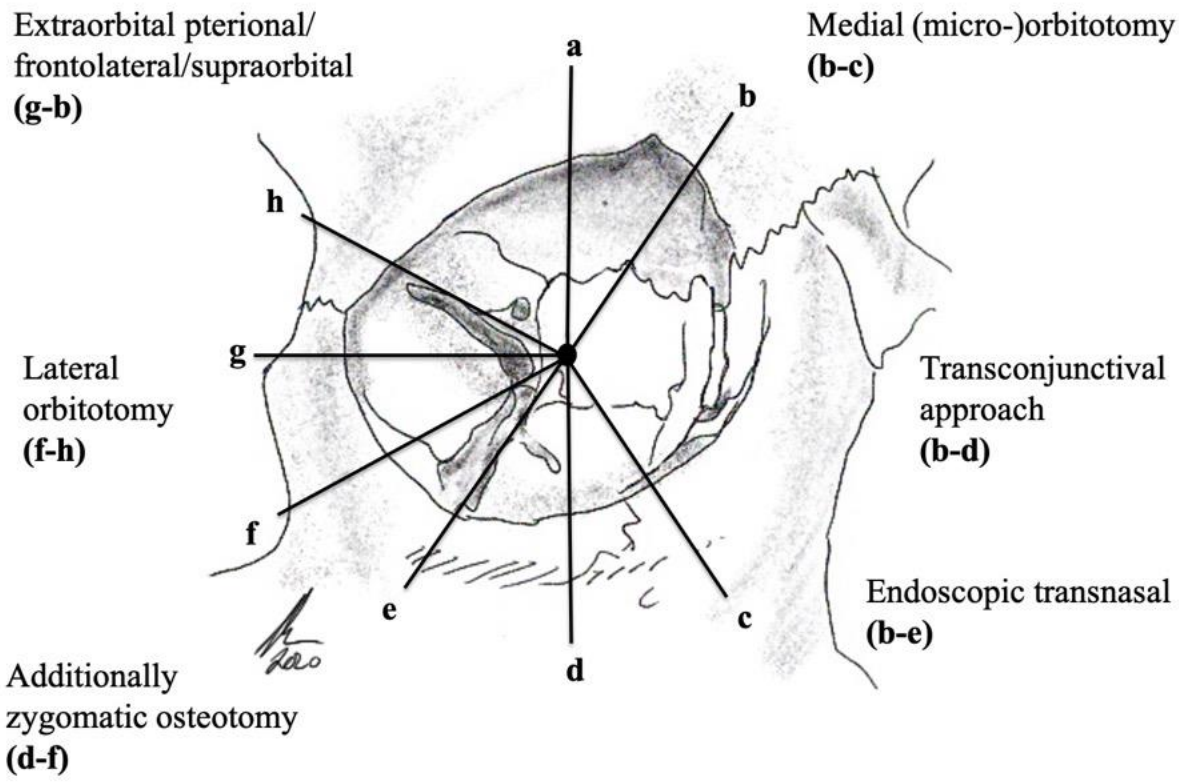
Results

We included 34 patients (median age 58 with range of 18-87 years, 55.9% [19/34] female, 44.1% [15/34] male). Preoperative proptosis was observed in 67.6% (23/34), visual impairment in 52.9% (18/34), diplopia in 41.2% (14/34) and ptosis in 38.3% (13/34). Intraconal tumors were found in 58.8% (20/34). Most common lesions were cavernous hemangiomas in 26.5% (9/34) and metastases in 14.7% (5/34). Gross total resection (GTR) rate was 73.5% (25/34). Planned biopsy was performed in 14.7% (5/34). Median follow-up time was 15.5 months (range 0-113). 23.5% (8/34) underwent a supraorbital approach, 52.9% (18/34) a pterional approach, 20.6% (7/34) a lateral orbitotomy and 8.8% (3/34) a transnasal approach. One patient underwent a combined technique (transnasal/lateral orbitotomy). Excluding planned biopsies, GTR was achieved in 80.0% (12/15) with a pterional approach, 100% (7/7) with a supraorbital approach, 83.3% (5/6) with a lateral orbitotomy, and 66.6% (2/3) via a transnasal approach. Complication rate requiring surgical intervention was 11.8 % (4/34).

Conclusion

Considering the low operative morbidity and satisfying functional outcome, GTR of intraorbital lesions is feasible. We support the use of classic transcranial and transorbital approaches. More invasive and complicated approaches were not needed in our series.

Fig. 1


Extraorbital pterional/
frontolateral/supraorbital
(g-b)
Medial (micro-)orbitotomy
(b-c)
a
b
h
g
Lateral
orbitotomy
(f-h)
Transconjunctival
approach
(b-d)
f
e
c
d
Endoscopic transnasal
(b-e)
Additionally
zygomatic osteotomy
(d-f)

P178

Metastasen in der Sellaregion und an der Hypophyse – eine Fallserie seltener Metastasierungswege
Sellar and pituitary metastasis – a case series of rare brain metastasis

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Objective

The sellar region is an unusual site for metastatic spread, but as patients with metastatic malignancy are living longer, it may become more prevalent in an interdisciplinary center. Compression of important anatomy adjacent to the sella may produce disabling symptoms and endocrine derangement, leading to significant morbidity.

Methods

To analyse the incidence of sellar metastasis, the authors reviewed their cases with sellar pathologies treated via an endonasal approach between January 2011 and October 2020. After identifying cases, further investigation was performed to evaluate patient demographic, symptoms at presentation, radiological and histological findings, management, and outcome.

Results

Seven of 332 patients (2.1 %) treated during this time period revealed in the final histopathology a metastasis. Thereby, malignant tumor history was known in one patient (14%). The preoperative MR and CT imaging suspected a malignant pathology or metastasis in two cases (28%). A biopsy was intended in two of these cases and a subtotal resection was intended in one case. In 4 of 7 cases (57%) the diagnosis was confirmed unanticipated in the histopathological final examination. Thereby, a subtotal resection was achieved in 3 cases and a near total resection in one case. The average age of the cases was 63.4 years, with histopathological diagnosis of two metastasis of lung cancer, one mestastasis of gastric cancer, one metastasis of kidney, one case of prostatic cancer, one lymphoma and one plasmocytoma. Adenohypophyseal dysfunction (3/7; 42%), abducens palsy (2/7; 28%) and visual field defects (2/7; 28%) were the most common findings at presentation. The mean follow up was 2.4 years. 5 of 7 patients (71%) died during this time period.

Conclusion

The sellar region should not be overlooked as a site of metastasis and sellar symptoms may be the first presentation of neoplastic disease. Any biochemical or clinical sign of pituitary pathology in a patient with known cancer should raise suspicion for sellar metastasis. Moreover, the development of hormonal dysfunction or ophthalmoplegia is suggestive of metastatic disease even in patients with no known primary. Further evaluation and metaanalyis of the cases reported in the literature are required to identify the incidence and treatment of these rare sellar metastasis.

P179

Fluoreszenzgesteuerte Hirntumorresektion mit einem 3D4K digitalen Exoskopsystem – erste Erfahrungen
Fluorescence guided brain tumour resection with a 3D4K digital exoscope system – first experiences

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Objective

Exoscopic 3D4K video systems (EX) have recently been introduced as an alternative to conventional operating microscopes (OM). However, experience in handling and setup remains scarce and superiority to OM has not yet been proven, inciting skepticism of the new technology. EX digital fluorescence modes may facilitate glioma resection, however it is unknown how this affects outcome. This study evaluated the practicability of exoscopic surgery in a wide range of cranial procedures, focusing on digital fluorescence guided resection of primary GBM.

Methods

All operations performed at a single neurosurgical center between 08/2018 and 05/2020 were evaluated. Exoscopic tumor resections were compared with operations using OM during the same period. Patient positionings, surgeons" comfort and fluorescence modes including ICG and 5-ALA were evaluated in a wide range of neurosurgical approaches. Duration of surgery, tumor localization and size, type of surgical approaches, extent of resection and postoperative deficits were assessed statistically as well as handling and optical issues by a standardized questionnaire. Follow-up data and extent of resection (EOR) by post-op MRI were analyzed for primary GBM.

Results

During this period, 513 EX operations were performed and compared to 101 OM surgeries. EX was generally rated as a valuable surgical tool, 3D optics in white light and fluorescence imaging were rated similar to conventional OM. EX operations were performed in 30 cases of metastases and 18 of recurrent glioma. EX resection of primary GBM occurred in *n*=8 cases using 5-ALA fluorescence. The median follow-up time was 161 days (range 114 – 208 days), 2/8 patients died after 31 and 303 days, respectively. Radiographic extent of resection, time of hospitalization, steroid use and median duration of operation (EX 156 min – OM 154 min) proved identical to conventional OM in primary GBM patients.

Conclusion

EX has been used and well established for a significant number of neurosurgical procedures. While presuming that the technical methodology as such when achieving identical EOR will not influence outcome of glioma surgery, proof of equipoise between different techniques expands the spectrum of surgical environments so that neurosurgeons have a choice to work according to their preferred ergonomics.

P180

Netzwerkbasierte Statistik zeigt motor-tumor bedingte Reduzierung der strukturellen Konnektivität
Network based statistics reveal motor-tumour related decrease of structural connectivity

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Objective

Cerebral tumors, which infiltrate the motor system lead to considerable disabilities. We have investigated how tumors in the motor system affect the patients" networks. Network-based statistics (NBS) allows to analyze global networks. NBS works on basis of the connectome, which defines a matrix representing all possible pairwise anatomical connections between neural elements of the brain.

Methods

We included 37 left- and right-handed adult patients in this study (15 females, 22 males, average age=48.24, SD=16.47, age range 20-78). Only patients with initial diagnosis of unilateral WHO grade II-IV gliomas were included. We used the NIHSS, a Nine-Hole Peg Test and a hand dynamometer to quantify tumor-related impairments. Probabilistic tractography was performed with Anatomically-Constrained Tractography. We computed 50'000'000 streamlines which were filtered to 10'000'000. We constructed symmetric connectome matrices with the Desikan–Killiany–Tourville node parcellation. Tractography and statistical analysis was performed by MRtrix3 for connectome group-wise edge level statistics using non-parametric permutation testing and control of family-level errors.

Results

NBS revealed significant edges with a structural connectivity decrease in pathological hemisphere matrices compared to healthy hemisphere matrices. Tumor localization-based subgroups showed distinct patterns of affected subnetworks. Especially frontal edges correlated with NIHSS, WHO degree or motor status.

Conclusion

Our findings suggest that we can use network-based statistics and connectome analyses to reveal global impacts of tumors on the network. Furthermore, our findings suggest that a functional decrease can be derived from the structural connectome. This method proved feasible and shows promising results to possibly further improve neurooncological and -surgical analyses.

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Algorithmen zur Perfusionsmessung – Geschwindigkeit gegen Genauigkeit?
Algorithms for perfusion measurements – Trading speed for accuracy?

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Objective

Singular value decomposition (SVD) is a fast and widely used algorithm for computing blood perfusion images from pCT, MRT, and ICG data. However, its speed is known to come at a price: The results, while mathematically correct, are not guaranteed to be physically plausible. We investigate four alternative algorithms for speed and accuracy and compare them with the SVD algorithm.

Methods

In perfusion imaging modalities, perfusion values (Tmax, rCBF, rCBV, and MTT) are computed per pixel from the residue function. The residue function is non-negative and, for the most part, monotonously decreasing, and has to be found numerically. SVD is not guaranteed to find solutions satisfying physical plausibility. Alternatively, solution can be found by pre-imposing a certain form on the residue function and/or using constrained optimisation. These methods are computationally more intensive. We investigated two imposed functional forms, bi-exponential (BE) and opposing logistics (OL), and applied two optimisation algorithms on each of them: unconstrained and with physically plausible constraints. We compared the performance to the SVD algorithm. All five algorithms were tested on a random set of pixels taken from intra-operative ICG videos of 11 patients with different diagnoses (SAH, trauma etc.). We measured 1) the execution time, 2) the average number of physically implausible results, 3) the mean error in reconstructing the contrast agent function, and, 4-7, the mean error in Tmax, rCBF, rCBV, and MTT. As the true value of these parameters cannot be known, we used the values computed by the cBE algorithm as the gold standard.

Results

SVD was, with 0.0017 s per sample image, by far the fastest method, while the constrained BE was the slowest (3.74 s). Regarding result plausibility, SVD had a 72% chance of producing physically impossible results, while both constrained algorithms were guaranteed to produce realistic results. However, in terms of clinically relevant parameters (Tmax, MTT etc.), OL turned to be the most accurate.

Conclusion

Imposing a functional form on the residue function can lead to more accurate results, but at high computationals costs (a factor of 100 or more). In clinical practice, these are unlikely to be justified. For real-time applications, SVD still seems to be the best compromise solution.

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Alien Hand Syndrom bei rupturierten Aneurysmen – eine systematische Übersichtsarbeit und Case Report
Alien hand syndrome in ruptured aneurysms – a systematic review and case report

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Objective

Alien hand syndrome (AHS) is a rare condition which is typically associated with lesions of the corpus callosum (CC) and of the supplementary motor area (SMA). Subarachnoid haemorrhage (SAH) due to cerebral aneurysm have been reported to be a potential cause for this condition. The pathogenesis and prognosis have been subject to controversies. In order to shed light on this rare condition we performed a systematic review and add a novel case to the literature.

Methods

We performed a literature search on PubMed and Medline using the search terms ("alien hand" OR "anarchic hand" OR "disconnection syndrome") AND "aneurysm". After screening all abstracts for inclusion, we identified additional papers for inclusion by hand-searching all references. We extracted all data on clinical presentation, treatment, radiological findings and follow-up. Furthermore, we added our own findings in a previously unpublished case.

Results

17 cases were eligible for inclusion, including the novel case from our centre. Aneurysms of the anterior communicating artery (ACoA) (10/17) were the most common origin of SAH that led to AHS, followed by pericallosal artery (PA) aneurysms (7/10). A majority of aneurysms underwent clipping (13/17), whereas 2/17 underwent coiling, and 2/17 were not treated interventionally. CC lesions were seen in all cases with computed tomography imaging (n=16), supplementary SMA lesions were described in 10/16 cases. 14/17 patients exhibited intermanual conflict and in 13/17 cases additional disconnection symptoms were described. The median follow-up was 4 months (range 0 – 72 months) and in 8/9 cases where follow-up findings were reported, the AHS symptoms improved.

Conclusion

Lesions of the CC and SMA caused by ruptures of ACoA or PA aneurysms may result in AHS. During treatment of these types of aneurysms damage to the mesial frontal cortex should be avoided in order to keep symptoms minimal. Mid-term follow-up indicates that commonly there is a favourable prognosis and regression of symptoms.

P183

Klinische und computergestützte volumetrische Analyse der Dekompression der hinteren Schädelgrube bei raumfordernden Kleinhirninfarkten

Clinical and computerised volumetric analysis of posterior fossa decompression for space-occupying cerebellar infarction

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Objective

To study outcomes after posterior fossa decompression for cerebellar infarction. The literature contains surprisingly little pertinent data with a 2018 meta-analysis describing only 283 patients pooled from 11 studies.

Methods

We retrospectively identified all patients undergoing posterior fossa decompression and necrosectomy for cerebellar infarction in our department from January 2012 – November 2020. We studied pertinent clinical data and performed computerized volumetric analyses (preoperative/postoperative infarction volume, necrosectomy volume, posterior fossa volume). A favorable functional outcome was defined as mRS 0-3. Standard statistical methods (Fisher exact and chi square test, ANOVA, regression analysis and Student's t-test) were employed.

Results

We studied 47 patients (68% male, median age: 68 years). 28 cases (60%) presented with hydrocephalus, 19 required temporary CSF drainage and a VP shunt was placed in one case. Bilateral and brainstem involvement was seen in 15 (32%) and 13 (28%) patients, respectively. 40 cases were operated for a GCS of ≤13 or GCS deterioration. 7 (15%) patients had preventive surgery (initial GCS 14-15, no preoperative GCS change). 35 (74%) patients had s GCS of 14-15 at admission. Prior to surgery only 14 (29%) cases had a GCS of 14-15. After surgery the number of patients with a GCS of 14-15 increased to 40 (85%), but only 23 (49%) patients had a mRS 0-3 at discharge. Predictors for a good outcome included a preoperative NIHSS<5 (p=0.018), no brainstem involvement (p=0.022), a >50% necrosectomy (p=0.031) and lesser postoperative infarction volume (p=0.044). The GCS at presentation, before surgery, preventive surgery and preoperative infarct volume did not correlate with functional outcome. A medical history of anticoagulation was a significant predictor of in-hospital mortality (p=0.005).

Conclusion

Posterior fossa decompression for cerebellar infarction is an effective life-saving procedure, but rapid recovery of the GCS after surgery did not necessarily translate into a good functional outcome. Functional outcomes seem primarily determined by the neurological deficit caused by the infarction. Computerized volumetric analysis provided some support for a positive role of aggressive infarct debridement.

P184

Sekundäre Leukoenzephalopathie und Fremdkörperreaktion nach endovaskulärer Behandlung von Patienten mit intrakraniellen Aneurysmen und aneurysmatischer Subarachnoidalblutung – Literaturübersicht und Fallvorstellung

Delayed leukoencephalopathy and foreign body reaction after endovascular treatment in patients with intracranial aneurysms and aneurysmal subarachnoid haemorrhage – systematic review of the literature and a recent case

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Objective

Delayed leukoencephalopathy and foreign body reaction are rare complications after endovascular treatment of intracranial aneurysms. However, cases are increasingly being described. Here we present a systematic review of the pertinent literature and an illustrative case.

Methods

Clinical presentation, differentials, diagnostics and treatment as well as formerly published data were reviewed in light of a recent case. A systematic search of the literature was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.

Results

We provide an extensive literature review and discuss causes and management of this rare delayed complication. Furthermore, we present the case of a 53-year-old female patient with a subarachnoid hemorrhage from a large anterior communicating artery aneurysm with tortuous cervical vessels who was treated with endovascular coiling. Post-Coiling MRI revealed partial anterior cerebral artery ischemia and scattered ischemic micro-emboli in the left central cortex. At discharge most symptoms were already resolved. Rehospitalization was necessary due to recurrent deterioration of the known symptoms six weeks after transfer to rehabilitation. A CT scan revealed substantial left hemispheric edema. MRI and MR-Angiography confirmed extensive vasogenic edema with contrast enhancing predominantly cortical lesions (Fig. 1 A - C) in the left ICA territory and no novel vascular obliteration. The patient recovered timely under high dose corticosteroid treatment and follow up MRI showed almost complete remission of the described lesions within 10 days (Fig. 1 D). Follow up MRI after 3 months demostrated almost complete remission (Fig. 2).

Conclusion

Foreign body reaction might result in delayed leukoencephalopathy, especially following complex endovascular aneurysm treatment. Early high dose followed by low dose ongoing corticosteroid treatment might result in timely remission.

Fig. 1

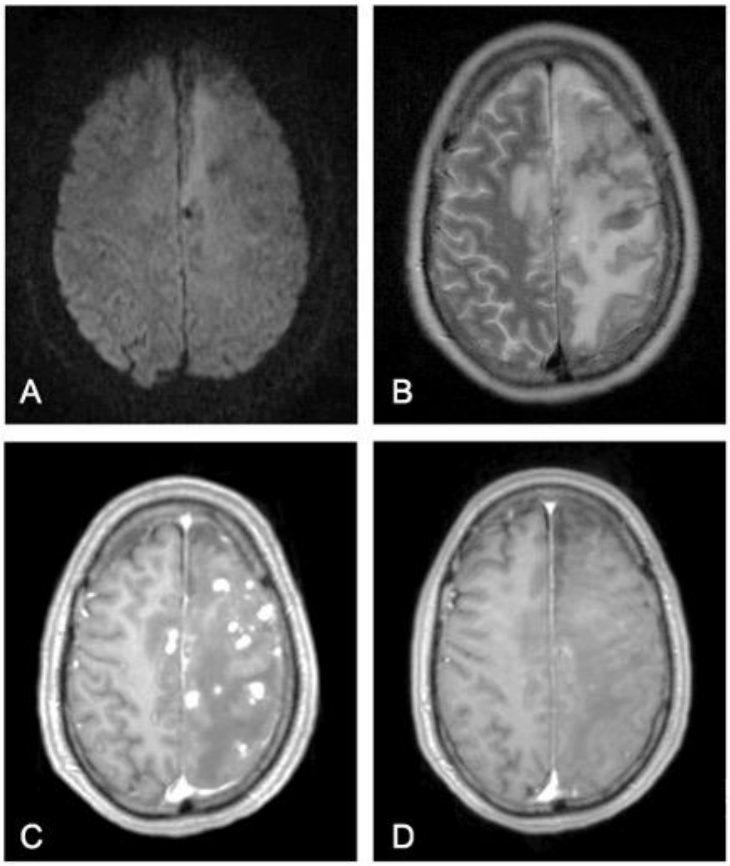
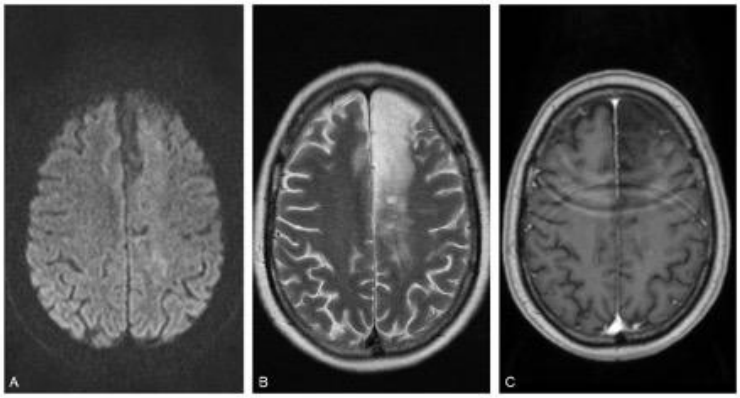


Fig. 2



Neurovaskuläre Chirurgie II/*Neurovascular surgery II*

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Entwicklung und Charakterisierung eines doppelten sacculären Elastase-degenerierten Aneurysma Kaninchenmodells
Development and characterisation of a dual saccular elastase-digested aneurysm rabbit model

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Objective

Intracranial aneurysm rupture is a devastating condition leading to high mortality and morbidity. The development of preclinical animal models with hemodynamic, morphologic and histologic characteristics close to humans one plays a key role in our understanding of the pathophysiological processes and in the development of new therapeutic strategies for treatment of intracranial aneurysm. This study aims to describe a new rabbit aneurysm model with different hemodynamic conditions, i.e. stump and bifurcation aneurysms, both with degenerated walls condition, in the same animal.

Methods

Five female New Zealand white rabbits with a mean weight of 4.0 (± 0.3) kg and mean age of 25 (±5) weeks underwent microsurgical stump and bifurcation aneurysm creation. Stump aneurysm was created by right common carotid artery (CCA) exposure at its origin at the brachiocephalic trunk. After temporary clip application at the CCA origin and 2cm above, the segment was treated with a local injection of 100 U Elastase for 20 minutes. Bifurcation aneurysm was created by suturing an elastase-treated arterial pouch into the end-to-side anastomosis of the right CCA to left CCA. Patency was controlled intraoperatively by fluorescence angiography and at follow up after 24±2 days by magnetic reasonnance angiography and macroscopic tissue inspection.

Results

The average duration of surgery was 221 minutes. The creation of two aneurysms in the same animal was successful in all rabbits. We observed no mortality during surgery and follow-up. One rabbit experienced postoperative complication with a vestibular syndrome, which recovered spontaneously within one day. All aneurysms were patent immediately after creation except for one bifurcation aneurysm which showed an extreme tissue reaction due to elastase incubation and an immediate thrombosis. Except this one, all aneurysms were patent at follow up.

Conclusion

We demonstrate for the first time the feasibility of creating a two-aneurysms rabbit model with stump and bifurcation hemodynamic characteristics and highly degenerated wall conditions. This model allows to study the natural course and potential treatment strategies on the basis of aneurysm biology and under consideration of different flow conditions.

P186

Entwicklung von singulären und multiplen intrakraniellen Aneurysmen – Was zählt?
Development of single and multiple intracranial aneurysms – What counts?

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Introduction

The prevalence of multiple intracranial aneurysms (MIA) has increased over the last decades. As MIA have shown a correlation with IA formation, growth and rupture risk, a more profound understanding of the underlying pathophysiology of MIA is needed. Our large institutional aneurysmal data base was analyzed to elucidate differences between single IA (SIA) and MIA carriers.

Methods

A total of 2453 patients were treated for IA at the University Hospital of Essen from 01/2003 to 06/2016. The patients' data were retrospectively screened for socio-demographic parameters, imaging modalities, pre-existing medical conditions, blood and cerebrospinal-fluid examination and medical prescriptions. These parameters were analyzed for correlation with MIA.

Results

MIA were identified in 853 (34.8%) patients. An increasing trend in MIA prevalence ($r=0,017$; $p=0,09$) was detected over the study period, alongside with a statistically significant increase in patients suffering from arterial hypertension (AHT) and tobacco addiction ($r=0,021$; $p=0,039$ and $r=0,035$; $p=0,002$, respectively). In multivariate analyses (MVA), MIA were independently associated with female sex ($p<0.001$), arterial hypertension ($p<0.05$), tobacco abuse ($p<0.05$), C-reactive protein elevation ($p<0.05$), elevated mean corpuscular volume (MCV, $p<0.01$) and elevated total serum protein ($p<0.01$), but not with the diagnostic modality (2D vs. 3D digital subtraction angiography, $p=0.0496$). Absolute number of IA showed a statistically significant correlation in MVA with female sex ($p<0.001$), AHT ($p<0.05$), familial intracranial aneurysms ($p<0.05$), tobacco abuse ($p<0.05$), elevated MCV ($p<0.01$) and high platelet number ($p<0.01$). IA location also showed a statistically significant difference, with 18% of IA being located in the posterior circulation in MIA cases and 26% of IA in SIA cases compared to the anterior circulation ($p<0.001$).

Conclusion

MIA prevalence is increasing. Alongside with previously reported MIA predictors like age, female sex, arterial hypertension, tobacco abuse and ADPKD, we found also specific location pattern for MIA and independent associations between certain rheological factors and MIA risk. Our findings indicate to the need for further research of underlying mechanisms of IA formation.

Neurovaskuläre Chirurgie II/*Neurovascular surgery II*

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Bewertung der fortgesetzten Anwendung von Acetylsalicylsäure (ASS, Aspirin) im Zusammenhang mit postoperativen Blutungen bei Patienten, die sich einem Aneurysma-Clipping unterziehen

Evaluation of continued application of acetylsalicylic acid (ASA, Aspirin) in relation to postoperative haemorrhage in patients undergoing aneurysm clipping

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Objective

There is increasing use of acetylsalicylic acid (ASA) among patients with heart disease or stroke, and additionally in primary prevention among aging populations. Does continued application of ASA lead to an increased risk for postoperative hemorrhage in patient undergoing aneurysm clipping. However, studies in the neurosurgical field dealing specifically with postoperative hemorrhagic complications due to continuous ASA application are very rare. In the present study, we have evaluated the incidence and risk of continued ASA use as it relates to postoperative hemorrhage in patients undergoing aneurysm clipping.

Methods

We have retrospectively analyzed 200 consecutive clipping procedures performed between 2008 and 2018. Two different statistical models utilizing Fisher"s exact test have been applied. The first model consists of two groups: (1) *No ASA effect*—which is made up only of patients who either hadn"t used ASA at all or patients who had stopped the use of ASA medication at or before the recommended time (>=7 days prior to operation); (2) *ASA effect*—all patients who had not discontinued ASA use within the recommended time frame. The second model consists of three groups: (1) *No ASA application*; (2) *Stopped ASA application* (>=7 days prior to operation); (3) *Continued ASA application* (did not stop use <7 days prior to operation or did not stop use at all). Data collected included demographic information, surgical parameters, aneurysm characteristics, and all hemorrhagic/thromboembolic complications. A postoperative hemorrhage was defined as relevant if a subsequent operation for hematoma removal was necessary.

Results

An ASA effect appears to have occurred in 32 out of 200 performed operations. In only one out of these 32 patients did a postoperative hemorrhage occur (3.13%). Postoperative hemorrhages in patients without any ASA impact were detected and treated in 5 out of 168 patients (2.98%). The difference between the two was minimal and thus not significant (*ASA effect* vs. *No ASA effect*: OR = 1.0516 [0.1187; 9.3132], p=1.000; RR = 1.0015 [0.9360; 1.0716]).

Conclusion

The results of this study indicate that continued ASA use is not associated with an increased risk of postoperative hemorrhage. In patients with high cardiovascular risk, and in the case of emergency surgery, ASA can safely be continued.

P188

Gesundheitsbezogene Lebensqualität bei Patienten mit medizinisch behandelter zerebraler kavernöser Fehlbildung bei Epilepsie

Health related quality of life in patients with medically treated cerebral cavernous malformation related epilepsy

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Objective

To estimate the health-related quality of life (HRQOL) in patients with untreated cerebral cavernous malformation related epilepsy (CRE)

Methods

We performed a prospective cross-sectional study on patients with CRE admitted to our hospital between 2018 and 2020 using standardized interviews such as the hospital anxiety/ depression scale (HADS-D-A/D), quality of life questionnaire (SF-36) and visual analogue scale (VAS) assessing subjective CRE disease burden. CRE patients surgically treated prior to our assessment, with incomplete clinical data and with insufficient knowledge of German language were excluded from the study. Health-related quality of life (HRQOL) data were analyzed and compared to an age- and sex-matched German normal population. Uni- and multivariate analyses were carried out to identify variables that show an impact on HRQOL outcome

Results

We included 37 CRE patients with a mean age of 46.7 ± 13.6 years (SD). 18 (48.6%) patients presented with symptomatic hemorrhage (SH) and 20 (54.1%) had multiple CCM. 15 patients (40,5%) suffered from comorbidities. 25 patients (67.6%) had only 1 seizure. 29 patients (78.4%) received anticonvulsive therapy at time of HRQOL assessment. The mean time between last CCM-related seizure and HRQOL survey was 41.7 ± 84.6 months (SD). CRE patients showed significantly lower scores in some of the SF-36 subdomains such as physical (RP) ($p = 0{,}007$), social (SF) ($p = 0{,}001$) and emotional functioning (RE) ($p < 0{,}001$), as well as in the mental health component score (MCS) ($p = 0.001$). Univariate and multivariate analysis identified multiple seizures, timeframe of more than 3 months between first and last seizure and comorbidities as predictors of HRQOL impairment. A significant correlation between VAS and MCS confirmed that the decreased HRQOL values are largely based on CRE manifestation.

Conclusion

We present an observational study on HRQOL in patients with untreated CRE. Patients with CRE revealed in some domains a decreased HRQOL compared to the normal population, even when not suffering from functional impairment. Our data reflects the disease burden of patients with CRE.

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Analyse der prognostischen Faktoren im Bezug auf das Hämatomvolumen für die Mortalität nach spontanen supratentoriellen intrazerebralen Blutungen

Survival analysis and identification of prognostic factors after spontaneous supratentorial intracerebral haemorrhage – a retrospective cohort study

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Objective

Supratentorial spontaneous intracerebral hemorrhage (sICH) remains associated with persistently high mortality and morbidity rates. A variety of risk factors influence the neurological outcome and survival of these patients. The impact of these factors may vary depending on the size of the hematoma. In this retrospective study, we investigated the impact on overall survival of these risk factors subject to hematoma size.

Methods

A retrospective cohort analysis of patients with sICH treated in our department from 2010 to 2012 was carried out. Depending on their initial hematoma volume, all participants were divided into subgroups of hematoma volume ≤50cc or > 50cc. Cumulative and volume-group-stratified short and long-term survival analysis was performed to evaluate the survival probability and hazard ratios for death. Uni- and multivariate cox proportional regression models were used to estimate the different covariates" odds ratios.

Results

Nearly a quarter of all patients (24.07%) died during their initial stay in the hospital. Hematomas larger than 50 cc showed a significantly higher mortality rate (log-rank test $p<0.0001$). A multivariate regression analysis revealed the patients' age as the decisive factor for the prediction in the case of hematomas smaller than 50 cc (hazard ratio=13.1, 95%CI:1.84 - 92.99, p=0.01). Radiographic signs of a cerebral herniation (p=0.004, hazard ratio= 14.71, 95%CI:2.35 - 91.90) and mydriasis (p=0.04, hazard ratio=6.96, 95%CI:1.02 - 47.4) have influenced the prognosis of larger hematomas. The long-term survival time of hematomas smaller than 50 cc was 70 months and was predominantly influenced by age and patient comorbidities. In hematomas larger than 50cc, median survival was reduced to 17 months, and their prognosis was correlated with the Glasgow Coma Scale score at the time of hospital discharge.

Conclusion

In larger than 50cc hematomas, the prognosis for in-hospital mortality is mainly influenced by the mass effect of the bleeding, especially in the presence of cerebral herniation. Their long-term prognosis is correlated with GCS at the time of hospital discharge. Patient comorbidities and age have a strong influence on the prognosis of smaller than 50 cc hematomas.

P190

Multiple intrakranielle Aneurysmen – die Anwendung und Genauigkeit des PHASES Scores bei 275 Patienten mit insgesamt 661 intrakraniellen Aneurysmen

Multiple intracranial aneurysms – the PHASES Scores applicability and accuracy in 275 patients harbouring 661 intracranial aneurysms

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Objective

The subgroup of patients with multiple intracranial aneurysms (MIA) accounts for about 20% of all patients suffering from intracranial aneurysms (IA). There are controversial findings regarding a higher rupture risk in patients with MIA, leading to uncertainties in assessment of individual risk for aneurysm rupture. We performed a subgroup - evaluation of the PHASES Score with respect to its applicability on patients with MIA.

Methods

We analyzed 275 patients harboring a total number of 661 MIA regarding the accuracy of the PHASES Score for prediction of SAH using Receiver Operating Characteristics (ROC). Additionally, we analyzed the patients with aneurysmal subarachnoid hemorrhage (SAH) more closely.

Results

The PHASES Score achieved an area under the curve (AUC) of 0.57 in prediction of SAH in patients with MIA with corresponding sensitivity of 60% and specificity of 46%. We observed the following distribution of corresponding 5-year rupture risk in patients with aneurysmal SAH: <1% risk (40%), 1-1.9% risk (30%), 2-4.9% risk (19%) and >5% risk (11%).

Conclusion

The PHASES Score shows low sensitivity and specificity in prediction of aneurysm rupture in patients with MIA. Patients harboring MIA and suffering from a SAH seem to be categorized as patients with singular IA. The use of new specific analytical tool to predict the rupture risk in patients with MIA is mandatory.

P191

Sekundäre dekompressive Kraniektomie bei vasospastischen Infarkten nach aneurysmatischer Subarachnoidalblutung – der Einfluss der Infarktgröße

Secondary decompressive craniectomy for vasospasm related infarction following aneurysmal subarachnoid haemorrhage – the influence of the size of infarction

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Objective

Aim of this study was to analyze the effect of secondary decompressive craniectomy (DC) on clinical outcome in patients with vasospasm related infarction following aneurysmal subarachnoid hemorrhage (aSAH) – regarding the influence of the size of infarction.

Methods

Between 01/2011 and 12/2019 28 consecutive patients with aSAH and vasospasm related infarctions underwent a decompressive craniectomy at our institution. Information including patient characteristics and outcome were prospectively collected in a computerized database. The size of infarction was measured by 19 segments, in which the territories of the major cerebral arteries were divided into. In addition, volumetric analysis of ischemic brain tissue preoperatively was performed. Outcome was analysed according to modified Rankin Scale (mRS) and dichotomized into favorable (mRS 0-3) and unfavorable (mRS 4-5) outcome after 1 year.

Results

Overall, favorable outcome was achieved in 6 of 28 patients (21%). In patients with infarction of 1 large vessel territory, favorable outcome was achieved in 6 of 10 patients (60%) and in none of 18 patients (0%) with infarction of > 1 large vessel territory ($p = 0.0006$). In patients with infarction of ≤ 2 segments favorable outcome was achieved in 6 of 8 patients (75%) and in none of 20 patients (0%) with infarction of > 2 segments ($p = < 0.0001$). Infarct volume was associated with an unfavorable outcome after exceeding a cut-off volume of 100 cm^3.

Conclusion

Our data indicates, that DC for vasospasm related infarction after aSAH seems to be a valid treatment option in a specified subgroup of these patients. Regarding long-term neurological outcome, patients with infarction in only one large vessel territory or ≤ two segments and patients with ischemic tissue volume £ 100 cm^3 seem to benefit from this treatment option. Careful decision making is needed in each individual case.

Neurovaskuläre Chirurgie II/*Neurovascular surgery II*

P238

ICT/IoT application to pre-hospital management of patients with stroke in acute stage

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Objective

After report of the usefulness of endovascular thrombectomy in acute stage of the stroke patients, the main issue to rescue the patients with stroke is to carry them to the suitable stroke center where the endovascular treatment staffs are available to do thrombectomy as short as possible. For emergency management in wide area of Hiroshima City, we started to use modified "JUST (Japan Urgent Stroke Triage) score" originally directed by Professor Yoshimura, Hyogo Medical University, from April 2019 to make suitable triage of the patients with high probability as stroke, especially as main trunk obstruction of the intracranial main arteries, LVO (large vessel occlusion). The objective was to estimate the efficacy of the JUST score handling.

Methods

We installed the application soft into the tablet and the patient"s condition boxes are checked by ambulance crew. After that, automatically the percentage of the probability of the stroke of the patient will be indicated, followed by the appearance of percentages of subtypes of the stroke. GPS function of the ambulance is combined with the location information of the stroke center will make suitable selection of the treatment location with distance between the ambulance and the stroke medical centers according to the shortness of distance and door to puncture time which are informed beforehand from the stroke center. We started clinical research to compare the outcome of such kind of patients before and after the introduction of this system. Prospective multicenter cohort study was carried out at total 13 stroke centers from April 1st ,2019 to March 30th ,2020. We investigated some issues between the periods before and after the use of JUST score.

Results

A total number of 5141 patients were enrolled in the cohort (2734 before; 2406 after). There were 1269 strokes (46.4%) including 140 LVO (5.1%), 394 ICH (intracerebral hemorrhage) (14.1%), 120 SAH (subarachnoid hemorrhage) (4.4%) and 615 CI (cerebral infarction) before use of JUST score. JUST score was used in 61.7% of the patients after implementation of JUST score, and there were 1267 strokes (52.7%) including 186 LVO (7.7%), 405 ICH (16.8%), 109 SAH (4.5%) and 567 CI (23.6%). The success rate at the first negotiation with a stroke center was significantly increased after JUST score introduction (76.3 % vs 79.7%, p=0.004). On-scene and transport time did not significantly change after JUST score. Among patients with acute LVO, door to puncture time was significantly shortened after JUST score (84 min vs 73 min, p=0.03), but outcome was similar between two cohorts at 90 days.

Conclusion

The modified JUST system is useful for prehospital triage of the patients with stroke in acute stage. The precise data will be shown in the meeting and I would like to introduce the new system, JUST 7, as simpler prehospital triage of the patients in the acute stage of the stroke.

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P193

Beurteilbarkeit der Ventrikelweite und der intraventrikulären Lage von Cerebralshunt-Kathetern mit Ultra-low-dose CT

Assessability of ventricular width and intraventricular CSF shunt catheter position with ultra-low-dose CT

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Objective

Whole body ultra-low-dose CT (ULD-CT) has replaced the radiographic shunt series as standard imaging method for ventriculoperitoneal or ventriculoatrial shunt at our institution. ULD-CT allows more precise assessment of distal shunt catheter with more confident depiction of potential complications such as disconnection, pseudocyst formation or extraperitoneal dislocation. However, full-dose cranial CT (cCT) remains the gold standard for the intracranial assessment of CSF-shunt. Patients with implanted CSF-shunt often require multiple cCT-scans in the course resulting in high radiation exposition. We retrospectively analyzed the feasibility of UDL-CT for evaluation of interventricular position of shunt-catheter as well as ventricular width.

Methods

Out of 358 ULD-CTs (100kV, 10mAs, care dose) of CSF-shunts performed at our institution between 2016 and 2019 267 ULD-CTs from 161 patients included the skull. Three blinded independent readers evaluated the assessability of the intraventricular catheter position using a Likert-type scale of 1-4 and measured the ventricular width on the level of anterior horns of lateral ventricles. The ventricular width quantificated in 67 ULD-CT was compared with full dose cCT done immediately before or after ULD-CT.

Results

An extraventricular position of the CSF-shunt as a complication was present in two individuals and correctly depicted by all readers. One intraventricular catheter was incorrect described as extraventricular. There were no missed dislocations. The assessabilty of the intraventricular position was rated "very good" or "good" in 246 (92%) and "limited" or "poor" in 21 (8%) examinations with a substantial inter-rater agreement (kappa: 0,61).

In comparison with full dose cCTs as gold standard mean deviation of the ventricular width was 2,13mm (5,42%; range 0-10,7mm).

The mean CTDI of ULD-CTs was 0,66 mGy and the mean DLP for the whole body 49,13 mGy*cm reaching 1,05% and 5,9% of the cCT radiation dose (mean CDTI: 62,62 mGy; mean DLP: 827,98 mGy*cm), respectively.

Conclusion

Intraventricular position of proximal CSF-shunt catheter can be evaluated by ULD-CT in the majority of cases. The assessability is limited e.g. in patients with slit ventricles, artifacts or hypodense defects. Moreover, UDT-CT allows accurate evaluation of the ventricular width. Further studies are needed to find the optimal (ultra) low-dose protocol for assessment of ventricular width (in patients with CSF shunt).

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Erfahrungen mit der Clavien-Dindo Klassifikation der chirurgischen Komplikationen in der Neurochirurgie
Experiences with the Clavien-Dindo classification of surgical complications in neurosurgery

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Objective

The standardized Clavien-Dindo classification of surgical complications is widely applied in various surgical disciplines, and it is declared as an effective instrument for quality management. This study aimed to evaluate the neurosurgical complications according to the Clavien-Dindo classification of surgical complications and represent the experiences with it in neurosurgery.

Methods

We retrospectively analyzed a period of care between June 2017 and December 2019 in our neurosurgical department. The evaluated complications were rated according to the Clavien-Dindo classification of surgical complications. The range of complications was compared with the length of stay and statistically analyzed using two-sided Spearman"s rank correlation coefficients.

Results

The study included overall 1681 operations at 1530 patients. Complications occurred in 17.7 % (n=271) of patients, of which 43,9% (n=119) had some postoperative neurological disturbances. 40.2% of complications were rated as grade 1, 15.1% as grade 2, 4.1% as grade 3a, 27.7% as grade 3b, 4.8% as grade 4a, 4.4% as grade 4b and 3,7% as grade 5. Patients with a higher rank of complications experienced significantly longer lengths of hospital stay. The severity level of postoperative occurred neurological disturbances didn't frequently match with the Clavien-Dindo ranking system.

Conclusion

The Clavien-Dindo classification can easily be used in neurosurgery to document the rates of general, surgical complications, but it is insufficient and can not be validated to describe the severity of postoperative occurred, neurological disturbances, which are so frequent in neurosurgery.

Fig. 1

Fig. 3

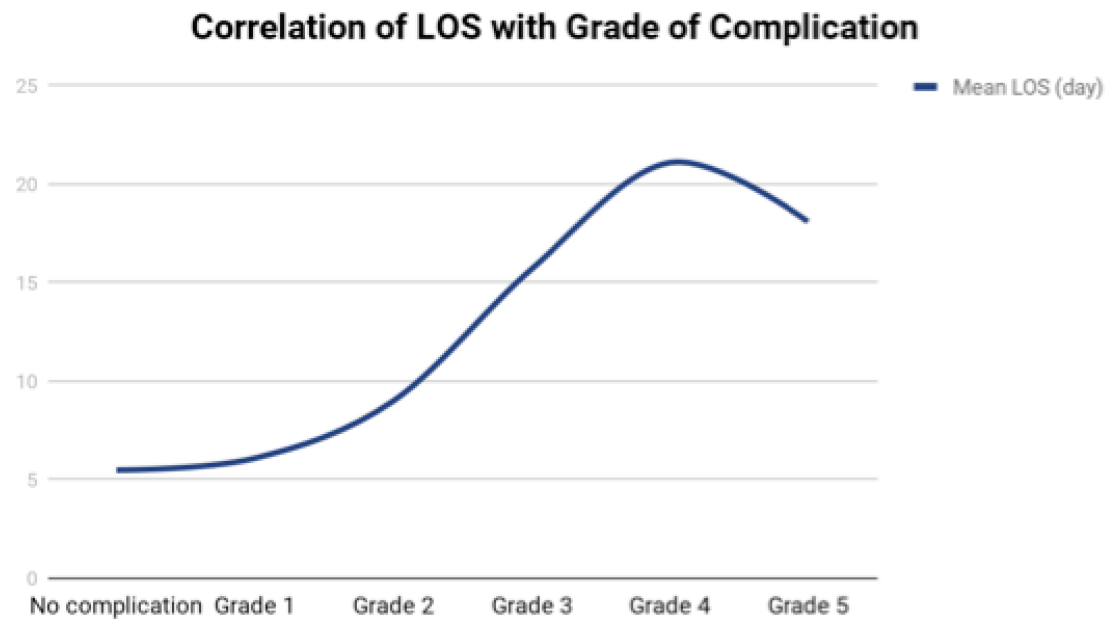
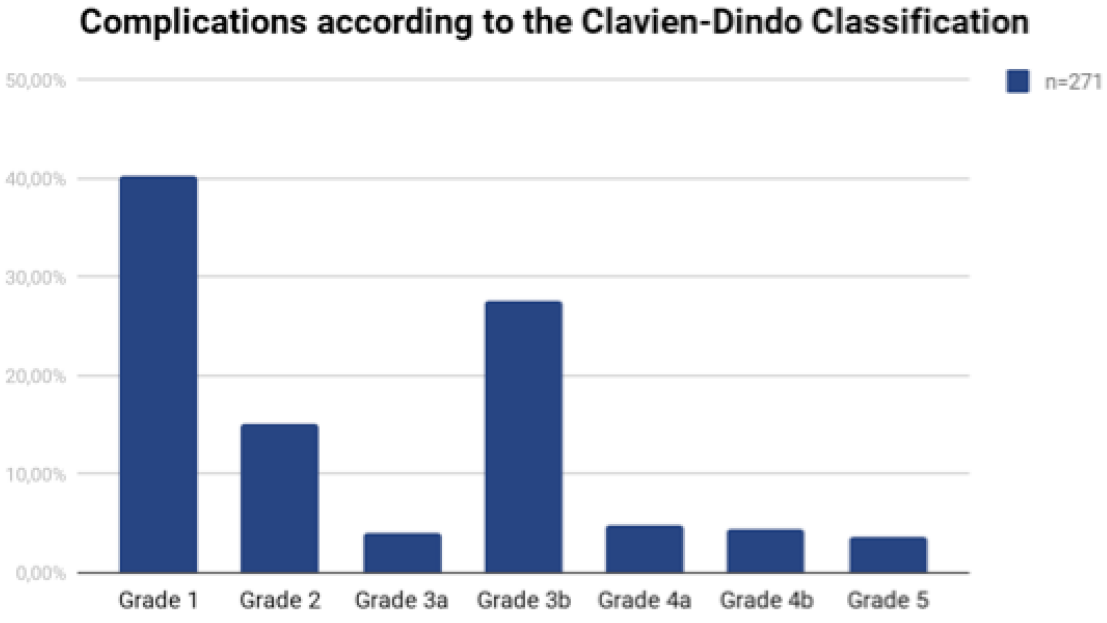


Fig. 2

Fig. 2.



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P195

Erweiterte Gerinnungsdiagnostik verringert die Nachblutungsrate nach kraniellen Eingriffen
Extended coagulation screening reduces postoperative haemorrhage rates in cranial neurosurgery

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Objective

Postoperative hemorrhage after cranial neurosurgery is a serious complication with substantial morbidity and mortality despite immediate intervention. We investigated the preoperative screening and substitution of previously undetected coagulopathies as a measure to decrease the risk of postoperative hemorrhage.

Methods

A study cohort of patients undergoing elective cranial surgery and receiving the extended coagulatory work-up were compared to a propensity matched historical cohort. Propensity matching was carried out in a 1:1 fashion according to age, gender and type of intervention. The extended work-up included a standardized questionnaire on the patient"s bleeding history as well as coagulatory tests of Factor XIII, von-Willebrand-Factor and PFA-100® in addition to the standard parameters consisting of the prothrombin time, partial thromboplastin time and thrombocyte count. Deficiencies in any parameter were substituted perioperatively. The primary outcome was determined as the surgical revision rate due to postoperative hemorrhage.

Results

The study cohort and the historical cohort included 197 cases each, without any significant difference in the preoperative intake of anticoagulant medication (p=.546). Most common interventions were resections of malignant tumors (41%), benign tumors (27%) and neurovascular surgeries (9%) in both cohorts. Replacement of coagulation factors was significantly more common in the study cohort (70 cases; 35.5%) than in the historical cohort (43 cases; 21.8%; p=.003). Imaging revealed postoperative hemorrhage in 7 cases (3.6%) in the study cohort and 18 cases (9.1%) in the historical cohort (p=.023). Of these, revision surgeries were significantly more common in the historical cohort with 14 cases (9.1%) compared to 5 cases (2.5%) in the study cohort (p=.034). Differences in mean intraoperative blood loss were not significant with 528 ml in the study cohort and 486 ml in the historical cohort (p=.376).

Conclusion

Preoperative extended coagulatory screening may allow for adequate substitution of coagulatory factors and thereby reduce the risk for postoperative hemorrhage in cranial neurosurgery.

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P196

Routinemäßige Entnahme von intraoperativen Abstrichen zur mikrobiologischen Testung mittels Kultur im Rahmen von Reoperationen aufgrund eines Rezidives degenerativer Wirbelsäulenerkrankungen – Sinnvoll oder entbehrlich?

Routine intraoperative smear testing for microbiological culturing in patients with reoperation due to recurrence after elective degenerative spine surgery – Useful or negligible adjunct?

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Objective

Subclinical surgical site infections (SSIs) are a rare, but feared reason for a recurrent symptomatology requiring reoperation after degenerative spine surgery. We analyzed a large series of patients to eliducate if routine intraoperative smear testing for microbiological culturing can be an useful adjunct in this situation.

Methods

We investigated the baseline characteristics, imaging/surgical parameters and outcome of patients with reoperation due to recurrence in index segment after elective degenerative spine surgery between 2000 and 2019 in our university neurosurgical clinic. Microbiological cultures via multiple intraoperative smear tests of the superficial and deep wound layers were routinely collected in those patients and correlated with imaging, laboratory and surgical findings for hints of subclinical SSIs.

Results

From altogether 7778 patients with degenerative spine surgery, a total of 488 patients needed reoperation during follow-up accounting for an overall reoperation-rate of 6.3%. Out of these patients, 60 patients underwent reoperation in the index segment due to recurrence of the degenerative pathology without any clinical, imaging or laboratory hints for SSIs. Median age of this patient cohort was 68.5years, with a predominance of the male sex (m:f=3:2) and the lumbar spine (90%). Mean time between index and re-operation was 18.1±37.2 months. In 11 of the 60 patients (18.3%), microbiological culturing of intraoperative smear testing during reoperation was positive: Minor bacterial growth of *Stap. epidermidis*, *Prop. acnes* and *Bac. circulans* was detected in 5, 4 and 1 patients without any intraoperative surgical hints for infectious findings and classified as "contamination"; none of these patients with watch&wait-strategy developed SSIs or second recurrence during follow-up. Only in a 42-years-old patient with reoperation due to recurrent cervical spinal canal stenosis 3 months after index operation, major bacterial growth of *Staph. epidermidis* was detected in combination with obvious intraoperative surgical hints for SSI that was immediately and successfully treated with rifampicin and vancomycin.

Conclusion

Routine intraoperative smear testing for microbiological culturing in case of reoperation due to recurrent symptomatology following degenerative spine surgery seems not to be diagnostically useful, unless there are clinical/imaging/laboratory and/or intraoperative surgical hints for SSIs.

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P197

Die halbsitzende Position bei Shunt-versorgten Patienten
The semi-sitting position in previously shunted patients

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Objective

The semi-sitting position is one of the preferred positions for posterior fossa surgery. Although posterior fossa or midline tumors are often associated with hydrocephalus, primary tumor removal with or without perioperative placement of an external ventricular drain is commonly favored since hydrocephalus may resolve after tumor resection. Shunting prior to tumor surgery is reserved for symptomatic cases, whereas there are limited data regarding perioperative management of such cases.

Methods

The medical records of all patients who underwent tumor removal in the semi sitting position over a decade after shunting for hydrocephalus were analysed retrospectively. Patients in whom an external ventricular drain was inserted prior to posterior fossa surgery in the semi sitting position were excluded.

Results

Twelve patients (10 women and 2 men) were previously treated for hydrocephalus and a total of 17 operations in the semi-sitting position were performed. The most common cause of hydrocephalus was acoustic neuroma (6/11). Nine patients had a programmable valve (valve setting range 6-14 cmH20, mean 7,5 cmH20), 2 patients had a medium pressure valve and in one case the valve could not be radiologically identified (not adjustable). In two patients the valve setting was adjusted from 8 to 16 cm H20 and from 14 to 20 cm H20 respectively after resolution of postoperative pneumocephalus revealed bilateral hygromas. In one case with a medium pressure valve bilateral asymptomatic subdural hygromas were found at 3 months follow-up and subsequently resolved spontaneously. In one case postoperative overdrainage with symptomatic slit ventricles was treated with ligation of the shunt catheter and implantation of an adjustable valve in a two stage procedure. In our series there were no cases of obstruction, disconnection, infection or hardware malfunction of the shunt system.

Conclusion

In cases of primary shunting for hydrocephalus associated with posterior fossa tumors a programmable valve set at a medium opening pressure is a valid option in the semi-sitting position. Special caution is necessary to detect overdrainage in cases without programmable valves.

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Shunt occlusion in der Hydrocephalus-Therapie – Welche Rolle spielen Protein-Gehalt und Zellzahl im Liquor?
Valve occlusion in CSF shunts therapy – Does protein and cell count in CSF matter?

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Objective

Shunt obstruction os a common cause of shunt failure in the treatment of hydrocephalus. Especially valve occlusion is traditionally believed to originate from elevated protein values or cell components in the CSF but detailed information is conflicting. The aim of this study was to explore the risk of shunt obstruction with regard to the levels of protein and cell counts in the CSF

Methods

274 patients who recieved shunt treatment between 2011 until 2018 with a follow up of at least one year were retrospectively explored for shunt malfunction due to valve obstruction. Age, the origin of hydrocephalus, the valve type, protein values and cell count in CSF at the time of shunt insertion and revision surgery were analysed.

Results

32 fo 274 patients needed revision surgery due to valve obstruction (11.7%) at a mean time interval of 143 days. WBC count in CSF but not protein in CSF were associated with overall valve obstruction. 25% of all obstructed valves showed protein values within the normal range, whereas 13.6% of all patients showed vastly elevated protein levels in CSF without evidence for valve obstruction. Seperating between early (<90 days) and late (>90 days) valve obstruction, a persisting elevated protein content in CSF at the time of shunt revision is significantly associated with early valve obstruction. Children with congenital and posthaemorrhagic patients are significantly overrepresented in the occlusion group especially in the early occlusion group.

Conclusion

Pathological CSF values such as WBC count and persisting elevated levels in CSF serve as a risk factor for ealry valve obstruction. Late obstruction occurs irrespective of normal CSF values. Especially infants are prone to early and late valve obstructions. The simple protein content in CSF at shunt insertion is not predictable for valve occlusions.

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P199

Subkortikales, monopolares Sprachmapping bei Tumoroperationen unter Wachbedingungen
Subcortical monopolar language mapping during awake surgery

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Objective

Intraoperative subcortical language mapping is traditionally performed with bipolar stimulation, which is characterized by frequent interruptions of the operative flow and intermittent mapping of the tumor cavity point by point. To overcome these limitations, we performed a continuous subcortical mapping using a monopolar suction device previously reported for motor tract mapping.

Methods

We present a consecutive case series of 15 patients with glial tumors (4 low grade/ 11 high grade) located in speech eloquent areas, who underwent awake surgery with neuropsychological support. Subcortical monopolar language mapping was performed with the Suction Probe by Raabe et. al. (short train, interstimulus interval 4 msec, pulse duration 500 µsec). Stimulation intensity, evoked temporary speech deficit as well as pre- and postoperative neurological findings were recorded.

Results

Thirteen of 15 procedures were technically successful. Two patients were not cooperative enough for awake surgery. Stimulation intensity ranged from 1 to 10 mA. Intraoperative temporary language errors (a.e. anomia, paraphasia) were evoked in 9 cases (82%) and a temporary total speech arrest in 3 (27%) cases. No seizure occurred during surgery. Gross total resection was achieved in 7 (47%), subtotal resection in 3 (20%) and partial resection in 5 (33%) cases. Postoperative language function deteriorated temporarily in only 2 patients.

Conclusion

Our preliminary data encourage the use of continuous dynamic monopolar language mapping as feasible and safe for localizing speech eloquent fibers adjacent to tumor boundaries.

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P200

Subkortikale Ischämien mit Relevanz für die Motorik sind im intraoperativen MRT innerhalb 1 Stunde nachweisbar – eine Fall-Kontroll-Studie

Subcortical motor ischemia can be detected by intraoperative MRI within one hour – a case-control study

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Objective

To achieve a maximum extent of resection, intraoperative MRI (ioMRI) scan is frequently performed. The present study evaluates the detection and clinical relevance of ischemia by ioMRI in patients with loss of motor evoked potentials (MEP) during glioma resection. Beyond its importance for neuro-oncology, such timewise highly accurate data is especially crucial for investigating early diagnostics of ischemic stroke.

Methods

Of 262 glioma patients between 07/2018 and 01/2020, eight patients (3.1%) showed an amplitude loss of continuous MEP monitoring during resection before the ioMRI scan (group loss of MEP=LOM). In these patients and a matched-pair cohort (MPC) of glioma resections without MEP loss, we performed additional ioMRI sequences including turbo-spin-echo (TSE)- and echo-planar-imaging (EPI)-diffusion-weighted imaging (DWI) with according apparent diffusion coefficient (ADC) maps and perfusion-weighted imaging (PWI). The clinical outcome was measured preoperatively, 5 days and 3 months after surgery.

Results

The mean±standard time between loss of MEPs and ioMRI was 63.0±8.7 min (range: 40-84). Ischemia within the motor system could be detected by ioMRI in group LOM in 100% EPI-DWIs, 100% EPI-ADCs, 75% TSE-DWIs, 87.5% TSE-ADCs, and 66.7% PWIs. No sequence showed motor ischemia in the MPC group. All patients of group LOM and no patient of group MPC suffered from permanent motor deficit.

Conclusion

Subcortical ischemia can be detected by ioMRI after MEP loss during the resection of motor-eloquent gliomas andwas clinically relevant in all cases. These findings are not only important in glioma surgery but of special interest in early diagnostics of ischemic stroke.

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P201

Der Effekt unterschiedlicher Stimulationsfrequenzen auf motorisch evozierte Potentiale im Rahmen des intraoperativen Neuromonitorings

The effect of different frequencies on motor evoked potentials in intraoperative neuromonitoring

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Objective

Intraoperative electrical transcranial and cortical stimulation is used to reduce the risk of damaging the motor system during neurosurgical procedures. In order to quickly identify a decline in the measured potentials it is necessary to install a continuous intraoperative monitoring with high temporal resolution. Therefore, measurements could be done continuously with high frequency. The objective of this study was to investigate whether high frequency motor evoked potentials can lead to a build-up effect of the measured potentials falsely showing stable or even rising potentials and therefore leading to false prediction of the postoperative neurological outcome.

Methods

We analysed data from 25 patients between April 2019 and July 2020. 13 patients underwent surgical resections of lesions in close proximity of motor eloquent structures using intraoperative MEP-monitoring with placement of cortical strip electrodes, 12 patients underwent surgery requiring the use of transcranial motor evoked potentials. In all cases stimulation was done with a frequency of 0,25Hz, 0,5Hz and 1Hz for 2 minutes each. In the cases using transcranial MEP-monitoring stimulation was done before craniotomy and in the cases using the strip electrode stimulation was done after placement of the electrode and before resection of the lesion. In almost all cases peripheral nerve recording electrodes were placed in the thenar muscle. Potentials were recorded and later the data of the first 10 curves and last 10 curves of each series of measurements were averaged and compared for all measurements to see whether a significant change in potentials could be shown for series of measurements done with different frequencies.

Results

In the analysis of the 13 cases of neurophysiological data obtained by using a strip electrode as well as in the 12 cases of transcranial MEP-measurement no significant increase of potentials could be shown for higher frequency recordings in the analysis. No other adverse events were noted.

Conclusion

Neither in the group of transcranial nor in the group of cortical stimulation did an increase of the frequency of electrical stimulation lead to a significant change of potentials. This suggests that intraoperative motor evoked potentials during neurosurgical procedures can be used safely in high frequency to provide continuous intraoperative monitoring with high temporal resolution quickly showing if a decrease of potentials happens without the occurrence of a build-up effect of potentials.

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P202

Der Frontal Aslant Tract – Ist er resektabel?
The frontal aslant tract – Is it resectable?

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Objective

The Frontal Aslant Tract (FAT) has not been described until recently. It connects the inferior frontal gyrus with the supplementary- and pre-supplementary motor areas. Its functions have not been entirely elucidated yet, however, there is evidence that the left FAT may play a role in language function.

The aim of our study was to evaluate neurological outcomes after partial or total resection of the FAT, as well as the functional connectivity of the FAT to language positive cortical areas.

Methods

23 patients, in which a partial resection of the left FAT was performed, were evaluated regarding their neurological outcomes. Out of those, 14 patients were operated awake and 9 under general anesthesia. In all patients, the FAT was visualized in both the pre-and postoperative MRIs, and the percentaged volume of FAT-resection was documented. Secondly, all patients were evaluated as regards their language function with the Aachen Aphasia Score (AAS) at 3 given time points: (1.) preoperatively, (2.) postoperatively and (3.) 3 months postoperatively. In addition, in 28 patients with tumors in the left perisylvian region, who were operated awake with direct electrical stimulation (DES), DTI fibertracing was performed from all DES postive language spots to visualize their potential integration into the FAT.

Results

Resection of the FAT had no immediate impact on the postoperative speech outcome in 87% of the patients. 13% showed a transient postoperative speech deterioration, which was associated with either semantic or dysarthric errors in the AAT. After 3 months, however, all FAT-resected patients showed a complete remission of their postoperative speech deficits.

Out of all 188 intraoperatively registered positive cortical language sites, only 15 sites integrated into the FAT. Those all originated from the frontal operculum. 11 originated from the pars triangularis, of which all consistently connected to pre-SMA; while 4 originated from the pars opercularis, of which all connected to SMA. As concerns the error categories connecting into the FAT, 47% were semantic errors, 27% anomias and 27% dysarthric errors.

Conclusion

While we did observe fiber-connections of language positive DES sites into the FAT, resection of the FAT did not result in permanent language deficits in any of the patients. It may thus be hypothesized that, while the FAT may play a contributory role within the language connectome, its role may not be essential for language function.

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P203

Potenzial und Problemfelder im Pioniergebiet "Privademics" in Deutschland – ein Insiderbericht
Potential and problems in pioneering privademics in Germany – an inside view

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Objective

Recent years have seen a surge in efforts to foster intersectoral collaboration between inpatient and outpatient medical care. In many countries, medical specialists combine their academic practice with a private outpatient clinic. This is a single-institution, single-surgeon report on developing a Privademics system emanating from a large German university center.

Methods

This is to describe the intersectoral collaboration between the department of neurosurgery of a large neurosurgical university center and a private practice with one board certified neurosurgeon. The neurosurgeon in charge of the private practice was also employed part time as an attending at the University Hospital. We undertook a strength, weakness, opportunities and threats (SWOT) analysis based on the first two years of this ongoing collaboration.

Results

From the University Hospital perspective, the benefit was that of having a seasoned surgeon cover calls and train residents. Academic output was also increased by the collaboration. Furthermore, residents may rotate through the private practice to obtain experience in outpatient medical care. From the private practitioner perspective, a continuous exchange with peers ensures being involved in new developments in the field. Especially complex cases benefit from the more intense inpatient and the more personal outpatient care afforded by the Privademic system. However, legal contractual challenges may impede the initiation or survival of such a collaboration.

Conclusion

Interconnecting private practice and University medicine in Germany is an onerous, but potentially rewarding undertaking. It provides benefits to academic development and patient care. For Privademics to thrive, a high degree of motivation is mandatory on the local level. As regulatory bodies are on the verge of softening intersectoral borders, we advocate Privademics as a viable future concept.

Neurovaskuläre Chirurgie III, Neurointensivmedizin/*Neurovascular surgery III, neurointensive care*

P204

Frühzeitige Mortalitätsprädiktoren für neurochirurgische Intensivpatienten mit isoliertem Schädel-Hirntrauma
Early predictors for intra-hospital mortality in neurosurgical intensive care unit patients with isolated traumatic brain injury

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Objective

Isolated traumatic brain injury (iTBI) is one of the leading causes of disability and mortality worldwide. The aim of the current study was to identify early predictors for intra-hospital mortality (IHM) in patients with iTBI.

Methods

A total of 200 patients with iTBI, admitted to our neurosurgical intensive care unit (NICU) between 09/2014 and 12/2016, were analysed retrospectively. Blood samples were taken on patients' admission to determine various serum biomarkers. Demographic and radiological data, Glasgow Coma Scale (GCS)-Score, Abbreviated Injury Scale (AIS)-Score, AIS-Head-Score, Acute Physiology and Chronic Health Evaluation (APACHE)-II-Score up on admission, intensive care unit parameters within the first 24 hours as well as the necessity for emergency surgery were analysed. Intra-hospital outcome was determined by the modified Ranking Scale.

Results

IHM was 27.5% (55/200). Lower levels of body temperature ($p<0.0001$), haemoglobin ($p=0.001$), haematocrit ($p=0.002$), partial thromboplastin time ($p=0.002$), cholinesterase ($p=0.031$), albumin ($p<0.0001$) and GCS-Score ($p<0.0001$), increased APACHE II-Score ($p<0.0001$), higher glucose level ($p<0.0001$), leucocyte count ($p=0.005$), partial thromboplastin time (PTT) ($p<0.0001$), urea level ($p=0.011$), troponin I level ($p=0.009$), C-reactive protein (CRP)/Albumin-ratio ($p=0.044$) upon admission as well as higher norepinephrine application rate (NAR) ($p<0.0001$), higher inspiratory oxygen fraction (FiO2) ($p=0.002$) and the necessity for emergency surgery ($p=0.006$) within the first 24 hours of NICU treatment were univariately associated with increased IHM. Furthermore, advanced age ($p<0.0001$), high AIS-Head-Score ($p=0.041$), the need for intubation ($p<0.0001$) and elevated lactate levels ($p=0.001$) were independent predictors of IHM in the multivariate analysis.

Conclusion

A higher need of NAR and FiO2 within the first 24 hours of NICU treatment were significantly associated with increased IHM. Furthermore, elevated serum lactate levels on admission were identified as a new independent predictor. These new predictors, especially in combination with well-known serum biomarkers, could be helpful to improve risk assessment of IHM in NICU patients with iTBI.

Neurovaskuläre Chirurgie III, Neurointensivmedizin/*Neurovascular surgery III, neurointensive care*

P205

Ist das Risiko für eine Luftembolie in halbsitzender Position bei Patienten mit schlechten ASA scores erhöht?
Is there an increased risk for air embolism in the semisitting position in patients with poor preoperative ASA grades?

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Objective

Many neurosurgical centers use the semisitting position in the surgery of various pathologies of the posterior cranial fossa. Despite of the many advantages of the semisitting position, venous air embolism represents possibly serious complication. We here examine, if patients with poor preoperative ASA grades have a higher risk for venous air embolism.

Methods

Over a 14-year period a total of 740 patients with various pathologies were operated on in the semi-sitting position. The perioperative clinical, surgical and anestheiogical data were collected to identify risk factors for the occurrence of venous air embolism. For this study, patients were dichotomized according to their preoperative American Society of Anesthesiologists (ASA) grade: Group A (ASA I + II), patients with no or mild previous illnesses. Group B (III + IV), patients with relevant previous illness.

Results

There were 404 women and 336 men. Mean age at surgery was 49 years (range 1-87 years). The medical condition according to ASA was classified as grade I =265 (35.8%), II=349 (47.2%) III=123 (16.6%) an IV=3 (0,4%). Venous air embolism was detected in 119 patients (16.1%) by Doppler /TEE. Twenty-three patients with VAE have a decrease of PtCO2 18 patients a drop in systolic blood pressure in and 23 patients had a combined drop in PtCO2 and systolic blood pressure. The following preoperative factors had no effect on the incidence of venous air embolism: hemoglobin value, BMI, body weight, height, gender and previous illnesses (arterial hypertension, heart disease). Surprisingly, There was a masked trend (P = 0.0532) however, that air embolism was less frequent in group B.

Conclusion

An unexpected result in our study was that in patients with a poorer preoperative physical condition (III and IV according to ASA classification) venous air embolism occurred less frequently. It is possible that ntraoperative surgical anestheisological measure were done with greater vigilance and attention in this group of patients.

Neurovaskuläre Chirurgie III, Neurointensivmedizin/*Neurovascular surgery III, neurointensive care*

P206

Langzeitverlauf nach Shunt-Implantation bei Normaldruckhydrozephalus – eine Analyse des Symptomverlaufs, des Evan's Index und der optimalen VP-Shunt-Einstellung

Long-term follow up after shunt surgery for normal pressure hydrocephalus – an analysis of symptom progression, Evan's index and optimal VP-shunt settings

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Objective

Ventriculoperitoneal (VP) shunt implantation is a well-established treatment method for patients with normal pressure hydrocephalus (NPH). This retrospective study aims to investigate the effects of this type of surgery on patients in the long-term and to find an optimal opening pressure of the programmable valve based on gender.

Methods

The data of NPH patients, who underwent VP-shunt implantation between 2004 and 2020, were retrospectively evaluated. Gait disturbance, cognitive impairment, urinary incontinence and Evan"s index values were analyzed preoperatively and 6, 12, 24 and 36 months postoperatively. The initial opening pressure of the programmable valve and every readjustment during the follow-up period was documented along with symptomatic changes at each pressure setting. Paired sample t-test and bivariate Pearson correlation were performed to analyze the data.

Results

The cohort consisted of 132 patients (87 male, 45 female) with a median age of 72.7. Median time of follow-up was 11.3 months. There was a significant reduction of the symptoms immediately after the implantation of the shunt system ($p<0.01$). However, no significant change was observed at the different time points during the long-term follow-up period up to three years. Similarly, Evan"s index was significantly reduced directly postoperatively ($p<0.05$), but showed no further improvement after that. No correlation between the reduction of symptoms and the Evan"s index was found. Valve opening pressure showed a significant relation to the gender of patients ($p<0.01$). The mean optimal opening pressure dependent on gender and overall symptom improvement was calculated to be 119.9±3.6 mmHg for women and 134.3±2.2 mmHg for men.

Conclusion

VP-shunt implantation is effective with regard to clinical and radiological outcomes of NPH patients, although these two factors seem to be independent of each other. In the long-term, patients show decreased rates of improvement when compared to immediate postoperative results. When choosing the opening pressure of the valve the gender of the patient should be taken into consideration.

Neurovaskuläre Chirurgie III, Neurointensivmedizin/*Neurovascular surgery III, neurointensive care*

P207

Routinemäßige postoperative Aufnahme auf die Neuro-Intensivstation nach mikrovaskulärer Dekompression – Notwendig oder nicht?

Routine postoperative admission to the neurocritical intensive care unit after microvascular decompression – Necessary or not?

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Objective

Postoperative admission of patients to neurocritical intensive care unit (NICU) who underwent craniotomy for close observation is a common neurosurgical practice. In this study we analyzed our data to determine if there is a real need of NICU admission after microvascular decompression (MVD) or whether it may be abandoned.

Methods

A series of 236 MVD surgeries for trigeminal neuralgia (213), hemifacial spasm (17), vagoglossopharyngeal neuralgia (2), paroxysmal vertigo (2), and pulsatile tinnitus (2) operated by a senior surgeon according to a standard protocol over a period of more than 10 years were included in this study. The pre and postoperative surgery and anesthesia records were analyzed. Patients were admitted routinely to NICU during the first phase of the study, while in phase II only patients with specific issues went to NICU.

Results

While 105 patients (44%) were admitted to NICU postoperatively (group I) 131 patients (56%) returned to the ward after a short stay in a postanesthesia care unit (PACU) (group II). There was no significant difference in ASA scores, presence of cardiac and pulmonary comorbidities like congestive heart failure, hypertension, previous MI, COPD in both groups. Specific issues for NICU admission in patients in phase I and II were: pneumothorax secondary to central venous catheter insertion (4 patients), AV block during surgery (1 patient), low blood oxygen levels during extubation (1 patient) and postoperative dysphagia and dysphonia (1 patient with vagoglossopharyngeal neuralgia). There were no differences with regard to side effects or outcome when comparing patients from group I (NICU) with patients of group II (PACU).

Conclusion

Our study shows that routine admission to NICU does not yield additional value. NICU admission can be restricted to patients with specific issues. When MVD surgery is performed according to a standard protocol in experienced hands, clinical observation on a neurosurgical ward is sufficient to monitor the postoperative course.

Neurovaskuläre Chirurgie III, Neurointensivmedizin/*Neurovascular surgery III, neurointensive care*

P208

Risiko-Score zur Früherkennung von Patienten mit einem Risiko für eine aseptische Knochendeckelnekrose
Risk score for early identification of individuals at risk for aseptic bone flap necrosis

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Objective

Aseptic bone flap necrosis (ABFN) is a common complication of autologous cranioplasty, necessitating a re-operation. Therefore, ABFN-prone individuals might be more eligible for direct cranioplasty using artificial bone flap implants. The aim of this work was to identify relevant demographic, clinical and laboratory markers of ABFN in a large cohort, in order to develop a risk score for ABFN occurrence.

Methods

All patients who underwent autologous cranioplasty after decompressive surgery between 2007 and 2019 were included. Laboratory data, initial clinical diagnosis and demographic parameters were identified that were retrievable at the time prior to craniectomy and prior autologous bone flap reimplantation. Univariant and multivariant analysis were carried out for the surveyed variables. Significant predictors of the multivariate analysis were used to determine the score.

Results

Of 412 patients that underwent craniectomy, 58 individuals (14% [32 female: 55.2%]) developed ABFN. The following independent predictors of ABFN were included in the risk score (0-6 points): craniectomy due to trauma or hemorrhagic stroke (2 points), younger age (< 40 years, 2 points), cranioplasty timing (> 94 days, 1 point) and an Alanin-Aminotransferase (ALT) < 18 U/L (1 point). The rates of ABFN in the patients scoring 0-2, 3-4 and 5-6 points were 4.2%, 16.1% and 34.6% respectively. The risk score showed a moderate diagnostic accuracy for ABFN prediction (area under the curve: 0.717).

Conclusion

We could identify independent predictors of ABFN, which were summarized in a risk score. The data indicate that future studies should focus on the value of metabolic syndromes in the occurrence of ABFN.

Neurovaskuläre Chirurgie III, Neurointensivmedizin/*Neurovascular surgery III, neurointensive care*

P209

Subdural Hematoma in the Elderly (SHE) score – ein zuverlässiger Prediktor für das Outcome bei akut subduralen Hämatomen im Rahmen leichter Traumata mit einem Status epileptikus als zusätzlicher unabhängiger Mortalität-Faktor

Subdural Hematoma in the Elderly (SHE) score – reliable predictor for outcome of minor trauma acute subdural haematoma with status epilepticus as additional independent mortality factor

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Objective

The aim of this study was the verification of the Subdural Hematoma in the Elderly (SHE) score proposed by Alford et al. as mortality predictor in patients older than 65 years with non-traumatic/minor trauma acute subdural hematoma (aSDH). Additionally, we evaluated further predictors associated with poor outcome.

Methods

The patients were scored according to age (1 point is given if patients were older than 80 years), GCS by admission (1 point for GCS 5-12, 2 points for GCS 3-4) and SDH volume (1 point for volume > 50 ml). The sum of points determines the SHE score. The multivariate logistic regression analysis was performed to identify additional independent risk factor associated with 30-day mortality.

Results

131 patients with aSDH were treated at our institution. We observed the same 30-day mortality rates published by Alford et al.: SHE 0: 4.3% vs. 3.2%, p = 1.0; SHE 1: 12.2% vs. 13.1%, p = 1.0; SHE 2: 36.6% vs. 32.7%, p = 0.8; SHE 3: 97.1% vs. 95.7%, p = 1.0 and SHE 4: 100% vs. 100%, p = 1.0. Additionally, 18 patients who developed status epilepticus (SE) had a mortality of 100% regardless of the SHE score. The distribution of SE among the groups was: 1 for SHE 1, 6 for SHE 2, 9 for SHE 3 and 2 for SHE 4. The only statistically significant risk factor for developing SE was surgery (RR=1.395; CI= 1.242-1.566; p=0.006). Furthermore, SHE 3 and 4 showed no difference regarding the outcome between surgical and conservative treatment.

Conclusion

SHE score is a reliable mortality predictor for non-traumatic/minor trauma acute subdural hematoma in elderly patients. Besides, we identified status epilepticus as a strong life-expectancy limiting factor in patients undergoing surgical evacuation.

Neurovaskuläre Chirurgie III, Neurointensivmedizin/*Neurovascular surgery III, neurointensive care*

P210

Die Rolle der medizinischen Vorgeschichte für den anfänglichen Schweregrad und das funktionelle Ergebnis einer Subarachnoidalblutung bei älteren Patienten

The role of previous medical history on the initial severity and functional outcome of subarachnoid haemorrhage in elderly patients

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Objective

Aneurysmal subarachnoid hemorrhage (SAH) presents a devastating diagnosis for elderly individuals. The clinical value of comorbidities for elderly SAH patients remains unclear. The aim of the study was to analyze the impact of previous medical history and medication on the course of SAH in elderly patients.

Methods

All consecutive SAH cases aged ≥65 years old who were treated in our hospital between 01/2003 and 06/2016 were eligible for this study. The data on comorbidities, previous medication, as well as initial severity, secondary complications of and the outcome after SAH were collected from the electronic medical records. The primary endpoints of the study were: [a] occurrence of cerebral infarcts; [b] in-hospital mortality, and [c] unfavorable outcome at 6 months after SAH defined as modified Rankin scale > 3. The associations were confirmed in the uni-and multivariate analysis.

Results

The final analysis included 246 elderly patients (mean age: 73.6 years, 71.1% females). The rates of cerebral infarcts, in-hospital mortality and unfavorable outcome were 55.6%, 29.7% and 60.2% respectively. Only cardiac morbidity was associated with initial clinical SAH severity, WFNS 4-5 (aOR=1.723, p= 0.046). Of all analyzed secondary complications, only aneurysm re-bleeding (aOR=7.63, p=0.008 / aOR=4.43, p=0.002 / aOR=3.05, p=0.109 for [a], [b] and [c] respectively) and pneumonia (aOR=2.21, p=0.027 / aOR=1.07, p=0.839 / aOR=1.73, p=0.302) were independently associated with one or more of the primary endpoints. In turn, patients with cardiac morbidity were prone to aneurysm re-bleeding (aOR=5.96, p=0.001) and individuals taking the medication with ACE inhibitors were at higher risk of pneumonia (aOR=1.93, p=0.049). The patients with the calcium channel blockers were at higher risk for cerebral infarcts (aOR=2.75, p=0.025). Finally, cardiac morbidity was independently associated with all primary endpoints (aOR=1.95, p=0.048 / aOR=2.25, p=0.014 / aOR=2.71, p=0.027).

Conclusion

Elderly SAH patients are at high risk for poor functional outcome. Particularly, the presence of cardiac comorbidity might complicate the course and outcome of SAH in elderly individuals.

Neurovaskuläre Chirurgie III, Neurointensivmedizin/*Neurovascular surgery III, neurointensive care*

P211

Zur Charakterisierung von transienten Hirndruckänderungen mittels der Allan Deviation
About the stochastic features during intracranial pressure transients – the Allan deviation

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Objective

The Allan deviation (AD) has not been generally used as a tool to determine the statistical properties of intracranial pressure (ICP) up to now. This fact is remarkable because concordance to modern analytic methods applied to ICP (i.e., the wavelet variance) exists. AD becomes important as it provides insight into the signal's properties in time, as is the degree of ICP's phase modulation originated by the cardiac "oscillator." This variability is the time difference between pulse-pressure subpeaks p1 and p2 (Δt12). We hypothesised AD to differ in stochastic properties between dynamic ICP changes and episodes of undynamic controls.

Methods

In 12 episodes of 50 min with distinct dynamics, ICP was recorded for diagnostis in patients with idiopathic intracranial hypertension (IIH). Offline analysis of PP waveforms was carried out, extracting the Δt12 parameter. Nine out of twelve episodes were assigned to 3 groups of notable ICP changes. Three episodes were rated controls because of no change in ICP dynamics. Allan deviation was calculated for nonoverlapping dyadic intervals (1,2,4...1024 samples). Linear regression was computed to determine stochastic properties within correlated group members' subsets (presets: high effect size, $R2>0.81$, $N=4$, $p<0.05$).

Results

Allan variance did not differ among groups; however, in longer intervals, differences between controls and dynamic episodes became apparent. A difference was found in the profile of AD, which showed almost concave, converging, and linear (controls) behavior over time intervals. For episodes of greater than 32 samples, controls showed minimum AD values. Stochastically, the dominant signal property was white noise, which was found in 6/144 subsets. Another 3 subgroups depict random walk and irregular properties. Seven subsets showed no effect size. The remaining subsets could not be unambiguously attributed to any stochastic properties.

Conclusion

The Allan deviation is a statistic portraying the dynamics through ICP measurements or derived parameters of it. The AD algorithm focussed on the nonstationarity. This limited study of an ICP parameter showed that different ICP dynamics had stochastic properties besides the deterministic ones. As irregularity was the leading signal characteristic, ICP should not only be rated by the magnitude and its fluctuations in time but also by the stochastic properties, which adds to the assessment of ICP curves as experienced in the patients with IIH and with other changes of ICP dynamics.

Neurovaskuläre Chirurgie III, Neurointensivmedizin/*Neurovascular surgery III, neurointensive care*

P212

Ein Knochenhormon – Osteocalcin im Gehirn
Bone-derived hormone osteocalcin in the brain

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Objective

Osteocalcin (OC), the bone-derived hormone is important in the regulation of brain development and aging. In the brainstem and hippocampus, OC promotes the synthesis of neurotransmitters, which contribute to cognition and anxiety. OC expression in the brain is contradictory: some reporting its synthesis in the brain and some explaining its brain presence by blood delivery. Presence of OC in the brain would give an opportunity to modulate its level and therefore also the cognition by certain drugs. Here we examined two brain regions, after treatment with an anti-inflammatory drug zileuton, for the OC peptide presence.

Methods

mRNA expression level of OC gene was analyzed using qRT-PCR from hypothalamic and hippocampal brain regions of ovariectomized rat treated with/without zileuton. For the peptide analysis, neuronal (4DIV), as well as neuronal stem cell (7DIV) cultures were developed from hypothalamic and hippocampal regions and protein extracts were made. Targeted mass spectrometry using parallel reaction monitoring (PRM) was used in order to detect and quantify OC.

Results

Level of OC mRNA in different brain regions varies after zileuton treatment. Cloning and sequencing of these amplified fragments detected an OC sequence, confirming the mRNA expression oscillation. Synthetic heavy isotope-labeled peptide was chosen as a probe for the detection and absolute quantification of OC. Targeted mass spectrometry using PRM and heavy isotope-labeled standards did not detect endogenous peptide down to a detection limit of 1 fmol, where the spiked heavy-labeled peptide was always detected.

Conclusion

This data support OC's blood delivery to the brain. The variations in the expression level of OC should undergo further study, like e.g. screening for the potentially homologues molecule(s) in the brain. Even more important is broader picture of OC: 1) how extracellular cues coming from the periphery-bones can affect brain function(s), 2) could the decrease in cognition during aging, be due to the reduction in circulating levels of OC, 3) can we reduce cognitive decline by OC supplementation.

Neurovaskuläre Chirurgie III, Neurointensivmedizin/*Neurovascular surgery III, neurointensive care*

P213

Neuronavigierte Standard subokzipitale retrosigmoidaler Zugang – Vergleich der chirurgischen Morphometrie des mikroskopischen und endoskopischen Zugangareals zum Hirnstamm

Neuronavigated standard suboccipital retrosigmoidal approach – morphometric comparison of the microscopical and endoscopical surgical area of exposure of the brain stem

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Objective

Microscopical and endoscopical surgical areas of exposure in the standard suboccipital retrosigmoidal approach (SSRA) vary widely. For surgical treatments of pathologies at the brain stem, the knowledge about the surgical area of exposure plays a crucial role. The aim of the anatomical study is to evaluate and to compare the surgical area of exposure for the microscopical SSRA and the endoscopical-assisted SSRA

Methods

Three adult human cadaver heads (6 sides) underwent a neuronavigated SSRA. Microsurgical and endoscopic (0 and 30 degree-optic) vector coordinates at the brain stem were marked and noted using neuronavigation. The surgical area of exposure and the corresponding angle of attack was calculated and compared.

Results

The mean endoscopic-assisted area of exposure (428, 43 mm2 ± 26,21 mm2 (Range: 386,23 – 457,29 mm2)) was more significant than the microcopical area of exposure (338, 97 mm2 ± 24,76 mm2 (Range: 311,72 – 361,45 mm2)). Notable, the endoscope increases the view located at the ventral brain stem. However the mean angle of attack for the microscope (39,89° ± 2,56° (Range: 36,31° - 42,06°)) and for the endoscope (39,56° ± 2,63° (Range: 36,14° - 41,88°) were almost equal.

Conclusion

Endoscopic-assisted SSRA helps to verify the microscopical complete resection of lesions and gives more additional surgical access to lesions located ventral to the brain stem provided that safe surgical maneuverability is given under this operative setting.

Neurovaskuläre Chirurgie III, Neurointensivmedizin/*Neurovascular surgery III, neurointensive care*

P214

Wie die COVID-19 Pandemie unser Leben verändert hat – Eindrücke aus dem klinischen Alltag
How the COVID-19 pandemic has changed our life – implications on patient care, triage and self-image

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Objective

The COVID-19 pandemic has definitely left its mark on the year 2020. Precautions, restrictions and lockdowns burden almost all people around the world. With hospital closures out of the question, physicians and nurses face a novel and particular challenge. Therefore, the authors' aim was to evaluate impressions and assessments of the medical staff of a tertiary referral hospital.

Methods

An online questionnaire addressing the current situation in daily clinical routine was created. The sheet consisted of 5 questions interrogating the participants' personal assessments towards the pandemic. Topics were changes in patient care and triage, corresponding workload, self image and expected negative consequences in the near future. All physicians from all departments of the hospital were invited to fill out the questionnaire.

Results

120 physicians participated and were divided into 3 groups: surgery, non-surgery and anesthesia. Two third (66.7%) of all physicians perceived an increased workload concerning patient care. In contrary, more than 90% of all surgeons and non-surgeons agreed that the majority of patients were reluctant to visit the hospital. This corresponded with the physicians" efforts to avoid elective admissions. With regard to the doctors" self-image in the current situation, more than 60% identified themselves as irreplaceable in the daily clinical routine. Interestingly, there was no significant difference between surgeons and non-surgeons. Another question focused on possible negative consequences of the pandemic in the future. Approximately the half (49.2%) of all physicians expected economic disadvantages for their department, whereas 45.6% of the surgeons and 61.4% of the non-surgeons anticipated disadvantages in their training program and career development.

Conclusion

The COVID-19 pandemic has meaningfully affected the daily clinical routine. The questionnaire revealed an increased workload despite less patient numbers, significant changes of patient care and triage as well as personal and economic worries. These impressions and assessments are probably based on imposed restrictions, bureaucratic hurdles, and hygienic precautions.

Neurovaskuläre Chirurgie III, Neurointensivmedizin/*Neurovascular surgery III, neurointensive care*

P215

Abnehmende Anzahl neurochirurgischer Notfälle an einem deutschen Universitätsklinikum während des Corona Lockdowns

Declining numbers of neurosurgical emergencies at a German university medical centre during the coronavirus lockdown

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Objective

The coronavirus pandemic due to SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) is posing unprecedented challenges to health care systems around the globe. Consequently, various lockdown scenarios have been politically imposed to get control over the spread of this disease. We examined the impact of the lockdown situation on the number of neurosurgical emergency patients admitted to our tertiary care center with a catchment area of approximately 2.2 million inhabitants in the south of Germany to ensure adequate neurosurgical emergency care during a pandemic lockdown.

Methods

All emergency admissions (with consecutive inpatient treatment) to the Department of Neurosurgery at the University Medical Center Regensburg, Germany, between 1 March and 8 May (69 days) of the years 2018, 2019, and 2020 were retrospectively identified and reviewed for this study. Demographic data, diagnoses, urgency of surgery, and duration of the journey to the emergency room were examined.

Results

Between 1 March and 8 May 2020, 59 emergency patients were neurosurgically treated at our department. Compared to 2018 and 2019, emergency admissions in 2020 had thus declined by 37.2% and 27.1%, respectively. The decline especially concerned non-traumatic spinal cases but also patients with other neurosurgical diagnoses such as intracranial hemorrhage. Evaluation of the overall disease severity of admitted patients by means of the urgency of surgery showed no difference between the baseline years and the lockdown period.

Conclusion

Our findings are in line with other observational studies of neurosurgical, neurological and cardiological centers in Europe that have described a drop in emergency cases. The reasons for this drop that seems to affect various medical fields and countries across Europe are still unidentified. Morbidity and mortality rates are still unknown, and efforts should be made to facilitate neurosurgical emergency care during a pandemic lockdown.

Funktionelle Neurochirurgie und Schmerz II, Chirurgie periphere Nerven/*Functional neurosurgery and pain II, peripheral nerve surgery*

P216

Neurophysiologische Untersuchung des Kortex bei Patienten mit chronischen refraktären Schmerzen und SCS-Therapie – erste Ergebnisse der Pilotstudie

Neurophysiological investigation of the cortex in patients with chronic refractory pain and SCS therapy – first insights of a pilot study

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Objective

Although spinal cord stimulation (SCS) is widely used in the treatment of refractory neuropathic pain, the underlying mechanisms of action are still not fully understood. The theory behind that mechanism is based on a simplified model, the gate control theory. It postulates that stimulation of the dorsal column leads to an activation of A-fibers, which closes the gate for nociceptive input via collaterals to the posterior horn and thus prevents the transmission of nociceptive information to the brain. Furthermore, activation of supraspinal centers also seems to play a role. Electroencephalography (EEG) allows the functional investigation of the nociceptive system by means of laser-evoked brain responses. In order to find non-invasive neurophysiological markers that objectify the clinical outcome of patients that underwent SCS implantation, we disentangled cortical generators and assessed frequency-specific oscillations using EEG.

Methods

We applied 40 noxious laser pulses (Nd:YAP, IR 1340 nm, 3 ms, 5mm, 2.00J) at the affected dermatome and its corresponding contralateral region in patients with neuropathic lower limb pain during on or off tonic electrical stimulation of the spinal cord. After each single pulse, patients were instructed to evaluate the perceived pain intensity on a numerical rating scale. EEG data were recorded after electrode implantation. For source analysis of the evoked cortical laser responses we used a distributed source model and evaluated nociceptive-induced oscillations using a wavelet analysis.

Results

In the cortical reconstruction, first results revealed pronounced activity in the on stimulation condition in the primary (S1) and secondary somatosensory cortex (S2) as well as in the posterior insula (pIC). While stimulation was switched off oscillatory low frequency activation could be observed in the contralateral pIC at the affected dermatome. Interestingly, in the tonic on stimulation condition enhanced low frequency activation was also additionally obvious in contralateral S1 as well as in S2.

Conclusion

Our results might elucidate the functional dynamics of tonic SCS at the supraspinal level. It appears that SCS might facilitate activation in the somatosensory cortices and thus help to engage feedforward inhibition processes for pain reduction.

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Organische Dünnschichttransistor basierte Elektroden zur Messung und Modulation intrazerebraler Nervenaktivität
Organic thin film transistor (OTFT)-based leads for recording and modulation of intracerebral neural activity

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Objective

Deep brain stimulation (DBS) is an accepted treatment option for various neurological diseases. Common commercial used leads enables only coarsemeshed stimulation and neurosensing due to the comparative big contacts and doesn"t meet the needed requirements for highly selective and adaptive modulation of fine neuronal circuits. To enable more precise and selective measurement and modulation of neural activity, we developed a high resolution organic thin film transistor (OTFT)-based lead.

Methods

The OTFT active matrix array of the lead acts as a voltage-controlled current source amplifier, whereby sensing is integrated to the stimulating contact and provides a high resolution, signal to noise ratio, sensitivity and selectivity. With a higher signal to noise ratio, the recording of neuronal action is more accurate. This OTFT matrix was fabricated using an organic semiconductor and organic dielectric with organic electronic technology. The flexible substrate was mounted on syringe needles to ensure a controlled insertion of the flexible probe.

Results

The proportion of current coming from each contact can be adjusted to range of 0-10mA amplitude, 50-500µs pulse width, 2-250Hz and support multipolar configuration. It is possible to localize and modulate the current shaping and reach better stimulation efficiency, less side effect and the therapeutic effect, hypothetically. The lead consists of 6x40 contacts in a length of 20mm with a diameter of 1.5mm was designed to enable a high resolution for stimulation/sensing in the target region.

Conclusion

A recent in vitro study showed a good biocompatibility of OTFT arrays regarding neuronal cell cultures and demonstrated that it is a pronouncing devise for neural bioengineering. This unique lead design allows a simultaneous and directional highly selective measuring of single neuronal cell action potentials and local potential fields inside the brain and a precise, directional stimulation dependent on physiological or pathological signals. In the next step, the lead will be implanted in animals to proof the feasibility and safety. Furthermore, a mathematical algorithm is needed to process and condense the high number of obtained data for clinical use.

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JM-PSN-03

Die Schwere der Schmerzen, die berichteten somatischen Symptome und ausgewählte Persönlichkeitsmerkmale sind mit Angstzuständen und Depressionen bei Patienten verbunden, die wegen Arthrose der Wirbelsäule operiert wurden – eine Pilotstudie

Pain severity, reported somatic symptoms and selected personality traits are associated with anxiety and depression in patients operated for spine osteoarthritis – a pilot study

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Objective

Pain, especially chronic pain, is associated with the experience of depressed mood and anxiety. In turn, experienced depression often leads to the occurrence of physical pain and somatic symptoms. The coexistence of emotional problems and pain can therefore lead to a "vicious cycle" of emotional and physical symptoms in patients. However, so far, there has been little research on experienced emotions and personality traits in patients operated on for pain resulting from degenerative diseases of the spine. The aim of our pilot study was to assess whether the severity of pain, reported somatic symptoms and selected personality traits are related to the experienced anxiety and depression in surgically treated patients.

Methods

Thirty-three patients (17 women and 16 men) qualified for spine surgery underwent psychological tests with HADS (Hospital Scale for Anxiety and Depression Assessment), FCZ-KT (Formal Characteristics of Behavior - Temperament Questionnaire), NEO-FFI (Personality Inventory), PSS-10 (Perceived Stress Scale) and subjective pain assessment using VAS.

Results

Statistically significant correlations were observed between the subjective severity of anxiety and the experienced pain ($p < .05$), as well as between the severity of depression and the reported somatic symptoms ($p < .05$), experienced stress ($p < .05$) and Perseverance (the tendency to repeat behavior after situation) ($p < .05$). In the study, women did not differ from men regarding the level of anxiety, depression, reported somatic symptoms and the level of experienced stress.

Conclusion

Our pilot study shows that pain intensity and reported somatic symptoms are related to the anxiety and depression experienced by treated patients. Further prospective research could elucidate whether any cause-effect relationships exist between them; the inclusion of psychotherapeutic or pharmacological interventions could reduce the intensity of experienced emotions and, possibly also reduce pain-related discomfort or the level of pain itself. However, this issue requires further research.

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Postoperatives Delir nach kombinierter tiefer Hirnstimulation im STN und NBM bei leichter bis moderater Parkinson-Demenz

Postoperative confusion state in combined STN and NBM DBS in mild to moderate Parkinson's dementia

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Objective

PD dementia (PDD) patients are excluded from the highly effective treatment of STN-DBS since dementia is an accepted contraindication. The DEMPARK study is an ongoing phase-1b trial at our institution with an exploratory endpoint on cognition by combined STN and Nucleus basalis of Meynert (NBM) DBS. Postoperative confusion state was frequently observed after implantation. Here we focus on lead location and its correlation with induction of postoperative delirium.

Methods

Patients received asleep STN and NBM DBS. Indirect targeting of the NBM considered landmarks such as convergence of the optic tract and the temporal crus of the anterior commissure and the level inferior to the external pallidum. Fusion of post-op CT to pre-op MRI and clinical protocols served for analysis of adverse events and sequels, of lead sites in relation to postoperative confusion.

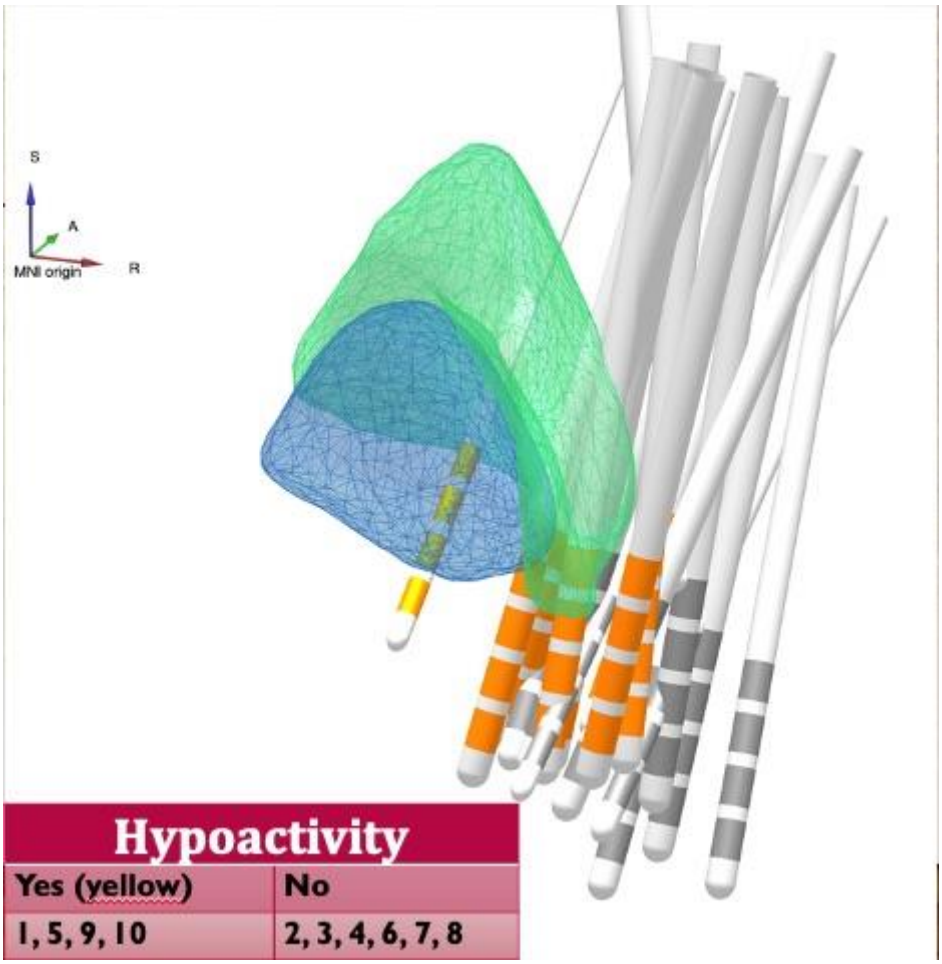
Results

Combined STN & NBM implantation was carried out in 10 patients (all male, Ø65.4 years, pre-op: MMST 22.6, UPDRS On/ Off 48.6 / 19.6, UPDRS Stim-On/ Med off 32.2). Any penetration of the ventricles or the caudate nucleus as well as crossing or disturbance of trajectories could always be avoided. Definite lead sites for the designated active contact were identified at 24.9 mm lateral, 7.6 mm anterior and 5.0 mm inferior to the midpoint. Transient delirium occurred in 7 patients (4 hypoactive, 3 hyperactive). Lead location of patients with hypoactive delirium was clustered with more medial lead placement.

Conclusion

Combined STN/ NBM implantation was conducted while critical surgical sequels such as hemorrhage or infection could be avoided. Of notice, more than half of the patients developed a postoperative confusion state. Currently it remains uncertain whether this is to be attributed to rather long anesthesia in pre-demented patients or related to a stun effect due to inhibition of cholinergic transmission which could be linked especially to hypoactive delirium.

Fig. 1



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RechargePSYCH – wiederaufladbare implantierbare Pulsgeneratoren bei Patienten mit Tiefer Hirnstimulation zur Behandlung psychiatrischer Erkrankungen

RechargePSYCH – rechargeable implantable pulse generators in patients with deep brain stimulation for psychiatric disorders

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Objective

The effects of Deep Brain Stimulation (DBS) for different psychiatric disorders have been explored in clinical trials. Implantable pulse generator (IPGs) replacements represent the most common type of scheduled follow-up surgeries as stimulation parameters are usually higher compared to movement disorder patients. Rechargeable IPGs offer longer battery life causing fewer surgical replacements combined with a smaller implant size. The impact of this technology on psychiatric patients as well as the amount of time necessary to maintain therapy are still unknown.

Methods

A single center database analysis was performed to identify all DBS patients who were implanted with a rechargeable IPG for a psychiatric indication from 2003 to 2019. Patients that were still implanted with a rechargeable device at the time of the trial were asked to complete a standardized online questionnaire. Primary endpoint was the rating of the convenience of recharging of the entire process and each individual step on an ordinal scale (0-10). Secondary endpoints were the rate of user confidence, user satisfaction, complications (failed recharges, interruptions of therapy) and the charge burden (minutes per week necessary to recharge the IPG). These endpoints were tested for differences in several subgroups (age, sex, indication, IPG model, confidence).

Results

N=21 patients completed the questionnaire including n=13 patients with major depression, n=6 patients with anorexia and n=2 patients with OCD. Mean age was 50.7 years with an average time of therapy with the rechargeable IPG of 31.8 months. Patients had undergone a median of 3 IPG replacements before receiving the rechargeable IPG. Convenience of recharging was rated high (8.0 out of 10.0 points). The mean charge burden was 286 minutes, which was regarded as acceptable by only 43% of patients. 81% of patients felt confident using the device. 66.7% would recommend and 62% would choose a rechargeable IPG again. 33% of patients experienced a failed recharge and 38% had an unintentional interruption of therapy. Depression patients rated the convenience of recharging significantly worse compared to OCD patients (p=0.027). Patients that did not feel confident were less likely to recommend (p=0.006) or choose a rechargeable IPG again (p=0.012).

Conclusion

Rechargeable IPGs can be safely implanted in DBS patients with psychiatric indications. Charge burden and complication rates are higher compared to movement disorder patients.

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P220

Periphere Nervenfeldstimulation in der kraniofazialen Region – eine monozentrische Studie
Peripheral nerve field stimulation in the craniofacial region – a single-centre study

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Objective

Peripheral nerve field stimulation (PNFS) emerged during the last decades as an effective treatment option for chronic pain refractory to conservative treatment. In contrast to other neuromodulation methods which stimulate the main nerve trunk, PNFS electrodes are placed subcutaneously to stimulate the small nervous endings in the region of the affected nerves. This method is particularly useful for targeting smaller and well-defined pain areas like the facial region. We aimed to report on the outcome of chronic PNFS in the craniofacial region for migraine, occipital neuralgia, atypical facial pain, atypical trigeminal neuralgia or trigeminal neuropathy.

Methods

We retrospectively analysed the records of patients who underwent subcutaneous implantation of electrodes during the last two years in the craniofacial area at our department. The reduction of pain through stimulation was measured with the numeric rating scale (NRS) preoperatively and postoperatively at different time-points.

Results

Eleven patients were included in this study. Patients had a mean age of 63.6 years (range 44-75) at the time of the implantation. One patient was diagnosed with chronic migraine, one patient with occipital neuralgia, three patients with atypical facial pain, four patients with atypical trigeminal neuralgia and two with trigeminal neuropathy. The preoperative mean pain intensity using the NRS was 8.0/10 points (SD±0.77), one week after the procedure, it was 2.8/10 points (SD±3.03) and at maximum follow-up (mean 9.33 months SD±4.88), was 5.0/10 points (SD±2.98). A significant pain reduction was documented in both time periods, one week after the procedure ($p<0.001$) and at maximum follow-up ($p<0.01$), compared to preoperative scores. Electrodes were explanted within the first month after surgery in two patients who did not significantly benefit from PNFS. One electrode in one patient was explanted after 7 months of stimulation due to a local infection. No further complications were documented.

Conclusion

PNFS can be an effective and safe alternative for patients with chronic pain in the craniofacial area refractory to conservative therapy methods.

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P221

Roboter-assistierte stereotaktische Implantation intrazerebraler Tiefenelektroden bei pädiatrischen und erwachsenen Patienten – Präzision, Komplikationen und epileptologische Ergebnisse

Stereotactic robot assisted placement of intracerebral depth electrodes in paediatric and adult patients – accuracy, complications and epileptological results

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Objective

The number of patients requiring depth electrode implantation for invasive video EEG diagnostics increases in most epilepsy centres. Here we report on our institutional experience with frameless robot-assisted stereotactic placement of intracerebral depth electrodes using the Neuromate® stereotactic robot-system.

Methods

We identified all patients undergoing robot-assisted stereotactic placement of intracerebral depth electrodes for invasive extra-operative epilepsy monitoring between September 2013 and March 2020. We studied technical (placement) and diagnostic accuracy of the robot-assisted procedure, associated surgical complications and procedural time requirements.

Results

464 depth electrodes were implanted in 74 patients (mean 6 per patient, range 1-12). There were 27 children and 47 adults (age range: 3.6–64.6 yrs.). The mean entry and target point errors were 1.82±1.15 and 1.98±1.05 mm. Target and entry point errors were significantly higher in paediatric vs. adult patients and for electrodes targeting the temporo-mesial region. There were no clinically relevant haemorrhages and no infectious complications. Mean time for the placement of one electrode was 37±14 min and surgery time per electrode decreased with the number of electrodes placed. 55 patients (74.3 %) underwent definitive surgical treatment. After a median follow-up of 24 (range 6-72) months 39/54 (72.2 %) patients were seizure-free (ILAE 1).

Conclusion

Frameless robot-guided stereotactic placement of depth electrodes with the Neuromate® stereotactic robot-system is safe and feasible even in very young children, with good in vivo accuracy and high diagnostic precision. The surgical workflow is time-efficient and further improves with increasing numbers of implanted electrodes.

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Burst Motorkortexstimulation zur Behandlung von Schlaganfall-assozierten Schmerzsyndromen
The impact of burst motor cortex stimulation on poststroke pain – a literature overview and single-centre experience

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Objective

A considerable percentage of patients with poststroke develop refractory pain with unfavorable responses to established conservative therapy. Brain stimulation, both non-invasive (transcranial magnetic stimulation, transcranial direct current stimulation, transcranial alternating stimulation, transcutaneous vagus nerve stimulation, minimally invasive motor cortex stimulation and invasive deep brain stimulation, has been reported to yield response rates ranging from 25% to 45%. Epidural MCS appears to be superior to DBS of the thalamus or brainstem, and it is used more frequently because of its easier and less invasive application and its wider range of indications.

Methods

We performed a review of human studies applying burst and conventional motor cortex stimulation (burstMCS and cMCS, respectively) on the basis of data sources identified through searches of PubMed, MEDLINE/OVID, and SCOPUS. Our aim was to review and discuss clinical data on the indications of burst MCS for various chronic pain states originating from central stroke (excluding trigeminal facial pain). In addition, we evaluated the efficacy and safety of burst versus cMCS for central poststroke pain with an extended follow-up of 5 years in a 60-year old male.

Results

Observational human cohort studies and one RCT using cMCS waveforms have revealed a meaningful clinical response; however, these studies lacked placebo groups and extended observation periods. In our case report, we found that 3 months of adjunctive cMCS reduced pain levels (visual analog scale (VAS) pre: 9/10 versus VAS post 7/10), whereas the pain decreased further under burst MCS (VAS pre: 7/10 versus VAS post: 2/10); the study involved a follow-up of 5 years and the following parameters: burst rate 40 Hz (500 Hz), 1–1,75 mA, 1 msec, bipolar configuration.

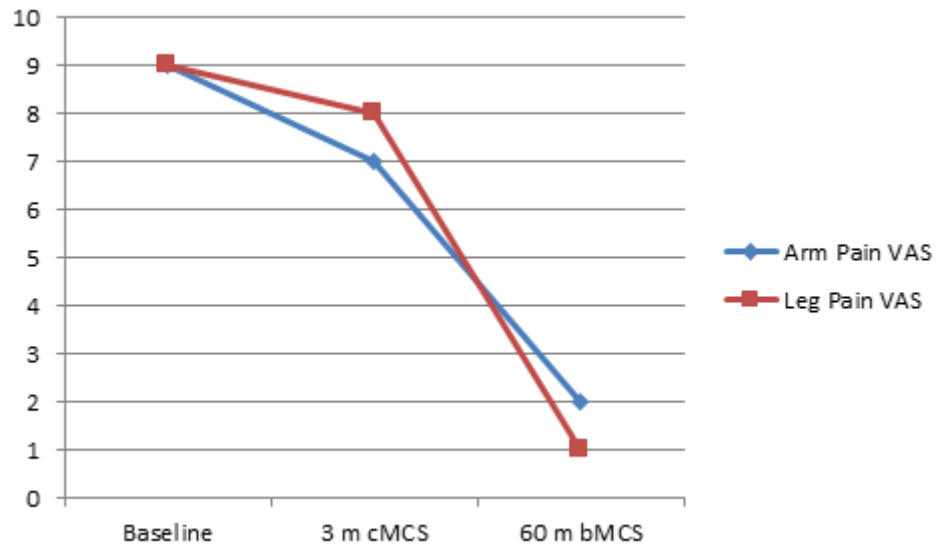
Conclusion

BurstMCS resulted in significantly decreased post-stroke pain observed after 5 years of cMCS. The available literature suggests similar efficacy to that of conventional (tonic) motor cortex stimulation, although the results are preliminary. Mechanistically, the precise mechanism of action is not fully understood. However, burstMCS may interact with the nociceptive thalamic-cingulate and descending spinal pain networks. To determine the potential utility of this treatment, large-scale sham-controlled trials comparing cMCS and burstMCS are recommended.

Fig. 1

Year	Study Design	Patient	Stimulation Protocol	Primary Endpoint	Secondary Endpoint	Outcome/Follow-up	SAE/AE
2017 [6]	Retrospective Analysis	16	rTMS MCS not described in detail	40% pain relief VAS	Influence of stroke type/location on pain relief	Significant reduction of pain intensity	Not reported
1993 [7]	Observational Cohort Study	11	MCS (pulse duration 0.1–0.5 msec, intensity 3–8 V)	Pain relief VAS	Barbiturate test/ morphine test	Significant reduction of pain intensity	No
2000 [9]	Retrospective Analysis	32	MCS not described in detail	Pain relief VAS	–	Significant reduction of pain intensity	No
2002 [10]	Retrospective Analysis	20	Various localizations by MRI, MEPs, bone landmarks; MCS not described in detail	Correct stimulation localization	–	Effective localization determination by using MRI and electrophysiological techniques	Not reported
2006 [11]	Retrospective Analysis	17	MCS not described in detail	Pain relief VAS	Double-blind testing with neurophysiological monitoring	Patients with TNP benefit more than those with PSP. Positive effects on pain can last 10 years	Not reported
2008 [13]	Randomized-controlled trial	11	MCS: bipolar stimulation at a 40-Hz frequency, 90-μsec pulse width, amplitude 2–7 V, and 1 hour on and 4 hours off	Pain relief VAS	–	Positive influence of subacute stimulation trials for correct electrode localization; Significant reduction of pain intensity	Not reported
2013 [16]	Case Report	1	MCS not described in detail	Pain relief after correct electrode replacement	–	Combining fMRI and PET can be helpful in detection of ideal stimulation points	Not reported
2015 [17]	Retrospective Analysis	14	MCS not described in detail	Pain relief VAS	Predictors of successful outcome	Significant reduction of pain intensity	Not reported
2018 [18]	Observational Cohort Study	18	MCS not described in detail	40% pain relief VAS	MQS, QoL, QLI	Significant reduction of pain intensity	Not reported
2019 [19]	Case series	6	MCS tonic vs. burst (example: 40 Hz/500 Hz/1000 μs/0.8 mA)	Pain relief VAS	Difference in treatment efficacy between tonic and burst stimulation	More effective pain relief in burst mode than in tonic stimulation mode	Not reported
2017 [21]	Literature Review	–	–	Improvement of MCS procedure	Discussed topics: inclusion and exclusion criteria; targeting and methods of stimulation; effects of MCS	More standardized protocols for MCS are needed regarding patient selection, implantation procedure, stimulation parameters and follow-up-course	Not reported
2007 [22]	Observational Cohort Study	14	MCS not described in detail	Pain relief VAS	Predictive factors: response of pharmacological tests, analgesic response achieved during the test period of MCS	Only 28% of patients experienced >40% pain relief	Yes
1999 [24]	Observational Cohort Study	32	MCS not described in detail	Pain relief VAS	–	75% pain relief; the positions of the stimulating poles effective on pain corresponded to the somatotopic representation of the motor cortex.	No
1991 [26]	Observational Cohort Study	12	MCS not described in detail	Pain relief VAS	Predictive factors: pain responsible for barbiturate and resistance to morphine	Significant pain relief	No
1991 [27]	Case series	7	MCS long-term inhibition of the burst hyperactivity	Pain relief VAS	Positive side effects	Significant pain reduction in all cases; Increase in regional blood flow of the cerebral cortex and thalamus	No
1994 [28]	Observational Cohort Study	6	Thalamic stimulation or MCS (pulse duration, 0.1–0.5 ms; intensity, 3–8 V)	Pain relief VAS	–	No satisfactory pain control with thalamic stimulation; 66% satisfactory pain control with motor cortex stimulation	Not reported
1997 [29]	Observational Cohort Study	39	MCS not described in detail	Pain relief VAS	Correlation between pharmacological tests and positive effects of MCS	Thiamylal and ketamine-sensitive and morphine-resistant cases displayed long-lasting pain reduction with MCS therapy	Not reported

Fig. 2



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P223

Entschlüsselung einer Black Box – eine fallgetriggerte histologische Untersuchung des Conus medullaris
Decoding a black box – a case triggered histological investigation of the conus medullaris

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[2]Martin-Luther-Universität Halle-Wittenberg, Institut für Anatomie und Zellbiologie, Halle/Saale, Germany
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Objective

The background for this investigation was the dramatic course of a 14-year-old girl with a spontaneous hemorrhage in the area of the conus medullaris resulting in a complete cross-sectional syndrome. Despite immediate surgical treatment, there was close to none postoperative improvement. The subsequent histopathological examination of the removed masses revealed a cavernoma. For a better understanding of the link between site and symptoms of conus medullaris lesions a literature research regarding the histological features of this structure was performed. This research did not lead to satisfying results. Although the conus medullaris syndrome is often described, this is, to our knowledge, the first investigation of its histological structure.

Methods

We present the histological examination of the conus medullaris of 18 body donors. The specific slide containing the ending point of the gray matter was noted. The distance between the caudal ending of gray matter in the conus and the macroscopical end of the conus medullaris could be defined as "gray matter to cone termination-distance" (GMCT-distance). Furthermore the greatest (a) and smallest (b) diameters of the conus medullaris were measured

Results

Gray matter displayed as butterfly figure was found almost along the entire length of the conus medullaris. However, there were great individual variations in the distance from the caudal ending of the gray matter and the macroscopical end of the conus medullaris. Additionally, the correlation of these differences with gender, body height, transverse diameter and area of the cross section at the end of the gray matter was analyzed.

Conclusion

This is the first description of the histological structure of the conus medullaris and can serve as basis for a better understanding of neurological deficits of a conus medullaris syndrome. Findings that the gray matter can be detected far into the conus medullaris with a great individual ending of the gray matter are important for operative care of intramedullary masses in this area and vascular malformations.

Fig. 1

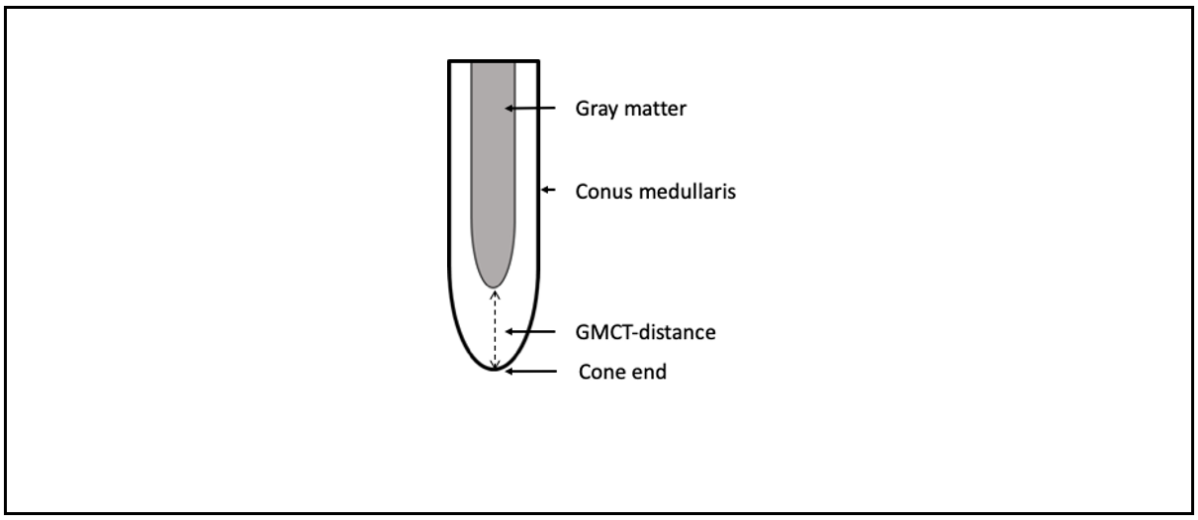
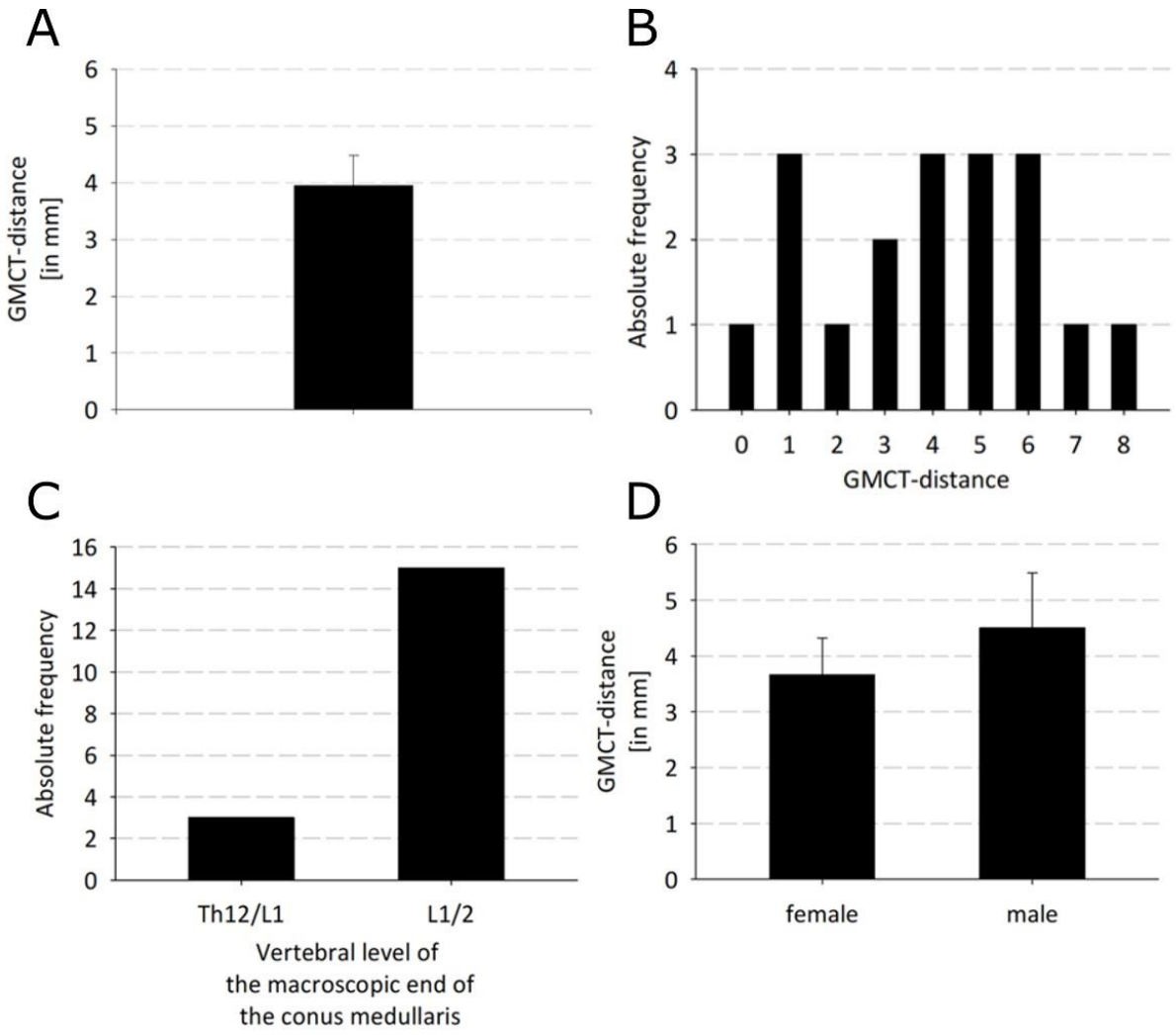

Gray matter
Conus medullaris
GMCT-distance
Cone end

Fig. 2


A
GMCT-distance [in mm]
0
1
2
3
4
5
6
B
Absolute frequency
0
1
2
3
4
0 1 2 3 4 5 6 7 8
GMCT-distance
C
Absolute frequency
0
2
4
6
8
10
12
14
16
Th12/L1
L1/2
Vertebral level of the macroscopic end of the conus medullaris
D
GMCT-distance [in mm]
0
1
2
3
4
5
6
female
male

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Behandlung der Meralgia paraesthetica in deutschen Krankenhäusern zwischen 2005 und 2018 – Diagnosehäufigkeit, Patientencharakteristika und Art der Intervention

In-patient treatment of Meralgia paresthetica in Germany between 2005 and 2018 – prevalence, patient characteristics and types of interventions

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Objective

Meralgia paresthetica (MP), a mononeuropathy of the lateral cutaneous femoral nerve (LCFN), was shown to occur in 32.6 per 100.000 patient years in a population based study between 1990 and 1999 in the United States of America. Since it is associated with diabetes mellitus (DM) and obesity, which are comorbidities with currently still increasing global prevalence, the prevalence of MP is expected to grow steadily in the coming years, as well. So far, no studies exist on the MP prevalence, patient characteristics and type of treatmen in Germany.

Methods

Data from patients with the International classification of disease (ICD) code G57.1 that were treated between 2005 and 2018 in disease related group (DRG) billing hospitals in Germany was analyzed. Ethical approval was granted by local authorities (EA1/275/20). The prevalence of MP, and patient characteristics in relation to patient age, comorbidities, as well as Operation and Procedure Classification (OPS) code were calculated.

Results

A median of 743 (687; 802) patients with MP as their main diagnosis were treated annually between 2005 and 2018 in hospitals in Germany. There was no increase over time in the prevalence of MP as main diagnosis. The prevalence of MP as a secondary diagnosis increased at a median annual rate of 81 patients (from 1365 to 1815). The rate related to 100.000 patients treated in German hospitals was stable between 3.9-4.6 % for main and 7.6-10.4 % for secondary MP diagnosis. As measured by 100.000 inhabitants, the rate of MP as main diagnosis remained stable (0.7-1%) but slightly increased for MP as secondary diagnosis from 1.7 to 2.2%. The median age of all patients with MP as a diagnosis was 52.6 years without obvious trends or significant differences between female and male patients. In 2018, the most frequent comorbidities were arterial hypertension (36.5 %), lipid metabolism disorder (12.3 %), DM (9.5 %), back pain (9.2 %) and depression (7.0 %). There was a trend towards a decrease of destructive nerve interventions (neurectomy) between 2005 and 2018 (8.3 % vs. 2.6 %, respectively). In 2018, decompressive surgery of the NCFL was performed in 21.9 % of hospitalized patients.

Conclusion

In-patient treatment numbers of patients with the main diagnosis of MP were relatively stable between 2005 and 2018 with a slight but subsecuent increase of patients with MP as secondary diagnosis. Numbers of destructive nerve interventions (neurectomy) decreased in that time-period.

Funktionelle Neurochirurgie und Schmerz II, Chirurgie periphere Nerven/*Functional neurosurgery and pain II, peripheral nerve surgery*

P225

Periphere Nerventumore – Schwierig zu diagnostizieren?
Peripheral nerve tumours – Difficult to diagnose?

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Objective

Peripheral nerve tumors are rare and sometimes difficult to diagnose. Despite recent advances in diagnostic tools and the more commonly use of ultrasound, MRI and electrophysiology, time until diagnosis of peripheral nerve tumors is quite long and they can be mistreated prior to diagnosis.

We therefore tried to analyze the frequency of misdiagnosed patients, treated as a spinal canal stenosis or a disc herniation.

Methods

Retrospective evaluation of patients treated in our department due to a peripheral nerve tumor between 2012 until 2018. Demographic, neurological symptoms, initial diagnosis, time of "false" treatment were analyzed.

Results

In total, 116 patients were treated (60 female, mea age: 50.3 ± 15.3 years of age). 43 neurinoma (37.1%), 18 neurofibroma (15.5%), 17 ganglioma (14.7%) 9 lipoma (7.8%) and 4 perineurioma (3.4%) analyzed. Peroneal nerve (n=21), sciatic nerve (n=11), ulnar nerve (n=11) and tibial nerve (n=10) were the most affected locations. First symptom was mainly pain (49.1%) followed by palpable lesion (27.6%).

False diagnosis and false treatment prior to diagnostic of a peripheral nerve tumor were seen in 26 patients (22.4%). Misdiagnosis was not significantly affected by the tumor (p=0.149) or the location of the tumor (p=0.233). False diagnose was detected in patients suffering from pain as the first symptom in majority (17/26, p=0.0001).

Conclusion

Symptoms of peripheral nerve tumors can easily be misinterpreted, mimicking degenerative spinal diseases, especially if pain is the first symptom.

Intraoperatives Monitoring II, Qualitätssicherung, Transsektorale Neurochirurgie/*Intraoperative monitoring II, quality management, trans-sectoral neurosurgery*

P226

7 Tesla Multi-Voxel Spektroskopie in der Detektion von fokalen kortikalen Dysplasien in therapieresistenter Epilepsie als Hilfestellung für die navigationsgeführte Resektion

7 Tesla high resolution spectroscopic imaging (MRSI) may detect focal cortical dysplasia in intractable epilepsy patients as neuronavigation targets for epilepsy surgery

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Objective

Structural 7 Tesla MRI has proven to enhance the diagnostic yield of detecting focal cortical dysplasia in refractory epilepsy patients. The aim of our study was to investigate if high resolution MR spectroscopic imaging (MRSI) using 7 Tesla may improve the detection rate even further.

Methods

We measured 10 patients suffering from medically refractory epilepsy using MRSI covering the whole brain with 3.4mm isotropic resolution in 15 min. Quantification used a basis set of neurochemical components including Choline, Creatine, NAA, myo-Inositol, Glutamate and Glutamine.

Results

Different patient specific patterns of investigated metabolites were detected. Increased focal total choline and creatine activity was found in 3 patients, corresponding to suspected areas of focal cortical dysplasia in the structural images as well as being in accord with previous MRS studies. These findings correlated strongly to the suspected epileptogenic zone defined by electro-clinical investigations and PET imaging. Other metabolite findings differed between these three patients. Intraoperatively, a tailored resection of these MRSI choline areas using neuronavigation and electro-corticography (ECoG) in these 3 patients was successfully performed and FCD I and IIb histology verified. Patients are seizure free so far.

Conclusion

Choline mapping using 7 Tesla MRSI may contribute to identify FCDs in patients with intractable epilepsy and guide the resection when included in the intraoperative neuronavigation. The observed different metabolic patterns could lead to improved preoperative classification during further investigation.

Intraoperatives Monitoring II, Qualitätssicherung, Transsektorale Neurochirurgie/*Intraoperative monitoring II, quality management, trans-sectoral neurosurgery*

P227

Intraoperative Anwendung einer Wärmebildkamera zur Detektion oberflächlich gelegener Hirntumore
Analysis of using a thermal imaging camera to detect superficial brain tumours – a pilot study

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Objective

Being able to reliably distinguish between physiological and pathological tissue constitutes an essential part of brain tumor surgery. Currently, surgeons can use various invasive and non-invasive methods to detect brain tumors. Achieving a balance between protecting healthy tissue versus maximizing the degree of tumour resection can be aided by a high degree of differentiation. Higher degrees of differentiation mean protecting more healthy tissue and increasing the amount of tumour resected. Aim of this pilot study is to evaluate whether a temperature difference between physiological and pathological tissue can be shown by means of a thermal imaging camera, focusing on superficially located gliomas.

Methods

During the course of 11 brain tumour extirpations, images (average of 14 images per patient) were taken at specific intervals (before and directly after Dura opening, then every 5 minutes) using a thermal imaging camera. All patients were treated according to an established, standard protocol using microsurgery, intraoperative monitoring and 5-ALA technique. Temperature data were compared and analysed with preoperative MRI and fluorescence images (5-ALA).

Results

During the first measurement the cortex"s temperature was 37.0°C (36.1 - 37.4°C). Tumour temperatures however were very inhomogeneous. Especially central parts were significantly colder (median: 35.8 °C) compared to surrounding cortex temperature. In 9 of 11 patients, the tumor margins displayed an increased temperature when compared to physiological tissue (mean: 37.2 °C). The remaining two patients showed no difference in temperature between the tumour margin and the surrounding cortex.

Conclusion

Our pilot study shows that by using a thermal imaging camera, a quick and uncomplicated differentiation between physiological and pathological tissue is probably possible. Since the degree of resection is essential for the patient's outcome, this probable correlation should be analysed in further studies to establish a new tool to further enhance the differention of tissue.

Intraoperatives Monitoring II, Qualitätssicherung, Transsektorale Neurochirurgie/*Intraoperative monitoring II, quality management, trans-sectoral neurosurgery*

P228

Die Architektur von Aneurysmen – die ersten *in vivo* Darstellungen zerebraler Aneurysmen mittels extravaskulärer, optischer Kohärenztomographie

Aneurysm architecture – first in vivo imaging of human cerebral aneurysms with extravascular optical coherence tomography

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Objective

The present study explores three-dimensional microscope integrated extravascular OCT as the first suitable intraoperative imaging modality of cerebral aneurysm (CA) and parent vessel wall morphology.

Methods

Incidental CAs (n=16) of the anterior circulation with indication for microsurgical clipping were scanned.

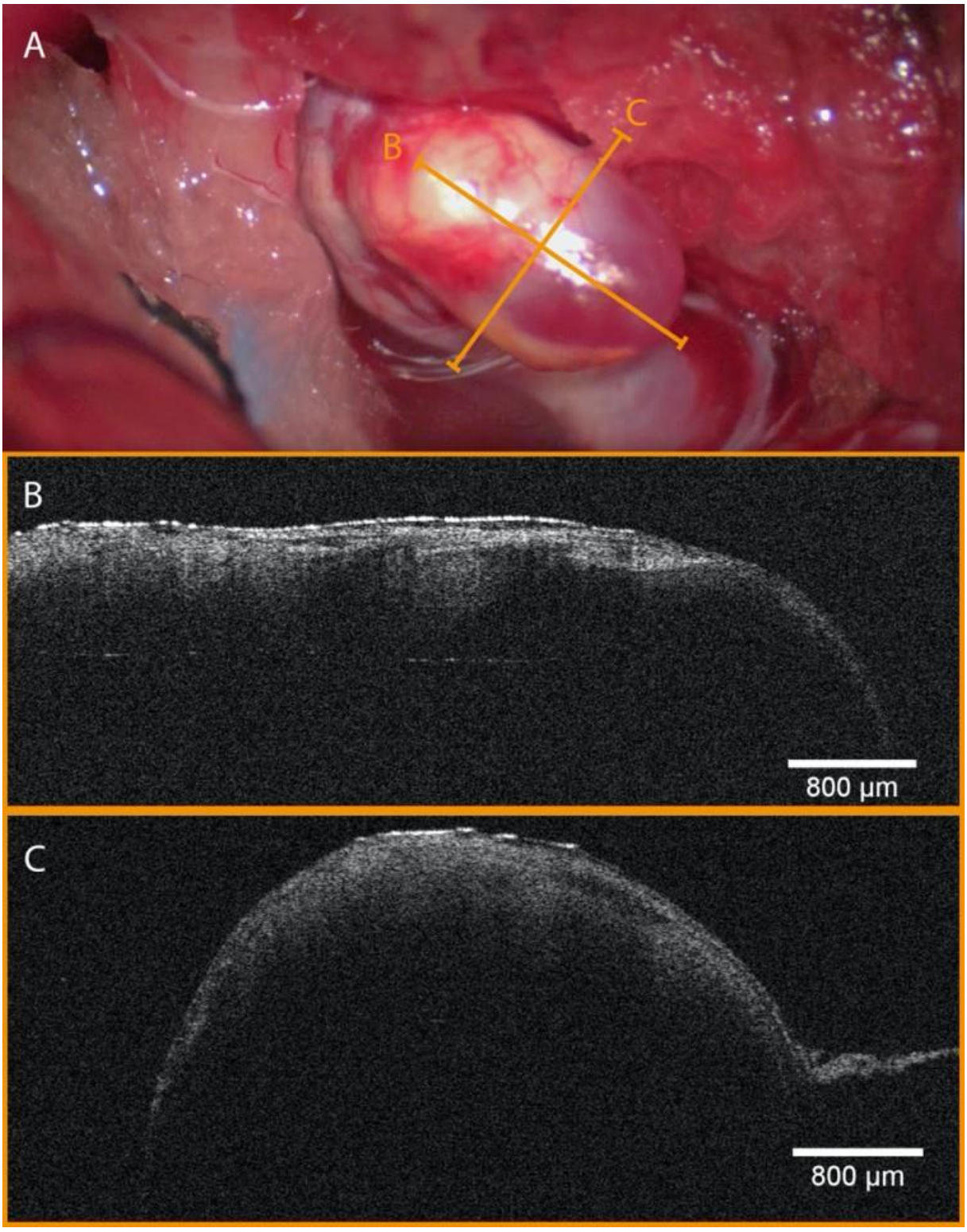
Results

Analysis revealed that intraoperative OCT achieved to delineate the microstructural composition of the parent vessel in all cases and the CA wall in 68,8 %. Clinical relevant characteristics like thickness, calcification, residual tunica media and atherosclerotic plaque of CA wall could be demonstrated with high image quality approaching spatial resolution of histopathology.

Conclusion

Our findings demonstrate that intraoperative OCT may hold promise as an additional imaging tool during neurovascular procedures.

Fig. 1



Intraoperatives Monitoring II, Qualitätssicherung, Transsektorale Neurochirurgie/*Intraoperative monitoring II, quality management, trans-sectoral neurosurgery*

P230

Diffusionstensorbildgebung oder hochaufgelöste Diffusionsmodelle zur Faserbahntraktographie – Evaluation der Genauigkeit bei der Chirurgie eloquenter Gliome unter Wachkraniotomiebedingungen

Comparison of diffusion signal models for fibre tractography in eloquent glioma surgery – determination of accuracy under awake craniotomy conditions

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Objective

Besides intraoperative electrostimulation methods(IOM), fiber tractography(FT) became an important non-invasive tool to ensure maximal safe tumor resection in eloquent glioma surgery. Intraoperatively applied FT is still predominantly based on Diffusion Tensor Imaging(DTI). However, multiple reconstruction schemes of high angular resolution diffusion imaging(HARDI) data for high resolution fiber tractography(HRFT) are becoming a focus of interest. However, clinical reasonability has to be considered. We evaluate the accuracy of HRFT based on q-ball imaging(QBI) and Constrained Spherical Deconvolution(CSD), compared with DTI-FT for the major language-associated pathways.

Methods

Ten patients with eloquent gliomas underwent surgery under awake craniotomy conditions. Points(AP) were acquired according to IOM results under repetitive neuropsychological examination. The distances of APs to fiber bundle margin and centerline (offsets) were calculated. Probabilistic HRFT models QBI-, and CSD were compared with conventional DTI-FT. The data was derived from a diffusion sensitized dataset of the clinical routine. Pairwise comparison of the methods was performed using the Wilcoxon signed rank test.

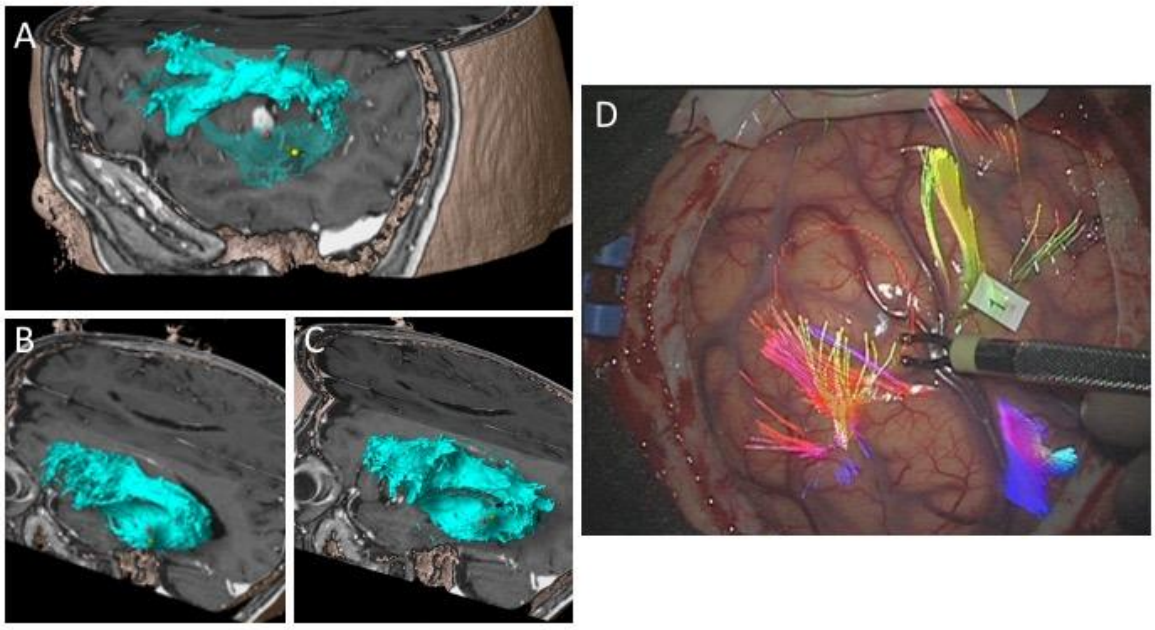
Results

Among the measured 183 min-offset values, 46% were located closer than 1cm to the estimated fiber bundle (CSD: 38%; DTI: 39% and QBI: 62%). However, only 10 min-offsets were further than 3cm away (5%). For QBI, lowest mean min-offsets (SLF: 7.7 ± 7.9mm; IFOF: 12.7 ± 8.3mm; ILF/MLF: 17.7 ± 6.7mm) were found. A significant advantage was objectified for QBI-FT compared with CSD and DTI ($p<0.001$). Comparing CSD-, and DTI-FT, there was no significant difference for the total fiber object ($p=0.105$), only for SLF ($p<0.001$) (illustrated with Figure).

Conclusion

Comparing HRFT techniques QBI and CSD for FT with DTI, QBI delivers significantly better results with lowest offsets and a good correlation to the IOM results. Besides, QBI-FT is still feasible for neurosurgical pre- and intraoperative applications. We consider a combined approach of QBI-FT and IOM under awake craniotomy for best preservation of neurological function in the presented setting. The implementation of well selected and sophisticated HRFT models into neuronavigation systems should be pursued.

Fig. 1



Intraoperatives Monitoring II, Qualitätssicherung, Transsektorale Neurochirurgie/*Intraoperative monitoring II, quality management, trans-sectoral neurosurgery*

P231

Endoskopische Assistenz in tiefen und engen Hirnarealen – mikrochirurgische Tumorchirurgie unterstützt vom neuen Mikro-Endoskop QEVO®

Endoscopic assistance in the deep and narrow spaces of the brain – microscopic tumour surgery supported by the new micro-inspection tool QEVO®

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Objective

To evaluate the feasibility and efficacy of the innovative micro-inspection tool QEVO® (Carl Zeiss Meditec, Oberkochen, Germany) as an endoscopic adjunct to microscopes for better visualization of the surgical field in complex deep-seated intracranial tumors in infants and adults.

Methods

We retrospectively assessed the surgical videos of 25 consecutive patients with 26 complex intracranial lesions (timeframe 2018–2020). Lesions were classified according to their anatomical area: 1=sellar region (n=6), 2=intra-ventricular (n=9), 3=IV.ventricle and rhomboid fossa (n=4), and 4=cerebellopontine angle (CPA) and foramen magnum (n=7). Indications to use the QEVO® tool were divided into five "QEVO® categories": A=target localization, B=tailoring of the approach, C=looking beyond the lesion, D=resection control, and E=inspection of remote areas.

Results

Overall, the most frequent indications for using the QEVO® tool were categories D (n=19), C (n=17), and E (n=16). QEVO® categories B (n=8) and A (n=5) mainly applied to intra-ventricular procedures (anatomical area 2).

Conclusion

The new micro-inspection tool QEVO® is a powerful endoscopic device to support the comprehensive visualization of complex intracranial lesions and thus instantly increases intraoperative morphological understanding. However, its use is restricted to the specific properties of the respective anatomical area.

Intraoperatives Monitoring II, Qualitätssicherung, Transsektorale Neurochirurgie/*Intraoperative monitoring II, quality management, trans-sectoral neurosurgery*

P232

Intraoperatives Optical Imaging mit sensorischer Reizung – ein technischer Bericht
Intraoperative optical imaging with tactile irritation – a technical note

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Objective

Resection of brain tumors near eloquent regions without causing additional neurological deficits for patients is challenging for the neurosurgeon in charge. Therefore, neuronavigation and intraoperative electrophysiological stimulation are established tools to increase patients" safety. A novel approach was shown recently with intraoperative optical imaging, to identify functional intact regions of the cortex near the tumor. Although this stimulation is highly accurate, the intraoperative setup is complex, cortex stimulation might cause epileptic seizures and specialized staff is needed. Therefore, we investigated, whether a direct tactile stimulation of different body parts shows also changes in blood flow during intraoperative optical imaging.

Methods

Two patients underwent a tumor resection in general anesthesia of a superficial glioma near the sensory cortex. Intraoperative optical imaging was performed before resection. Patients were stimulated bipolar in the median nerve at the wrist. Afterwards, the hand region, arm region, the abdomen and leg region were brushed with a surgical rubber for tactile irriation. Image data were acquired with a charge-coupled device camera attached via a beam splitter to a surgical microscope. For each stimulation site, image data of a 30s rest period, 30s stimulation period and 85s poststimulus period were acquired from the cortical surface.

Results

The tactile irritation of the hand revealed equal cortical activation compared to bipolar stimulation of the median nerve. Furthermore, a plausible topographic distribution along the sensory cortex during tactile irritation of different body regions was observed, whereby the abdominal stimulation showed no cortical activation. The difficulty of this method remain the motion artifacts during brushing the different body regions and the associated irritation of the skin.

Conclusion

We showed for the first time, that tactile irritation of different skin regions in general anesthesia leads to changes of blood flow during intraoperative optical imaging. With this new method, a patient individualized and simpler intraoperative setting is possible. Further studies are ongoing to standardize this method to enable a broader usage within the neurosurgical society.

Intraoperatives Monitoring II, Qualitätssicherung, Transsektorale Neurochirurgie/*Intraoperative monitoring II, quality management, trans-sectoral neurosurgery*

P234

Das intraoperative Neuromonitoring und die Bedeutung für die chirurgische Behandlung von Hirnstammkavernomen

Predictive value of intraoperative neuromonitoring in brainstem cavernoma surgery

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Objective

Intraoperative neuromonitoring is an established tool for distinct neurosurgical procedures but the predictive value of motor or somatosensory evoked potentials (MEP/SSEP) in brainstem cavernoma (BSCM) surgery is still a matter of debate. This study aimed to evaluate the use of MEP and SSEP in surgically treated BSCM patients.

Methods

62 consecutive patients (≥18 years-old) of a single institution that were surgically treated for BSCM were included. All patients received intraoperative MEP/SSEP monitoring and postoperative follow-up of >3 months. The study endpoints were new postoperative motor or somatosensory deficits and postoperative functional disability at discharge or follow-up. Diagnostic accuracy was determined by receiver operating characteristic (ROC) analyses with area under the curve (AUC) metrics.

Results

Intraoperative decrease of MEP/SSEP was associated with a new postoperative motor (discharge: OR=11.9, p=0.017; follow-up: OR=5.3, p=0.039) or somatosensory (discharge: OR=7.7, p=0.001; follow-up: OR=8.4, p=<0.001) deficit. Binary classification testing revealed sensitivity and specificity values for MEP (discharge: 31% and 93%; follow-up: 33% and 91%) or SSEP (discharge: 82% and 80%; follow-up: 85% and 79%) respectively. ROC analysis and AUC metrics exhibited acceptable performance of intraoperative neuromonitoring for MEP (AUC=0.75, p=0.02) and SSEP (AUC=0.72, p=0.004) values. Subsequent analysis identified an association between intraoperative MEP (OR=6, p=0.047) or SSEP (OR=4.09, p=0.009) decrease and increased postoperative functional disability.

Conclusion

Intraoperative neuromonitoring can reliably predict early postoperative motor or somatosensory deficits after brainstem cavernoma surgery.

Intraoperatives Monitoring II, Qualitätssicherung, Transsektorale Neurochirurgie/*Intraoperative monitoring II, quality management, trans-sectoral neurosurgery*

P235

Qualitätssicherung in der CT-navigierten Wirbelsäuleninstrumentierung – Genauigkeit der postoperativen Schraubenpositionierung in Bezug auf die 3D-navigierte Trajektorienplanung

Quality assurance in CT-navigated spinal instrumentation – accuracy of postoperative screw positioning in relation to 3D-navigated trajectory planning

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Objective

Screw accuracy in spinal instrumentation has so far mainly been evaluated from a clinical point of view according to positioning within cortical bone compartments or in relation to nervous structures. In the light of the anticipated advancements of robotic assistance devices for spinal instrumentation however, it is important to also evaluate the screw accuracy in relation to a preoperative 3D-trajectory plan for quality assurance in navigated screw implants. We sought to evaluate how accurate a 3D-trajectory plan for lumbar pedicle screws can be transferred to the surgical site using CT-Navigation.

Methods

This retrospective analysis was performed on 15 consecutive cases of CT-navigated spinal instrumentations for lumbar spondylosis between February 2014 and June 2016. Intraoperatively, a dedicated 3D-trajectory was planned for all screws using a commercial navigation system. On postoperative CT, implanted screws were manually segmented to derive achieved screw positions. Comparison of 3D-trajecotry plans and implanted screws was performed on the Medical Imaging Interaction Toolkit (MITK) by computing minimal absolute differences (MAD) of screw head and tip points (in mm) and screw axis (in degree), respectively. The percentual overlap of planned and implanted screws was calculated for each screw (Dice-Coefficient). Clinical acceptability of each screw was evaluated by the Gertzbein-Robins classification. Results were evaluated considering the registration error obtained during navigation.

Results

We obtained data for 104 screws covering levels L2-S1. A median axis deviation of 5° (range 1-22°) was shown between planned and implanted screws. Screw head and tip points showed median MAD of 2mm (range 0-11mm) and 4mm (range 0-16mm), respectively. Median Dice Coefficient between planned and implanted screws was 65% (range 34-99%). Screw positioning was clinically acceptable in all cases using the Gertzbein-Robins classification, showing no or only minor (<2mm) cortical breach in 83 (80%) and 21 (20%) cases, respectively. Mean registration error was 7mm (range 5-9).

Conclusion

Despite the clinically acceptable screw placements in all the reviewed screws, considerable deviation between planned and actual trajectory was observed, which exceeded the mean registration error. Hence, factors contributing to screw variations should be evaluated in the future, helping to improve CT-navigated as well as robot-assisted placement of spinal screw implants.

Intraoperatives Monitoring II, Qualitätssicherung, Transsektorale Neurochirurgie/*Intraoperative monitoring II, quality management, trans-sectoral neurosurgery*

P236

Risikofaktoren für das Auftreten einer intraoperativen Somnolenz und einer postoperativen Desorientiertheit bei der Tiefen Hirnstimulation von Parkinson-Patienten

Risk factors for intraoperative somnolence and postoperative disorientation in deep brain stimulation for Parkinson's disease

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Objective

In many centers deep brain stimulation for Parkinson´s disease is performed on awake patients to obtain reliable microelectrode recordings and to perform intraoperative clinical testing. However, some patients become somnolent after the testing or the implantation of the first electrode, some during the testing for the second electrode, thus, hindering reliable evaluation of the optimal stimulation site. In addition, intra- and postoperative disorientation may occur. The aim of our study was to investigate possible influencing factors.

Methods

We retrospectively analyzed 122 patients with Parkinson's disease having received implantation of a DBS system at our centre. Patient age ranged from 42 -75 years (mean 61,8 years). The occurrence of intraoperative somnolence and postoperative disorientation was correlated with the duration of disease prior to surgery, number of microelectrode trajectories, AC-PC-coordinates of the planned target, UPDRS-scores, intraoperative application of sedative drugs, duration of the surgical procedure, perioperative application of Apomorphin and the preoperative L-DOPA, equivalence dosage.

Results

Patients in whom intraoperative somnolence occurred were significantly older than patients without this effect (p=0,039). Patients with intraoperative somnolence had a longer duration of the disease prior to surgery (p=0,080) and their preoperative off-medication- UPDRS was higher (p=0,071). If the planned target was more medial (p=0,060) and more inferior (p=0,051) intraoperative somnolence occurred more often. Sedative drugs, applied to cover skin incision and burr hole trepanation, again, led to more pronounced somnolence (p=0,019). The same was true for longer durations of the surgical procedure (p=0,020). Higher numbers of microelectrode trajectories were more likely associated with postoperative disorientation. Perioperatively applied Apomorphin could reduce the occurrence of somnolent phases during the operation (p=0,026), whereas the amount of the preoperative L-DOPA-equivalent dosage did not seem to have any major effect.

Conclusion

Several influencing factors were found to seemingly increase the risk of intraoperative somnolence and postoperative disorientation. These factors should be taken into account and adjusted, if possible, to permit reliable interpretations of the intraoperative clinical and electrophysiological findings.

Schädelbasiszentren/*Skull base centres*

V183

Evaluation der perioperativen Risiken durch Luftembolien und des postoperativen Outcomes nach Operationen in halbsitzender Position – eine neurochirurgisch-anästhesiologische Analyse

Evaluation of the perioperative risks due to air embolism and postoperative outcome in patients operated in the semisitting position – a neurosurgical and anaesthesiologic analysis

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Objective

The semisitting patient position offers perioperative surgical advantages for selected neurosurgical cases. However, overall benefit may be questioned due to additional risks such as perioperative venous air embolism (VAE) or postoperative pneumocephalus. The aim of this study was to evaluate peri- and postoperative complications and patient outcome from an anesthesiologic and neurosurgical point of view in patients operated in the semisitting position.

Methods

From 2008 to 2018 a total of 827patients were included and retrospectively analyzed. All patients were monitored my continuous transesophageal echocardiography for the detection of VAE. The number and severity of VAE according to the Tübingen classification were documented by the anesthesiologist. Postoperative CT scans were analyzed for complications such as bleeding or pneumocephalus and indication for revision surgery or subdural/ventricular air exchange was noted. Overall outcome by means of Karnofsky index and duration of the in-patient stay were evaluated from the patient charts.

Results

The mean patient age was 47.4 years with a range of 4 to 85 years. A persistent foramen ovale or other right-left shunt was present in 17.1% of patients. Any VAE was detected in 50.7% of patients, a change in expiratory CO2 (Tübingen grade II-V) occurred in 10.0%. No patient presented with hemodynamic instability (grade V). Patients with more than one detected VAE event had a significantly higher risk of showing a clinically relevant grade II-IV ($p=0.001$). The duration of the surgery did not correlate with the severity of the VAE. However, patients with a VAE grade II-IV required longer postoperative ventilation at the ICU ($p=0.01$). An ARDS was diagnosed in 0.4% of all cases and was associated with perioperative VAE ($p<0.001$). Overall outcome did not differ between patients with and without VAE, however patients with an VAE grade II or higher required a significantly longer in-patients stay ($p=0.03$). A postoperative pneumocephalus requiring air exchange was detected in 3% of patients, one subsequently treated with a subdural hygroma drainage (0.1%). No patient presented with new permanent neurological deficits due to paradox VAE or pneumocephalus.

Conclusion

If indicated, the semisitting position can be safely performed in an experienced interdisciplinary team. No fatal adverse events attributable to the positioning were observed in this large patient collective.

Schädelbasiszentren/*Skull base centres*

V184

Therapie von Sinus-Cavernosus WHO Grad I Meningeomen – Langzeitanalyse
Management of meningiomas (WHO I) involving the cavernous sinus – long-term tumour control and functional outcome

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Objective

Preservation of function in patients harboring meningiomas WHO grade I involving the cavernous sinus (CSM) is crucial in the light of sufficient tumor control. Concise data on the functional outcome of an interdisciplinary, multimodal treatment concept are scarce. We analyzed functional outcome and long-term tumor control in CSM patients following microsurgical tumor resection, fractionated stereotactic radiotherapy (FSRT) or a combination thereof.

Methods

Patients with CSM treated between 2003 and 2017 were included in this retrospective study. Prior to FSRT a 68Ga-DOTATATE PET/CT was performed for radiation planning. Volumetric analysis was performed on gadolinium enhanced MRI (BrainLab elements software). Progression-free survival (PFS) was analyzed using the Kaplan-Meier method, the log-rank test was performed to test differences between groups. Cranial nerve function including visual acuity and visual field were analyzed at baseline and during follow-up.

Results

A total of 85 patients with CSM matched the inclusion criteria. Following interdisciplinary tumor board recommendation, 48 patients underwent microsurgical tumor resection (group A), 25 patients received a resection followed by FSRT within 6 months (group B) and 12 patients were treated with FSRT alone (group C). Median total tumor volume and intracranial tumor volume were significantly higher in group A (11.4 cm3/9.5 cm3) and B (13.5 cm3/10.3 cm3) than in group C (4.32 cm3/2.3 cm3). The median follow-up time was 47 months in group A, 46 months in group B and 45 months in group C. 18 patients (37.5%) of group A developed a tumor recurrence whereas no progression was observed in group B and C. PFS at 5-years was 55.7%, 100%, and 100% in groups A, B, and C ($p<0.001$). Indications for maximal surgical resection were space occupying tumors and compression of the optic nerve. Incidence of optic nerve compression was significantly higher in Group A (n=43) and B (n=19) than in group C (n=0). Post-therapeutic new onset or deterioration of double vision was observed 29 % (group A), 17 % (group B) and 0% in group C. A deterioration of visual field occurred in 9% (A),17% (B) and 0% (C) of patients.

Conclusion

In large meningiomas with involvement of the cavernous sinus, a combination of tailored resection and subsequent radiotherapy provides very good results concerning tumor control and functional outcome. In small lesions without the necessity of surgical intervention, radiotherapy alone leads to excellent outcome.

Schädelbasiszentren/*Skull base centres*

V185

Hörerhalt nach der Operation von Vestibularis Schwannomen durch die prophylaktische Gabe von Nimodipine – Studienprotokoll einer randomisierten, multizentrischen Phase III-Studie "AkniPro 2"

Prophylactic nimodipine treatment for hearing preservation after vestibular schwannoma surgery – study protocol of a randomised multi-centre phase III trial – AkniPro 2

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Objective

A previously performed phase III trial on 112 subjects investigating prophylactic nimodipine treatment in vestibular schwannoma (VS) surgery showed no significant effects on preservation of facial and cochlear nerve functions, though it should be considered that protection of facial nerve function was the primary outcome. However, the risk for postoperative hearing loss was halved in the nimodipine group compared to the control group (OR: 0.49; 95%-CI: 0.18-1.30; p=0.15). Accordingly, this phase III extension trial investigates the efficacy and safety of prophylactic nimodipine for hearing preservation in VS surgery.

Methods

This is a randomized, multi-center, prospective, two-armed, open-label phase III trial with blinded expert review and two-stage with interim analysis. 336 adults with the indication for microsurgical removal of VS (Koos I-IV) and serviceable preoperative hearing (Gardner-Robertson scale (GR) 1-3) are assigned to either therapy (intravenous nimodipine 1-2 mg/h from the day before surgery until the fifth postoperative day and standard of care) or control group (surgery only and standard of care). The primary endpoint of the trial is postoperative cochlear nerve function measured before discharge according to GR 1-3 versus GR 4-5 (binary). Hearing function will be determined by pre- and postoperative audiometry with speech discrimination, which will be evaluated by a blinded expert reviewer. Furthermore patient-reported outcomes using standardized questionnaires will be analysed.

Results

Prophylactic parenteral nimodipine treatment may have a positive effect on hearing preservation in VS surgery and would improve patient`s quality of life. Further secondary analysis are planned. Except for dose-depending hypotension nimodipine is known as a safe drug.

Conclusion

In the future, prophylactic nimodipine treatment may be recommended as a routine medication in VS surgery. VS can be considered as an ideal model for clinical evaluation of neuroprotection, since hearing outcome can be classified by well recognized criteria. The beneficial effect of nimodipine may be transferable to other surgical procedures with nerves at risk and may have impact on basic research.

Trial registration: EudraCT-No.: 2019-002317-19, DRKS00019107

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Schädelbasiszentren/*Skull base centres*

V186

Retrospektive Analyse mikrovaskulärer dekompressiver Methoden in der Therapie der Trigeminusneuralgie – Sling vs. Wrapping Technik

Retrospective analysis of microvascular decompression methods for treatment of trigeminal neuralgia – sling vs. wrapping technique

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Objective

Microvascular decompression (MVD) following the technique of neurosurgical pioneer Peter Jannetta, by means of wrapping the nerve with a Teflon felt, has been proven to be the most effective treatment for typical trigeminal neuralgia (TGN) for over 50 years. Yet, a small number of patients experience recurrence of pain, following correct exhibition of operative treatment. Granulomatous and inflammatory reactions to interposed material have been suspected to be responsible for recurrence of pain. As a consequence, we have been performing the sling technique in our institution for the last four years, which aims at permanently displacing the offending vessel, without contact to the trigeminal nerve (CNV).

Methods

We retrospectively examined patients, who had been operated on TGN by means of MVD in our clinic between 2008 and 2020. Sling technique was carried out, by fixating the offending vessel either to the tentorium cerebelli or mastoid bone by means of a Teflon wick. 188 patients (114 wrapping cohort, 74 sling cohort) underwent surgery and were compared for trigeminal pain containment at discharge as well as at follow up, by means of the Barrow Neurological Institute (BNI) Pain Intensity Score (I = No pain, no medications; II = Occasional pain, no medication; IIIA = No pain, continued medication, IIIB = Some pain, adequately controlled with medication; IV= Some pain, not adequately controlled with medication; V = Severe pain/no pain relief) and postoperative complications.

Results

No significant differences were observed between both techniques, neither concerning postoperatively described pain (BNI Score I-III 93.9 vs. 97.3% at discharge and 85.6 vs. 81.8% at follow up; wrapping vs. sling group respectively) nor postoperative complications at a mean follow-up time of 68 vs. 18.6 months. Most frequent complications were facial numbness (20.2 vs. 16.2%) and hypoacusis (5.3 vs. 6.8%).

Conclusion

The sling technique is a safe and effective operative technique to treat typical TGN and poses an elegant alternative to classical wrapping of CNV.

Schädelbasiszentren/*Skull base centres*

V187

Chirurgisches und funktionelles Outcome nach Resektion von 64 petroclivalen Meningeomen
Surgical and functional outcome after resection of 64 petroclival meningiomas

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Objective

The management of petroclival meningiomas (PM) remains notoriously difficult due to their close association to neurovascular structures and complex anatomy. We analyzed surgical and functional outcome of a consecutive series of patients.

Methods

We reviewed patient charts and imaging data of patients with a PM resected at our institution and compared surgical and functional outcomes between subgroups stratified by surgical approach.

Results

A consecutive cohort of 64 patients from 2006 to 2018 were included, of which 67.2% were female with mean age was 55 years (range 21 – 84). Follow-up data were available for 68.8% and reached a mean 42.3 months (range 1 – 129) with a median 28.5 months. Most tumors were WHO grade I (95.3%) with an average size of 37 ± 15 mm. Infiltration of the cavernous sinus was observed in 53.1% of cases and the lesion reached the brain stem in 82.8% of cases. Preoperative cranial nerve palsy was observed in 73.4%, of which trigeminal neuropathy (42.2%), hearing loss (32.8%) and impairment of vision (18.8%) were the most common. A retrosigmoid approach was employed in 78.1% of cases, a pterional in 15.6%, combined petrosal in 3.1% and transnasal as well as subtemporal in 1.6% each. Fifteen cases (23.4%) were resected in a two-staged fashion. Gross total resection (GTR) defined as Simpson grades I and II was achieved in 71.0%, with surgical complications in 21.3% of cases most commonly constituting meningitis (6.3%). Postoperatively, 87.5% of patients had cranial nerve palsy, of which 63.6% had improved or resolved on last follow up. Trigeminal neuropathy had the highest resolution rate with 15.6%, while visual impairment only improved in 1.6% and hearing loss in 4.7%. Achieving GTR was not significantly associated with higher rates of surgical complications (p=.288) or postoperative cranial nerve palsy (p=.842). Tumor progression was observed in 15.9% of patients after a mean 102 months.

Conclusion

Despite the substantial technical challenge, resection of PMs represents the mainstay of tumor control with favourable resolution of perioperatively prevalent cranial nerve palsies.

Schädelbasiszentren/*Skull base centres*

V188

Chirurgische Strategien zur Behandlung von petroclivale Meningiom und Auswertung prognostischer Faktoren, die das klinische Ergebnis beeinflussen

Surgical strategies for petroclival meningioma and evaluation of prognostic factors influencing clinical outcome

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Objective

Despite the advances in skull base surgery, surgical removal of petroclival meningioma (PCM) remains a major neurosurgical challenge in terms of postoperative neurological morbidity and long-term oncological outcome. To date, there are still controversial surgical strategic treatment concepts and limited knowledge about adjuvant radiotherapy, prognostic factors and their influence on the course of the disease.

Methods

The purpose of this study was to evaluate prognostic factors influencing the progression-free survival (PFS) rates of petroclival meningiomas, with a particular focus on the role of the extent of resection and postoperative adjuvant radiotherapy.

Results

Between 1998 and 2018, 89 patients with petroclival meningiomas were treated in our Department of Neurosurgery, of whom 19 patients underwent gross total resection (GTR) and 70 patients underwent subtotal resection (STR). Thirty-one patients received postoperative adjuvant radiotherapy of the residual tumour and fifty-eight were treated with surgery alone. Gross total resection (Simpson Grades I and II) was associated with significantly improved PFS (hazard ratio = 4, CI (95%) 1.3–12, p-value = 0.0107). Adjuvant radiotherapy showed an improvement in PFS (hazard ratio = 2.9, CI (95%) 1.1–7.1, p-value = 0.014). Even the subgroup analysis of extended PCM with infiltration of the cavernous sinus showed an advantage for PFS after GTR of the posterior fossa, i.e. near total resection (NTR). (Hazard ratio = 3.9 , CI (95%) 1.7–9.2, p-value = 0.0017). The additional radiotherapy of the residual tumour in the cavernous sinus in this subgroup also showed a beneficial effect on PFS (hazard ratio = 3.1, CI (95%) 1.2–7.9, p-value = 0.012).

Conclusion

Safely maximising the extent of resection for petroclival meningiomas correlates with a better outcome. Until now, the extension of surgical resection is still the most important prognostic factor in relation to oncological outcome. However, gross total resection of extended petroclival meningioma with infiltration of the cavernous sinus is associated with significant neurological morbidity and requires additional adjuvant therapy concepts.

Schädelbasiszentren/*Skull base centres*

V189

Zeitverlauf der Symptombefreiung nach mikrovaskulärer Dekompression bei Hemispasmus facialis – die Greifswalder-Erfahrung

Time course of symptoms resolution following microvascular decompression in hemifacial spasm – the Greifswalder-Experience

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Objective

Microvascular decompression (MVD) success rates reach 90% in hemifacial spasm (HFS). However, the postoperative course and duration of resolution of the symptoms remain quite variable. The aim of this study is to analyze the different prognostic factors that might determine the postoperative patterns and duration needed until the final recovery is reached.

Methods

A retrospective review of our microvascular decompression database was performed, 287 patients following de-novo MVD, with a minimum follow-up of 6 months were included. Data of the second operation in patients who were operated more than once were excluded. The overall trend of postoperative recovery was modeled. Patients were grouped according to the recognizable recovery patterns. Uni- and multivariable regression analysis was used to identify the factors affecting allocation to the identified patterns, the time needed to initial and final resolution of the symptoms and relapse.

Results

The overall trend of the postoperative course showed improvement by <6 months, followed by relapse peaking around 8 months with a steep remission starting at the 13th postoperative month. Five main recovery patterns were identified: Among statistically significant independent predictors of allocation to the defined patterns was the location of grooving. 257 patients (89,5%) completely recovered postoperatively. Regarding time to initial recovery, AICA (HR: 1.42; CI 1.03-1.98), or >1 vessel compression (HR: 1.42; CI 1.06-1.90), showed a lower hazard of not recovering, and peripheral grooving showed an increased hazard of not recovering (HR: 0.56; CI 0.38-0.81). 114 patients (39.9%) experienced one or more relapses. A statistically significant protective factor for relapse was brainstem grooving (OR: 0.43; CI 0.19-0.90).

Conclusion

We recommend at least 1 year before evaluating the outcome following MVD and deciding to re-operating. In contrast to central brain stem indentation of the facial nerve, peripheral indentation as well as compressions caused by PICA are associated with delayed recovery. Brainstem grooving might be protective against relapse of the symptoms following initial recovery.

Schädelbasiszentren/*Skull base centres*

V190

Transnasaler transmaxillärer prälakrimaler Zugang für Tumore in der Fossa Pterygopalatina – erweiterte Schädelbasischirurgie in einem interdisziplinären Team

Transnasal transmaxillar prelacrimal approach for tumours in the pterygopalatine fossa – extended skull base surgery in an interdisciplinary team

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Objective

The pterygopalatine fossa is located between the posterior wall of the maxillary sinus and the pterygoid plates and therefore deep in the skull base. Surgical access to tumors arising from or invading this region is therefore challenging. The endoscopic transnasal transmaxillar approach provides a minimal-invasive route to access this region. It is associated with less morbidity than traditional microscopic transcranial or transfacial approaches, while providing better visualization. We aimed to explore the feasibility of this approach based on our clinical experience.

Methods

Patients harboring pathologies involving the pterygopalatine fossa were evaluated in this study. The surgical corridor included a mega-antrostomy and medial maxillectomy with removal of the posterior wall of the maxillary sinus. A prelacrimal window maximized the access to the anterolateral maxillary sinus while preserving the inferior turbinate and the nasolacrimal duct. The surgical treatment was performed by an interdisciplinary skull base team comprising one neurosurgeon and one otorhinolaryngologist. Neuronavigation and neurophysiologic monitoring, including dynamic electromyography (EMG), motor evoked potential (MEP), and somatosensory evoked potential (SSEP) of the Vth nerve was furthermore applied. A micro-doppler probe was utilized to locate important vessels.

Results

A total of four patients (n=4) were operated via this approach in our department between September 2019 and November 2020. Patients" age ranged from 14 to 79 years of age. The tumor pathologies comprised meningiomas (n=2), a neurinoma (n=1) and one juvenile nasopharyngeal angiofibroma (JNA) (n=1). No postoperative complications could be registered. In two cases a submaximal resection was achieved due to V3 involvement and the associated risk of nerve injury. In the patient harboring a JNA, a small residual tumor adherent to the internal carotid artery was left to avoid rupture. Overall, a good surgical reduction of tumor tissue and in one case a complete removal was achieved.

Conclusion

The endoscopic transnasal transmaxillar approach with rod lens endoscopes to the pterygopalatine fossa is a feasible surgical corridor with low morbidity. The prelacrimal route is an essential improvement to traditional endoscopic transmaxillar approaches that increases access and freedom of movement to the anterolateral maxillary antrum. An experienced interdisciplinary team is the essential backbone for this type of surgeries.

Freie Themen/*Free topics*

V191

Antiapoptotische und neuroprotektive Wirkung von Thiaminderivaten *in vitro*
Antiapoptotic and neuroprotective effects of thiamine derivatives in vitro

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Objective

During surgery, cells of the nervous system (NS) are exposed to various stressors, which can lead to consequential damage to nerve tissue. So far, there is little knowledge about neuroprotective substances that can prevent surgically induced nerve damage. Thiamine (TM) is an essential cofactor in energy metabolism and the deficiency reduce conduction speed in neuronal cells and can lead to Wernicke Encephalopathy. In addition, an anti-apoptotic function of TM has been described before. Therefore, the aim of study was to investigate the neuroprotective influence of different TM derivatives and the associated anti-apoptotic cellular mechanisms.

Methods

Immortalized Schwann (SW10) and neuronal cells (RN33B) were seeded and four hours pretreated with 10 µM thiamine hydrochloride (TIH), 5 µM sulbuthiamine (SBT), 5 µM dibenzoylthiamine (DBT) or 5 µM benfothiamine (BFT). Then the cells were stressed with 150 mM NaCl (osmotic stress (OMS)) or 2 % Ethanol (oxidative stress (OXS)). After 24 hours, the cellular release of lactate dehydrogenase (LDH) was measured. The LDH release of total lysed cells was set to 100 %. Proteins of treated and untreated cells were separated using SDSPAGE. In western blot analysis, the amount of total and phosphorylated protein of AKT(Ser473), CREB(Ser133), and ERK1(Tyr202) and ERK2(Tyr204) was investigated.

Results

Under TIH treatment, reduced cell death was measured in neuronal and Schwann cells during OXS. According to western blot analysis, treatment with TIH resulted in increased amount and phosphorylation of CREB(Ser133) in SW10 cells during OMS. After treatment with SBT, reduced LDH release was observed in neuronal cells during OMS, which was associated with an increased AKT(Ser473) and CREB(Ser133) protein level. Treatment with DBT reduced LDH release in Schwann cells during OMS and also led to an increased amount of CREB(Ser133). Under BFT treatment, reduced LDH release was measured in SW10 cells during OMS. In the same time the total amount of CREB(Ser133) was increased..

Conclusion

The measured cell death reduction in a surgical-like stress model suggests that TM and its derivatives may have a beneficial effect on the survival of NS cells by associated increased levels and activation of anti-apoptotic proteins. The influence of TM on these and other antiapoptotic proteins should be further investigated.

Freie Themen/*Free topics*

V192

Kranioplastik nach VP-Shunt – ein riskanter Eingriff
Cranioplasty following ventriculoperitoneal shunting – lessons learned

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Objective

Cranioplasty (CP) is considered as a straightforward and technically unchallenging operation; however, complication rates are high reaching up to 56%. Presence of a ventriculoperitoneal shunt (VPS) and timing of CP are reported risk factors for complications. Pressure gradients and scarring at the site of the cranial defect seem to be critical in this context. The authors present their experiences and lessons learned.

Methods

A consecutive series of all patients who underwent CP at the authors" institution between 2002 and 2017 were included in this retrospective analysis. Complications were defined as all events that required reoperation. Logistic regression analysis and chi-squared test were conducted to evaluate the complication rates according to suspected risk factors.

Results

A total of 302 patients underwent cranioplasty between 2002 and 2017. The overall complication rate was 17.5%. Complications included epi-/subdural fluid collection (7.3%) including hemorrhage (4.6%) and hygroma (2.6%), bone graft resorption (5.3%), bone graft infection (2.0%), and hydrocephalus (5.7%). Overall, 57 patients (18.9%) had undergone shunt implantation prior to CP. The incidence of epi-/subdural fluid collection was 19.3% in patients with VPS and 4.5% in patients without VPS, OR 5.1 (95% CI 2.1–12.4). Incidence of hygroma was higher in patients who underwent early CP. Patients with temporary shunt ligation for CP did not suffer from complications.

Conclusion

CP in patients with a VPS remains a high-risk procedure. Any effort to understand the pressure dynamics and to reduce factors that may trigger the formation of a large epidural space must be undertaken.

Freie Themen/*Free topics*

V193

Ist die Aufwärtsbewegung des Liquors wichtig für den ETV-Erfolg?
CSF upward motion crucial for ETV success?

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Objective

ETV is indicated for treating obstructions of major CSF pathways, ventricular dilation and hydrocephalus complaints. Despite these parameters the outcome evaluation yields success rates of not more than 60-70% for shunt independency. Hence compromised CSF absorption seems to occur more often than expected. Beside the time scale of obstruction, we have extended the search for parameters suitable to assess involved CSF dynamics.

Methods

Prospective study in 55 pediatric patients (8 yrs. mean) between 2000 and 2020 with aquaeductal stenosis, Chiari- and Dandy Walker malformation showing different grades of ventricle outlet obstruction with escalating head circumference, elevated Evans- and FOH-Ratios, spontaneously perforated septum pellucidum over 5 years mean follow up time. All patients underwent MRIs pre- and postoperatively. Success was defined as abatement of complaints, papilledema and elevated head circumference, flow void signals through the stoma. Social outcome like protected education was documented. Four patients were studied pre-and postoperatively by real time (RT) MRI CSF flow studies.

Results

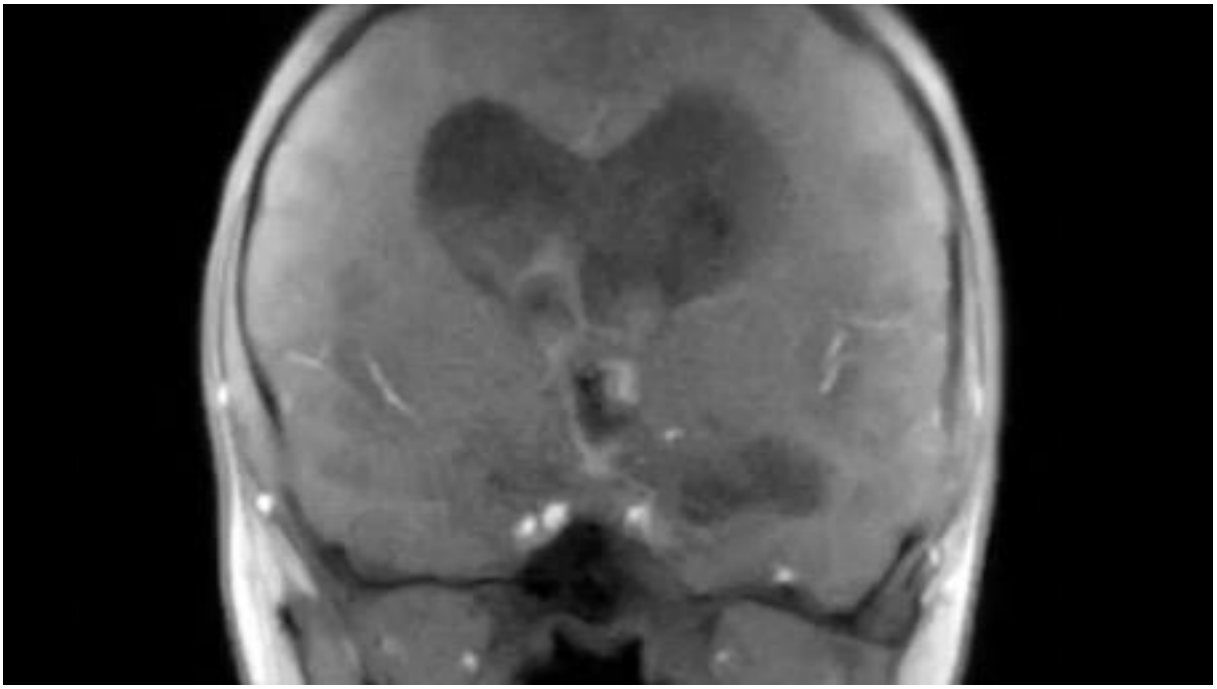
In 70.9% bowing of the floor of the 3rd ventricle was observable. 49% of the children had spontaneous septal perforations, parachute signs or an open aqueduct before ETV (36%). ΔER and ΔFOHR were reduced by ETV for 0.04 and 0.06 (mean) respectively. Opened stoma with flow void signs were found in 81%. Previously obstructed aqueducts post ETV open without addressing the aqueduct occurred in 12.7%. Increase of head circumference stopped in 65.4%. Shunt insertion in cases of developmental delay and persistent papilledema was estimated as 29%, re-ETV in 2 cases. The mean interval for shunt insertion after ETV was 97 days (Max=556d). CSF upward motion intraoperatively was regularly observed (video1). Flow passing the patent stoma could be demonstrated by RT-MRI in 3 patients (video2) in contrast to one failed ETV. Regular education correlated significantly ($p<0.05$) with ventricular volumetry and postoperative size ratios.

Conclusion

Challenging concepts of CSF dynamics have come into focus during the last 5 years. Understanding hydrocephalus with perturbated resorptive capacities of the glymphatic system focus on sustained alterations induced by obstructive structures. Enabling CSF upward flow driven by inspiration seems crucial for successful ETV and restored resorptive capacity.

Fig. 1

Fig. 2



Freie Themen/*Free topics*

V194

Intrakranielles Hirndruckmonitoring in der Diagnose des Pseudotumor cerebri Syndroms
Intracranial pressure monitoring in the diagnosis of pseudotumor cerebri syndrome

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Objective

Pseudotumor cerebri syndrome (PTCS) mostly occurs in obese women of childbearing age. Usually, the diagnosis is established based on the presence of papilledema, an elevated opening pressure measured at lumbar puncture, a normal CSF composition and on the absence of pathological findings in MRI. Although it has been shown that continuous ICP monitoring can be a helpful adjunct, especially when findings are inconclusive or medical treatment fails, data on ICP dynamics in PTCS are sparse and their interpretation remains uncertain. The aim of this study is to highlight the utility of continuous ICP monitoring in diagnosing PTCS.

Methods

All adult patients with presumed PTCS in which ICP monitoring with an epidural sensor (Neurodur®, Raumedic) was performed between 2010 and 2020 were included. Clinical findings and ICP dynamics, emphasizing on baseline ICP, ICP fluctuations and the presence of ICP oscillations (A- and B-waves) were analysed. Baseline ICP values were defined as follows: normal (0-10 mmHg), elevated (11-20 mmHg), highly elevated (21-40 mmHg) and severely elevated (> 40 mmHg).

Results

Epidural ICP monitoring was performed in 42 patients (35 women and 7 men), with at least one nocturnal recording in every patient (range 1-5, median 2). There were no procedure related complications. Dislocation of the sensor occurred in 4 patients. Aided by the ICP dynamics the diagnosis of PCTS was confirmed in 35 patients, which subsequently received a ventriculoperitoneal shunt. ICP values in this group were normal in 4 (11,4 %), elevated in 9 (25,7 %), highly elevated in 16 (45,7 %) and severely elevated in 6 (17,1 %) patients. ICP-oscillations in the form of A-, B- and complex-waves formations were found in 10 (28,5%), 35 (100%) and 25 (71,4%) patients respectively. In 7 patients ICP investigation revealed normal values and guided the decision not to proceed with further surgical treatment.

Conclusion

Continuous epidural ICP monitoring is a safe and useful diagnostic tool for investigating PTCS patients especially in atypical cases and when surgical treatment is considered. An increased baseline ICP, large ICP fluctuations as well as the presence of ICP oscillations (A- and B-waves) during recordings can support the diagnosis of PCTS.

Freie Themen/*Free topics*

V195

Nicht-invasive Ultraschall (US) basierte Abschätzung von intrakraniellem Druck (ICP) und Ventrikelweite als ideale Erst- und Verlaufsdiagnostik bei Patienten mit Hydrocephalus

Non-invasive ultrasound (US) assessment of intracranial pressure (ICP) and ventricular size as an ideal first-line and follow-up diagnostic tool in patients with hydrocephalus

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Objective

The aim of this project is to use non-invasive ultrasound technology to research essential and fundamental physiological and pathophysiological relationships between intracranial pressure, ventricular width and individual factors. Furthermore we aim to establish reliable, non-invasive examination methods for patients with hydrocephalus.

Methods

239 children and 132 adult patients with hydrocephalus of different origin were included. Transorbital US measurement of the optic nerve sheath diameter (ONSD) was performed to assess ICP and transtemporal US measurement of the third ventricle diameter (TVD) provided insights into the ventricular system. US investigations were done initially, after therapy and repeatedly during the course of the disease and were correlated with MRI/CT findings, opthalmological, clinical and invasive ICP-parameters.

Results

In 81 patients, ONSD was compared to invasively measured ICP and correlated well ($r= 0.65$, $p< 0.01$). In 215 patients, ONSD and TVD values measured at initial diagnosis or at shunt failure, were increased (mean ONSD 5.9±0.6mm, mean TVD 7.86±5.86mm) and decreased significantly ($p<0.001$) after therapy (mean ONSD 5.2±0.4mm, mean TVD 4.86±4.57mm). Shunt or ETV failure led to significant and quick re-increase of both ONSD and TVD.

Conclusion

Transorbital US ONSD and transtemporal US TVD are an excellent, non-invasive first-line screening tool if hydrocephalus is suspected in any age-group and can be used to reliably follow-up hydrocephalus patients after therapy.

Freie Themen/*Free topics*

V196

Shuntoskopie-gesteuerte versus freie-Hand-Technik bei der Anlage des intraventrikulären Katheters
Shuntoscope-guided versus free hand technique in ventricular catheter placement

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Objective

The position of the intraventricular catheter is essential for a proper function of the cerebral shunt system or external ventricular drainage. Placement of the catheter usually depends on the skills of the surgeon using Free-Hand-Technique and can lead to position-dependent complications. However, a camera-assisted method using the semi-rigid shuntoscope can be helpful. Shuntoscope-assisted ventricular catheter placement has been reported to reduce shunt failure in uncontrolled series. We investigated the efficacy of both techniques in a retrospective monocentral study.

Methods

Between September 2018 and August 2020, in 55 pediatric and adult procedures an intra-ventricular catheter with two different techniques were implanted; the shuntoscope-guided technique (n=29) and the free-hand technique (n=26). The records were reviewed retrospectively. Catheter positioning was graded on postoperative imaging using three-point scale from Hayhurst et al. 2010. All patients were operated by the same surgeon. Complications and revisions rate were compared between the two groups.

Results

29 patients, 6.3 years old in average, range 1.4 – 27.7 years, 48.3% female and 51.7% male, received intra-ventricular catheter using the shuntoscope-guided technique. 26 patients, 28.6 years old in average, range 1.0 – 79.5 years, 73.1% female and 26.9% male, received intra-ventricular catheter using the free-hand technique. The success rate for the optimal placement of the intra-ventricular catheter with a grade I on the Hayhurst scale was significantly higher in the shuntoscope group (93.1%) than in the free-hand group (80.2%), p <0.029. 20.7% of the patients in the shuntoscope group had a revision operation, one revision was due to wound infection, on the contrary, the revision rate was in the Free-Hand-Group higher with 31.8%.

Conclusion

Our current study confirms that insertion of the intra-ventricular catheter using shuntoscope-guided technique in pediatric and adult patients is a safe and effective procedure with high success rate of a correct position and fewer related complications and revisions.

Reference:

Hayhurst C, Beems T, Jenkinson MD, Byrne P, Clark S, Kandasamy J, Goodden J, Nandoe Tewarie RD, Mallucci CL. Effect of electromagnetic-navigated shunt placement on failure rates: a prospective multicenter study. J Neurosurg. 2010 Dec;113(6):1273-8. doi: 10.3171/2010.3.JNS091237. Epub 2010 Apr 16. PMID: 20397892.

Freie Themen/*Free topics*

V197

Die ersten Neurochirurginnen in Deutschland
The first female neurosurgeons in Germany

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Objective

Women in leading positions in neurosurgery are still underrepresented. In 2016, only 14 % of the neurosurgery departments in German hospitals listed woman in leading positions (chief and senior physicians). In our project we present the lives of the first female neurosurgeons in Germany who achieved their specialization in a time when neurosurgery as a discipline was still new in Germany. This project is embedded in current international research on the history of women in neurosurgery. The beginning of neurosurgery in Germany was shaped by Fedor Krause, Otfrid Foerster und Wilhelm Tönnis, among others. But who were the first female neurosurgeons in Germany?

Methods

Personal interviews, telephone interviews and literature research.

Results

Alice Rosenstein (1898-1991) was the first woman who worked as a female neurosurgeon in Germany in the 1920s when German neurosurgery was in its infancy. She was a student of Otfrid Foerster and in 1930, opened the new operation theatre in Karl Kleist"s "Nervenklinik" in Frankfurt. In 1933, she was expelled from Germany and escaped to the US. Thirty-five years after Alice Rosenstein had left Germany, the first woman became a specialist of neurosurgery in Germany: In 1968, Gisela Liermann (now Ludwig) finished her training in neurosurgery in Berlin-Buch (GDR) under Friedrich Weickmann. Her colleague Immetraut Ferchland (now Kalweit) succeeded in 1976, whereas the first certified West German female neurosurgeon was Ruth Ilse Kahl in 1969. Margareta Klinger and Jutta Krüger were the first women in (West) Germany who achieved the habilitation in neurosurgery in 1980. Gabriele Schackert, neurosurgeon since 1984, is the first female neurosurgeon who in 1993 became a chair holder in a university hospital.

Conclusion

All these women faced similar struggles even though their career paths have been different. Despite the difficulties at that time, they achieved their goals. Young female neurosurgeons can still take them as role models because only few of them are represented in leading positions in neurosurgery though women account for more than half of all medical students.

Funktionelle Neurochirurgie und Schmerz II/*Functional neurosurgery and pain II*

V198

Interosseus anterior Syndrom – Ein nervenchirurgisches Problem?
Interosseous anterior syndrome – No space left for surgery?

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Objective

Since the first description by Nevin and Kiloh the compression syndrome of anterior interosseous nerve has been the subject of controversial discussion. Recently, the use of MR-neurography (MRN) and high-resolution neurosonography (HRNS) spawned the idea of neuritis as only agent causing a fascicular motor lesion.The co-existence of a "real" mechanic compression neuropathy is severely called into question, and consequently surgical treatment is losing importance.

Methods

Retrospectively, we analyzed medical charts of n= 9 treated surgically for interosseus anterior syndromepatients. Demographics, clinical and imaging features, intraoperative findings and outcome were assessed.

Results

Overall n= 9 patients were assessed, of these n= 4 were female and n= 5 male. Mean age was 38 years (range 7-67 years). Clinical symptoms consisted of pain in n= 4, typical pinch grip weakness in n= 10 and sensory deficits in n= 8 patients. N= 3 suffered from prior traumatic arm fractures. N=1 was treated unsuccessfully with immunoglobulins before. N= 10 patients were assessed by HRNS and n= 8 with MRN. The preoperative imaging correlated in all cases with intraoperative findings. Specifically, in n= 6 patients' compressive fascia, in n= 2 additional nerve crossing vessels and in n= 3 a massive scar was found and released. Open surgery was performed in n= 7 and endoscopic assisted surgery in n=2 patients. No complications occurred. Mean follow-up 6.75 months in the surgical group with n=1 lost to follow-up. All other patients reported on pain relief and in n= 6 motoric function improved significantly.

Conclusion

In our experience mechanical compressive interosseous anterior syndrome exists besides the recently described causal neuritic proximal fascicular lesion. Imaging techniques such as MRN and HRNS facilitate the correct identification of the causal lesion, unraveling the presence of either compressive neuropathy or neuritis. Therefore, meticulous preoperative work-up is mandatory to decide on the appropriate therapy.

Funktionelle Neurochirurgie und Schmerz II/*Functional neurosurgery and pain II*

V199

Kartierung kortikaler Sprachareale mittels Doppelpuls-TMS – eine Proof-of-Principle Studie
Mapping cortical language regions using paired-pulse TMS – a proof-of-principle study

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Objective

Assessing the cortical representation of language in the individual patient, e.g. by means of repetitive transcranial magnetic stimulation (rTMS), is of high importance in the preoperative context. We could recently show that rTMS with a frequency of 30 Hz is superior to the most commonly used protocol of (5-)10 Hz. Nevertheless, the still relatively low number of evoked language errors and the discomfort evoked by the stimulation drive the need for a further improved stimulation protocol. We, therefore, tested whether paired pulse (pp-)TMS is also suitable for inducing language errors.

Methods

13 healthy, right-handed subjects (f=6, 25-41 years) were investigated using two different rTMS protocols: (i) the 30 Hz rTMS as control and (ii) the novel pp-TMS (interstimulus-interval: 7 ms). TMS protocols were applied in a pseudo-randomized order during a picture naming task (picture-to-trigger interval: 0 ms) over cortical language areas. Language errors were post-hoc analysed by two independent raters and were assigned to eight different error categories. The level of pain was assessed on a subjective 0-10 numeric rating scale (NRS).

Results

30 Hz rTMS evoked a significantly higher number of errors than the pp-protocol, i.e., 18 ± 12 % vs. 10 ± 7 % ($p<0.05$). However, pp-TMS was significantly better tolerated with a mean NRS of 2.3 ± 1.6 vs. 3.4 ± 1.5 ($p<0.05$, FDR-corrected). Of note, pp-TMS evoked a higher number of anomias (15 ± 15 %) than 30 Hz rTMS (4 ± 7 %; $p<0.1$, FDR-corrected).

Conclusion

We could show that single pp-TMS is capable of inducing language errors whilst being well-tolerated by the subjects. Therefore, pp-TMS might be an alternative protocol for language mapping, also when considering safety aspects (lower total amount of electric current). Nevertheless, the pp-TMS protocol need to be further evaluated to optimize its potential use in preoperative language mapping.

Funktionelle Neurochirurgie und Schmerz II/*Functional neurosurgery and pain II*

V200

Methodische Überlegungen zur Vorhersage des "sweet spots" für die tiefe Hirnstimulation basierend auf probabilistischer Traktographie

Methodological considerations on predicting the sweet spot in deep brain stimulation based on probabilistic tractography

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Objective

Deep Brain Stimulation (DBS) has evolved to a standard treatment of various movement disorders. As DBS of specific neuronal structures also affects distant areas connected via fibres travelling through the volume of tissue activated, these fibre tracts themselves are also gaining specific interest for planning of DBS surgery and could serve as a base for patient-specific targeting. Probabilistic tractography is a powerful tool to reliably predict subcortical fibre tracts based on diffusion tensor imaging. We investigated possible methodologic influences and pit-falls in probabilistic tractography and their implications for clinical studies in DBS patients.

Methods

We retrospectively analysed 14 patients suffering from Essential Tremor and 19 patients suffering from Parkinson's disease having received implantation of DBS systems at our centre. A workflow for probabilistic tractography was established using FSL 6.0.3 (fsl.fmrib.ox.ac.uk). DWI-images were acquired at a 3T MRI scanner (Magnetom Skyra, SIEMENS) with 64 gradient directions. Patients were under general anaesthesia during image acquisition. We defined subcortical seed- and target regions to exemplarily track the dentato-rubro-thalamic tract (DRTT). DBS electrodes were reconstructed using LeadDBS (lead-dbs.org). We evaluated possible influences in the workflow and their implication on measured distances to the specific electrode poles.

Results

Several pit-falls were identified in the workflow. Main influences on the measured distance of electrode poles to the DRTT were normalization into the MNI standard space and the method of definition of thresholds of the obtained probability maps. Additionally, the definition of criteria for evaluation of thresholds resulted in non-linear effects regarding distances from electrode poles. The way of measuring these distances either manually in a semi-objective manner or based on automated algorithms yielding to local distance maps resulted in slightly different findings.

Conclusion

Probabilistic tractography has been used multiply with respect to different questions in the field of DBS. As a variety of different parameters has to be defined for various steps in the workflow, special attention should be paid to possible influences on measurements used for these studies, which are often underestimated. Due to the lack of standardization, scientists should be aware of these influences regarding adequate interindividual comparability of results and objectively define individual standards.

Funktionelle Neurochirurgie und Schmerz II/*Functional neurosurgery and pain II*

V201

Psychologische Faktoren und deren Einfluss auf Outcome-Parameter nach peripherer Nervenfeldstimulation (PNFS) bei Patienten mit chronischer Lumbago

Psychological parameters and their influence on outcome measures of peripheral nerve field stimulation (PNFS) in chronic low back pain

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Objective

PNFS is effective in patients with chronic low back pain. As the treatment of low back pain strongly depends on psychological factors, this study evaluates the impact of such factors on outcome measures after lead- and neurostimulatorimplantation.

Methods

Between 2014 and 2019 a prospective cohort study of 40 patients with chronic lumbar pain was conducted. Symptom checklist-90 (SCL-90) measured the subjective psychopathology. Hospital Anxiety and Depression Scale (HADS) score was assessed at baseline to measure symptoms of anxiety and depression. Pain intensity (NRS), SF12v2 with Physical Component Summary (PCS) and Mental Component Summary (MCS) scores, and Oswestry Disability Index (ODI) were assessed pre- and postoperatively as well as 3 and 6 months after PFNS implantation. All outcome values were compared to baseline data. Statistical analysis was performed using depending t-test and analysis of variance (ANOVA). A p-value <0.05 was considered significant.

Results

The cohort consisted of 40 patients (19 females, 21 males) with a median age of 60.5 years (IQR25-75 52-67 years). NRS, ODI, and SF12v2 showed significant improvement in the whole follow up period compared to baseline values ($p<0.05$). Elevated HADS scores for anxiety were seen in 64%, for depression in 77% of the patients at baseline. SCL-90 was pathologic in 72% of the cases. A one-way ANOVA revealed no differences between elevated HADS- and SCL-90 values and all outcome measures after PNFS implantation in the whole follow up period ($p>0.05$).

Conclusion

Chronic low back pain is often associated with mental health problems. Highly elevated levels for anxiety and depression as well as subjective mental stress in patients with chronic low back pain had no negative impact on NRS, ODI, and SF12v2 in the whole follow up after PNFS implantation.

Funktionelle Neurochirurgie und Schmerz II/*Functional neurosurgery and pain II*

V202

Lebensqualität nach der Behandlung peripherer Nerventumoren – Ergebnisse des retrospektiven Studienarms eines multizentrischen Registers

Quality of life after treatment of patients with tumours of peripheral nerves – results from the retrospective study arm of a multicentre registry

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Objective

Peripheral nerve tumors are rare diseases. So far, no multicenter data on long-term outcomes, efficacy of treatment and diagnostics or on life quality exists. The establishment of the peripheral nerve tumor registry (PNTR) in 2017 allows for systematic analysis of patients with tumor in association to peripheral nerves. To what extent life quality might be affected by the disease has never been studied.

Methods

Quality of life was assessed by the Euro-Qol-5D-5L (EQ-5D-5L) and Euro-Qol visual analog scale (EQ-VAS) survey at follow-up in the retrospective study arm in 2 out of 8 participating study centers. An index is calculated based upon EQ-5D-5L for quantification of health state (<0: worst possible state of health, 1: best possible state of health). The EQ VAS ranges from 0 (worst possible health status) to 100 (best possible health status). Patient characteristics (age, sex) as well as disease (histopahology) and treatment (pre- and postoperative symptoms, type of treatment) specific data was analyzed.

Results

EQ-5D-5L survey were sent to 96 patients. Response rate was 35 % (n=36, mean age of 44 years, 14 female, 22 male patients). Most frequent histopathology w schwannoma(n=24) and perineurioma (n=5). Other histopathologies were neurofibroma (n=2), malignant peripheral nerve sheath tumor (MPNST) (n=2), non-hodgkin lymphoma (n=1), plexiform neurofibroma (n=1) and fibromyosarcoma (n=1). Prevailing preoperative symptoms were pain in 44 %, motor deficits in 28 %, and sensory deficits in 50 %. Patients were treated by complete tumor resection (89 %) or biopsy (11 %). Reported symptoms in the actual survey were pain in 17 %, motor deficits in 36 % and sensory deficits in 56 %. Quality of life was assessed at a mean of 48 months after initial presentation and treatment. Only 22% of patients reached the highest index score of 1.0 in EQ-5D-5L. Patients with MPNSTs and perineurinoma reported severe problems in the dimension anxiety and pain(Table 1). In the Euro-Qol Visual Analog Scale (VAS) patients rated their overall health with a median of 80 (25-100).

Conclusion

Measures of life quality in patient with peripheral nerve tumors reported higher numbers of problems in the 5 dimensions of EQ-5D-5L compared to the General population in Germany. Type of tumor might be the most significant factor affecting life quality in the dimension of pain and anxiety.

Fig. 1

	Mobility n (%)	Self-Care n (%)	Usual Activities n (%)	Pain n (%)	Anxiety n (%)
Level 1 (No problems)	26 (72,22)	33 (91,67)	24 (66,67)	12 (34,29)	29 (80,56)
Level 2 (slight problems)	5 (15,89)	1 (2,78)	7 (19,44)	13 (37,14)	2 (5,56)
Level 3 (moderate problems)	5 (15,89)	1 (2,78)	2 (5,56)	8 (22,86)	4 (11,11)
Level 4 (severe problems)	0 (0)	1 (2,78)	3 (8,33)	1 (2,86)	1 (2,78)
Level 5 (extreme problems)	0 (0)	0 (0)	0 (0)	1 (2,86)	0 (0)
Total	36 (100)	36 (100)	36 (100)	35 (97,22)	36 (100)

Funktionelle Neurochirurgie und Schmerz II/*Functional neurosurgery and pain II*

V203

Lebensqualität nach Dekompression des Nervus pudendus – Macht die chirurgische Behandlung Sinn?
Quality of life QoL after decompression of the pudendal nerve – Is surgery a viable therapeutical option?

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Objective

Pudendal neuralgia can be caused by a rare compression neuropathy. Affected patients suffer from severe impairment of their social and personal life. Surgical decompression of the nerve is a treatment option. We evaluated outcomes of our operated patients in terms of patient"s satisfaction.

Methods

From 2015-2020 n=29 patients were operated for pudendal neuropathy, n=25 (n= 31 procedures) could be included in this retrospective study. Patient data and patient"s satisfaction were assessed using an adapted questionnaire.

Results

Mean age was 54 years, n=15 were female, n= 10 male. Pain was present in all patients, n= 5 presented with sensory, n=6 with motor deficits. All patients received preoperative nerve block. In n= 29 surgeries, we performed dorsal transgluteal decompression (n=13 unilateral/ n=12 bilateral) and in n=2 transperineal ventral. The identified compression site was in n=15 a hypertrophic sacrotuberal ligament. Additionally, n n=16 cases we found scarring and fibrous tissue, varicosis, and a sacrospinal ligament compression. No perioperative complications occurred. Overall postoperative pain intensity dropped significantly from 7.96 on Visual Analogue Scale VAS to 5.96 ($p<0.0002$). Pain medication could be reduced in n=10, n=11 improved their free time life activity and n=17 patients overall well-being.

Conclusion

In our experience, surgical pudendal nerve decompression led to a significant improvement if patient"s life quality. Careful patient selection and meticulous workup are mandatory for a successful treatment. Further studies with larger patient groups and longer follow-up are required.

Funktionelle Neurochirurgie und Schmerz III/*Functional neurosurgery and pain III*

V204

Radiofrequenzdenervierung für Facettengelenksarthropathie hat bessere Ergebnisse in der Schmerzreduktion und Lebensqualität im Vergleich zur chemischen Neurolyse (Ethylalkohol 95% oder Glycerol 20%)

Radiofrequency denervation therapy for lumbar facet joint arthropathy – enhanced outcome compared with chemical neurolysis (ethyl alcohol 95% or glycerol 20%)

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Objective

Chronic low back pain is a major source of disability and loss work productivity worldwide.Treatment modalities of back pain due to facet joint arthorpathy include chemical neurolysis (Ethyl Alcohol or Glycerol) and radiofrequency denervation of lumbar facet joints. Long-term outcome of these semi invasive techniques are currently unclear. We hypothesize that radiofrequency denervation is associated with superior pain abolishment and less complications than chemical neurolysis

Methods

Prospective study between 01.12.2017 and 01.12.2019. Adult patients with recurrent chronic low back pain, resistant to non-invasive therapy were included. Spinal imaging was performed to exclude alternative diagnoses. Patients were grouped based on treatment Modality into radiofrequency denervation (Gr. RFD), chemical neurolysis with Ethyl-Alcohol 95% (Gr. EA-95) and Glycerol 20% (Gr. Gly-20). The Core Outcome Measures Index for the back (COMI), WHO pain ladder level and VAS (Visual Analog Scale)-scores were determined.Outcome was determined pre-interventional, after 6 weeks, 6 and 12 months.

Results

95 patients with a mean age of 63.7 years were included. Prior to intervention, a mean COMI-score of 8.31 and a VAS-score of 8.01 were encountered. A total of 30 patients underwent RFD, 35 patients were treated with EA-95 and 35 patients were exposed to Glycerol 20% neurolysis. No statistically significant differences were found between the three groups. Upon intervention however, patients treated by RFD had significantly lower VAS-levels compared with Ethyl Alcohol after 6 weeks (VAS: 4.33 vs.6,12 (P<0.05)). Also, after 6 months both VAS and COMI-scores were significantly decreased in RFD-patients than those treated by Gly-20 (respectively VAS:4.42 vs.6.64, P

Conclusion

The Radiofrequency denervation in therapy recurrent chronic lower back pain is associated with better results in pain reduction and quality of life compared to chemical neurolysis. High complication rate after chemical neurolysis with EA-95 compared to alternatives. In our view, in the absence of contraindications radiofrequency denervation should be considered as the treatment of choice in patients with symptomatic facet arthropathy.

Funktionelle Neurochirurgie und Schmerz III/*Functional neurosurgery and pain III*

V205

Wiederherstellung Laser evozierter Potentiale bei chronischen neuropathischen Schmerzen durch Dorsalganglienstimulation – Nur ein elektrisches Phänomen oder Neuroplastizität?

Restored laser evoked potentials in chronic-neuropathic pain patients under dorsal root ganglion stimulation treatment – Mere electrical phenomenon or neural plasticity?

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Objective

Dorsal root ganglion stimulation (DRGS) relieves pain in patients with chronic neuropathic pain. However, its neurophysiological mechanism remains unclear. We used laser evoked potentials (LEP) to verify our hypothesis that the recovery of LEP may reflect DRGS induced neuroplasticity of the nociceptive system.

Methods

Nine patients (mean age 56.8 years, range 36 to 77 years, 2 females) diagnosed with chronic neuropathic pain were enrolled in the study. We measured each patient"s LEP at the painful limb and contralateral healthy limb on the first, fourth, and seventh day after implantation of the DRGS system. Their pain assessment was performed according to the numeric rating scale (NRS) at the same time.

Results

The LEP amplitude of the N2-P2 complex in these patients showed a significant increase at day 7 compared to day 1 ($Z = -2.666$, $p = 0.008$) and day 4 ($Z = -2.547$, $p = 0.011$), respectively. There was no significant difference in the N2-P2 complex amplitude between the ON and OFF states of the DRGS. Compared to the preoperative assessment, the patients" NRS significantly decreased after 1 day ($p = 0.007$), 4 days ($p = 0.007$), and 7 days ($p = 0.007$).

Conclusion

In this study, we showed that under DRGS treatment, the LEP of neuropathic pain patients recovers within a period of 7 days. The DRGS treatment has a lasting rather than a temporary effect. DRGS can also significantly reduce the NRS in patients with chronic neuropathic pain. This reflects DRGS induced neuroplasticity in the nociceptive system.

Fig. 1

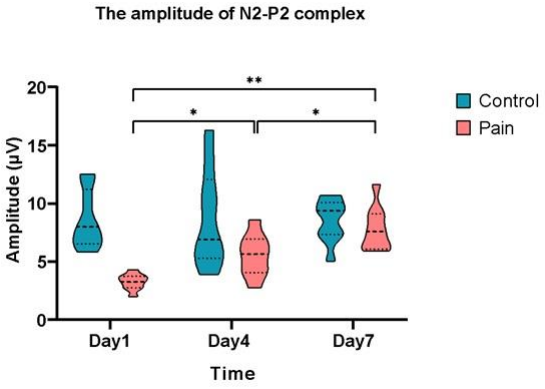
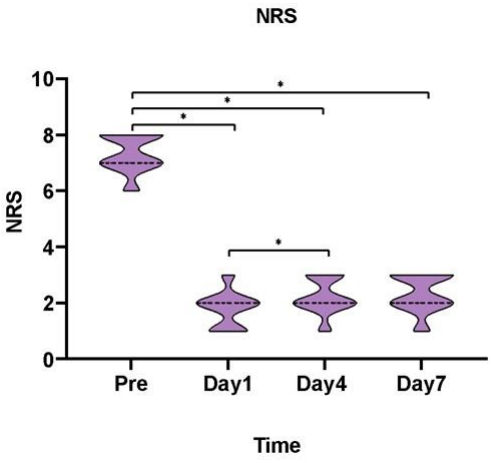

The amplitude of N2-P2 complex
Amplitude (μV)
20
15
10
5
0
**
*
*
Control
Pain
Day1
Day4
Day7
Time

Fig. 2


NRS
NRS
10
8
6
4
2
0
*
*
*
*
Pre
Day1
Day4
Day7
Time

Funktionelle Neurochirurgie und Schmerz III/*Functional neurosurgery and pain III*

V206

Spinal Cord Stimulation – Eine alternative Therapie bei symptomatischer adulter Skoliose, wenn die Operation nicht geeignet ist?

Spinal cord stimulation – A reasonable alternative treatment in patients with symptomatic adult scoliois if surgical therapy is not suitable?

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Objective

In adult scoliosis the asymmetric loading of weight-bearing structures promotes progressive degeneration causing lower back pain (LBP) and additional regional pain (RP). For patients who do not respond to conservative therapy dorsal instrumentation and fusion can provide significant improvement of pain and impairment scores, however complication rates of up to 39% have been reported. We therefore we aimed to evaluate the use of neuromodulation, in particular spinal cord stimulation (SCS), in a larger cohort of adult scoliosis patients

Methods

We prospectively analyzed 18 adult scoliosis patients receiving SCS treatment in our institution between February 2019 and May 2020. Adult scoliosis was defined as a Cobb angle of >10° in the coronal plane in skeletally mature patients. Clinical follow-up was performed at 3,6 and 12 months following implantation of an epidural SCS System. Patients reported NRS values for the categories of LBP and specific regional pain both at rest and in motion. Further, Short form-36, Short form of the Profile of Mood States, Pittsburgh Sleep Quality Index and Oswestry Disability Index were collected. The study was approved by the institutional Ethics Committee (EA2/093/13).

Results

The average patient age was 71 years old (range 33-85) with a BMI of 29 kg/m2 (range 22-37 kg/m2). Scoliotic deformity of the thoracolumbar junction was most commonly reported (66%). Compared to preoperative values, NRS of lower back pain (LBP) at rest was significantly reduced following SCS at three (43% lower, p=0.005) and six (49% lower, p=0.027) months follow-up. LBP in motion was also reduced at three (32% lower, p=0.005) and six (36% lower, p=0.010) months. RP at rest was reduced at three (42% lower, p=0.002) and six (52% lower, p=0.014) and in movement at three (29% lower, 0.004) and six (34% lower, p=0.012). Sleep quality and symptoms of depression were significantly improved at 3 months after implantation, and disability scores improved significantly at six months following implantation.

Conclusion

Our cohort was comprised of adults for whom the risks of corrective surgery must be carefully considered. In these patients, neuromodulation can significantly reduce LBP as well as RP in the first six months following implantation indicating that neuromodulation may provide a reasonable alternative in poor surgical candidates.

Funktionelle Neurochirurgie und Schmerz III/*Functional neurosurgery and pain III*

V207

Verschiedene Varianten oxidierter regenerierter Zellulose verursachen ein unterschiedliches Ausmaß an Zellschäden bei organotypischen Hippocampus-Schnittkulturen

Variants of oxidised regenerated cellulose cause different cellular damage on organotypic hippocampal slice cultures

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Objective

Hemostasis is one of the challenging problems in neurosurgery. Based on oxidized regenerated cellulose (ORC) several hemostyptic materials like Tabotamp®, Equicel® and Equitamp® have been developed. The present study compared ORC that differ in their compositions and properties. In organotypic hippocampal slice cultures (OHSC) the cytotoxicity and damage on neuronal tissue was evaluated.

Methods

Properties like structure, solubility and pH values of different ORC were analyzed. The cytotoxicity was detected via DNA-binding fluorescence dye in Schwann cells, astrocytes and neuronal cells. Detachment of cells caused by ORC treatment was examined using crystal violet staining. Additionally, organotypic hippocampal slice cultures (OHSC) were treated for 24 and 48 hours with ORC. Propidium iodide, haematoxylin-eosin and isolectin B4 staining was used to analyze the cellular damage, cytoarchitecture and microglia activation.

Results

Cell death analysis showed a better compatibility of Equitamp® compared to Equicel® and Tabotamp® ($p<0.001$). Furthermore, Equitamp® treatment led to equivalent cytotoxicity of neuronal cells compared to the non-oxidized control material (cotton gauze). Additionally, OHSC damage was stronger after Tabotamp® and Equicel® treatment in comparison to Equitamp® or gauze ($p<0.01$). In contrast to the other ORC, Equicel® led to a very early and strong increase of microglia cells after 24 hours ($p<0.001$). Immunofluorescence staining was not detectable after Tabotamp® treatment, which might be due to an artifact caused by strongly reduced pH. In contrast to Tabotamp®, Equicel® displayed a neutral pH in aqueous solution but was not soluble within 48 hours. Equitamp® led to a less decreased pH of 4.8 at concentration of 500 mm^2/ml ($p<0.001$) with a comparable solubility to Tabotamp®.

Conclusion

The application of Equitamp® resulted in significantly decreased damage and cell death of neuronal tissue compared to Equicel® and Tabotamp®. Therefore, ORC like Tabotamp® or Equicel® should be carefully used in eloquent areas.

Funktionelle Neurochirurgie und Schmerz III/*Functional neurosurgery and pain III*

V208

Drahtlose periphere Nervenstimulation bei refraktärer Trigeminusneuralgie
Wireless subcutaneous trigeminal nerve field stimulation for refractory trigeminal pain – a single-centre experience

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Objective

Subcutaneous trigeminal nerve field stimulation (sTNFS) is a neuromodulatory treatment for neuropathic trigeminal pain with the ability to reduce the intensity and frequency of pain attacks. However, the published case series of sTNFS report hardware issues including lead migration, skin erosion, infection, so- called pocket pain at the site of the implanted neurostimulator. Furthermore, traditionally used systems are not MR-compatible. New wireless neuromodulation technology, promises not only an even less invasive sTNFS treatment and thinner electrodes better suited for facial implants, but also provides further advantages such as lack of an implantable neurostimulator and 3-T MRI compatibility.

Methods

All patients received stimulation with subcutaneous leads in the concerned trigeminal regions that were connected wirelessly to an extracorporeal neurostimulator. During the follow-up VAS-scores, attack rates, oral pain medication, complications and side effects of sTNFS were recorded and documented.

Results

According to the 3rd edition of the International Classification of Headache Disorders (ICHD-3) N=2 of the patients were classified with TN with concomitant persistent facial pain and N=1 patient with multiple sclerosis associated TN. All three patients received at least 24 days of stimulation with subcutaneous leads in the concerned trigeminal regions that were connected wirelessly to an extracorporeal neurostimulator. All patients (n = 3) responded to sTNFS (i.e. ≥50 % pain reduction) during the test period. The time of the test period was 44 ± 31.24 days (mean ± SD). The length of stimulation per patient per day amounted 2.5 ± 2.2 hours (mean ± SD). The pain intensity (as defined by VAS) was reduced by 80% ± 17 % (mean ± SD). Reduction or cessation in pain medication was observed in all patients. No surgical complications occurred in the long-term follow-up period of 18.84 ± 6 (mean ± SD) months.

Conclusion

The new wireless sTNFS device is a safe, effective and reliable therapy with apparently few complications. Compared to conventional devices, the equipment permits longer trial stimulation periods. Furthermore, the daily stimulation duration was much shorter compared to previous reports.

Funktionelle Neurochirurgie und Schmerz III/*Functional neurosurgery and pain III*

V209

Die Langzeitergebnisse der direkt implantierbaren Nervus peronaeus Stimulation bei 33 Patienten mit zentral bedingten Fußheberparese

Long term results following electrical stimulation of the peroneal nerve using the implanted peroneal nerve stimulator in 33 patients with central drop foot

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Objective

Direct electrical stimulation of the peroneal nerve, using the implantable peroneal nerve stimulator, enables a therapy of the centrally caused drop foot, improving the gait of the patients. In this paper, we present long-term results at 36-month follow-up post implantation.

Methods

A total of 33 patients, 27 stroke and 6 multiple sclerosis (MS) patients, suffering from spastic drop foot were implanted in our center and assessed in terms of gait endurance, speed, risk of fall and life quality at baseline and 36 months following implantation.

Results

The six min gait endurance test increased from 202±41 m to 380±30 m in 81% while using the implant. Gait speed measured over 20 m increased in average in 41.8 %, the time needed decreased from 31.8±10.2 s without to 18.5±4.6 s by using the implantable peroneal nerve stimulator. Gait steadiness improved, measured by the Timed Up and Go (TUG) test in 36.6%. Thirty-one of 33 patients reported remarkable improvements of their quality of life following direct electrical nerve stimulation.

Conclusion

These findings confirm previously published efficacy data at 12 month after implantation and underline the long-lasting effect of the implant.

Neuroonkologie V/*Neurooncology V*

V212

Problematisch oder praktikabel? Histopathologische Diagnose von primären cerebralen Lymphomen nach präoperativer Kortikosteroidtherapie

Problematic or practical? Histopathological diagnosis of primary central nervous system lymphoma after preoperative corticosteroid therapy

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Objective

Primary central nervous system lymphoma (PCNSL) is a rare disease that usually requires a surgical biopsy to verify the diagnosis. High-dose corticosteroids (CS) are an effective symptomatic treatment for PCNSL-patients with severe neurological symptoms. However, CS may disguise the histopathological diagnosis necessitating multiple surgeries. The aim of our study was to investigate the impact of CS treatment on histopathological diagnostic accuracy.

Methods

This retrospective single-centre observational study, comprised all patients diagnosed with PCNSL that were treated at our institution between October 2008 and June 2020. Data extracted from digital patients records included demographics, surgical techniques and treatment with CS before surgery.

Results

125 patients were included into the analysis. The majority of the patients were male (59.2%), mean age at diagnosis was 54,5 years. Surgical techniques included stereotactic biopsy (n=78), open biopsy (n=20), endoscopic biopsy (n=5), and partial or total tumour resection (n=19). Forty-six patients received CS before the respective neurosurgical intervention. CS treatment was discontinued between 0 to 75 days prior to surgery. PCNSL-diagnosis could be verified in the initial histopathological analysis in 41 (89.1%) patients with CS and in 77 (97.5%) patients without CS (χ^2 fisher p=0.09), respectively. Six patients were operated on while undergoing CS treatment and in 18 patients, CS treatment was discontinued less than ten days before surgery, rendering histopathological analysis significantly less accurate (success rate of 79%; χ^2 fisher p=0.003). Patients with unsuccessful initial diagnosis stopped taking CS 4 to 8 days before surgery (n=5) or were not treated with CS (n=2). Interestingly, we did not observe a difference regarding successful tissue sampling between stereotactic and open surgery techniques (χ^2 fisher p=0.67).

Conclusion

If clinically justifiable, CS should be discontinued ten days before the surgical biopsy to significantly improve diagnostic accuracy. However, even after CS therapy, PCNSL could be diagnosed in almost 90% justifying immediate biopsy in cases where rapid causal therapy is mandatory. A second biopsy ten days after CS therapy appears to be a valid option if the initial diagnosis fails.

V213

Initiale PCV-Chemotherapie in der Behandlung von Oligodendrogliomen WHO Grad 2 – verlängertes progressionsfreies Überleben und niedriges Risiko einer histologischen Malignisierung

PCV chemotherapy alone for WHO grade 2 oligodendroglioma – prolonged disease control with low risk of malignant transformation

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Objective

The role of chemotherapy alone in WHO grade 2 oligodendroglioma (OD) after biopsy, incomplete or gross total resection remains controversial. We here analyze the clinical outcome of four cohorts being treated with either procarbazine, CCNU and vincristine (PCV) or temozolomide (TMZ) compared to a wait and scan strategy and resection only.

Methods

142 patients with molecular characterized OD (WHO 2016) were treated within four cohorts: (W&S) wait-and-scan after stereotactic biopsy (n=59); (RES) wait-and-scan after resection (n=27); (TMZ) temozolomide after biopsy (n=26) or (PCV) PCV (n=30) after biopsy. Presurgical MRI T2 tumor volumes were obtained by manual segmentation. Progression-free survival (PFS), post-recurrence PFS (PR-PFS) and rate of malignant transformation were analyzed.

Results

PFS was longest after PCV (9.1 years), compared to 5.1 years after W&S, 4.4 years after RES and 3.6 years after TMZ. The rate of malignant progression within 10 years was 9% in PCV, 29% in W&S, 67% in RES and 75% in TMZ (p=0.01). In W&S, patients treated with PCV at first relapse had a longer PFS from intervention than those treated with TMZ (7.2 vs 4.0 years, p = 0.04). Multivariate analysis identified smaller tumor volume prior to any intervention (p = 0.02) and initial PCV therapy (p=0.01) to be prognostic for progression-free survival.

Conclusion

PCV chemotherapy alone is an effective treatment option for WHO grade 2 oligodendroglioma with long PFS and low rate of malignant transformation.

Fig. 1

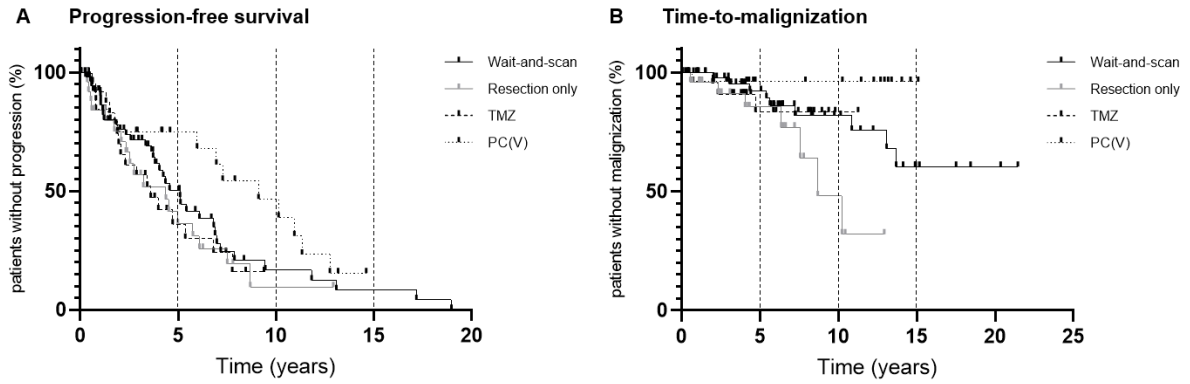

Fig. 2. Progression-free survival (PFS, $p = 0.15$) (A) and Time-to-malignization (TTM, $p = 0.04$*) (B). Four different groups were compared: wait-and-scan versus resection only versus temozolomide only versus procarbazine + CCNU (+/- vincristine) (PC(V)) only.

Neuroonkologie V/*Neurooncology V*

V214

Kartierung des genomweiten Methylierungsmusters identifiziert eine Hochrisiko-Untergruppe der intraventrikulären Meningeome
Mapping of genome-wide methylation pattern identifies a high-risk subgroup of intraventricular meningiomas

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[6]Universitätsklinikum Hamburg-Eppendorf, Neuropathologie, Hamburg, Germany

Objective

Intraventricular meningiomas (IVMs) are a rare subgroup accounting for less than 5% of all intracranial meningiomas. Recent studies showed evidence that IVMs are marked by a distinct chromosomal alteration with a combined loss of chromosome 22q and 1p. Here, we aim to map epigenetic patterns of IVMs in a multicenter cohort of 50 patients

Methods

For biomathematical analysis methylation profiles from 850k methylation arrays were imported using the minfi package, followed by a batch correction (lima batch effect removal) and normalized resulting in a methylation intensity matrix of beta-values. We removed CpG sites from X, and Y chromosomal regions and selected the most variable 2000 probes for PCA analysis. The number of non-trivial components was obtained by comparison to a randomly arranged matrix of beta values. A non-trivial component was defined by a larger eigenvalue than random values. Dimensional reduction and clustering were performed for subgrouping of IVMs. In order to map the IVM into a reference dataset of meningioma, we imported the raw *.idat files of all 149 methylation profiles of meningioma in the recently launched methylation classifier (Capper et al., 2018)

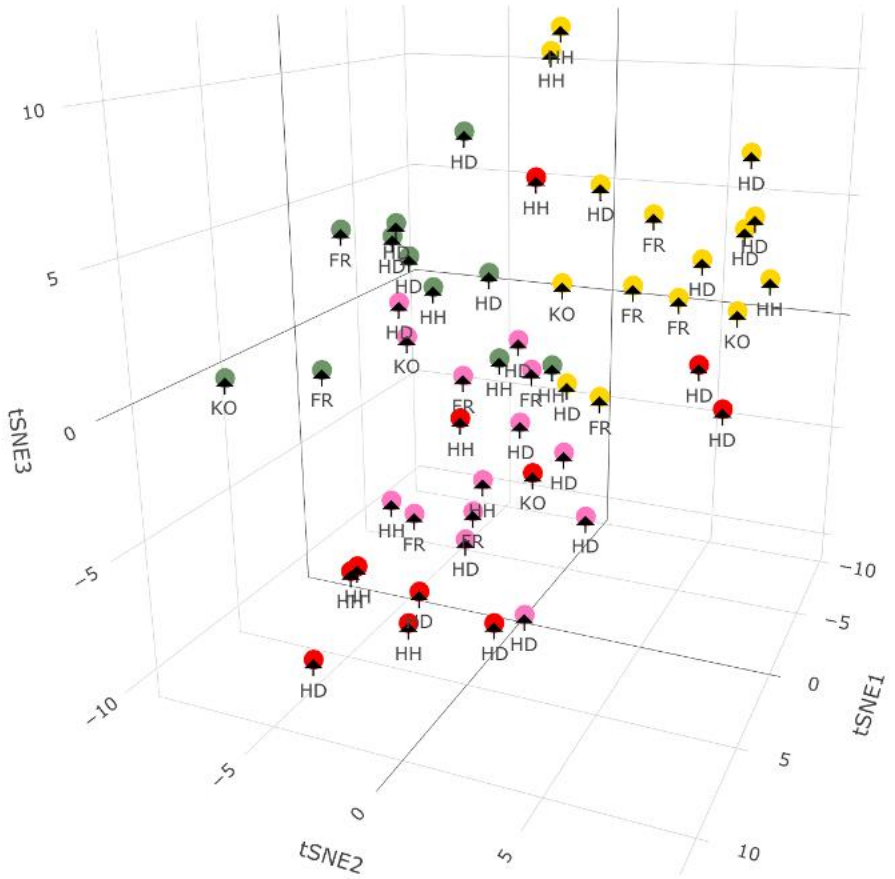
Results

We were able to confirm that IVMs are more frequently marked by a loss of chromosome 22q compared to its reference cohort. Clustering of the methylation pattern revealed 2 different subcluster, one cluster contained a high number of copy number alterations and lead to tumor relapse in all patients within 48 months. This was significantly increased compared to the remaining IVMs (p=0.023) with a median PFS of 64 months (relapse in 2/3 of the group). We found a hypermethylation of gene promoter regions that regulate hormone binding and DNA repair mechanism within cluster1. In comparison to the reference cohort, most of the IVMs (76%) clustered separately, which suggest that IVMs are driven by an unique molecular program

Conclusion

Our findings showed two different groups of IVMs with a significant difference of progression-free survival. The malignant phenotype was marked by an increased genomic instability driven by hypermethylation of DNA repair mechanism and hormone binding sites. Based on our data, we provide the possibility for early prediction of a relapse probability by genome-wide methylation in IVM"s

Fig. 1



Neuroonkologie V/*Neurooncology V*

V215

Immunophänotypisierung von Tumor-infiltrierenden T Zellen im primären ZNS Lymphom
Immunophenotyping of tumour-infiltrating T cells in primary CNS lymphoma

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Objective

Primary CNS lymphoma represents a malignant disease with dismal prognosis. Standard of care is high dose chemotherapy and radiation. However, this combination cannot be applied to the elderly and fragile population. Immunotherapy holds great promise to be effective in these patients. This study therefore aims to explore the phenotype of tumor-infiltrating lymphocytes (TIL) in order to analyze the potential for immune checkpoint inhibition.

Methods

We performed ex vivo multicolor flow-cytometry on surgical specimens of nine patients with intracerebral lymphoma (n=9), including seven with primary CNS lymphoma after isolation of TILs following standard protocols. Data was analyzed using a Fortessa LSR flow cytometer and Diva software. Multiparameter analysis was performed using GraphPad Prism. The study was approved by the local ethics committee (PV4904).

Results

Our ex vivo phenotyping demonstrated a predominant infiltration of CD8+ T cells, which outnumber CD4+ T cells by a ratio of 2:1 ($p<0.01$). Regulatory T cells (Tregs) were not increased in the tumor microenvironment and the NK cell frequency was reduced compared to the peripheral blood. While CD4+ T helper cells displayed significantly increased surface expression of multiple activation and checkpoint markers, including TIGIT, PD-1, Tim3 and CD57, cytotoxic CD8+ T cells predominantly expressed only TIGIT and PD-1. On average 70% and 80% of CD8+ T cells expressed PD-1 and TIGIT, respectively, compared to 35% and 60% of PD-1 and TIGIT on CD4+ T cells ($p<0.05$). CD8+ T cells further showed and increased expression of CD39 and a simultaneous downregulation of CD73, both ectoenzyms involved in the modulation of intratumoral ATP metabolism, thereby indicating an either metabolic adaptation or immune modulation by the tumor cells. In addition, tumor-infiltrating T cells highly expressed HLA-DR, reflecting their overall activation status.

Conclusion

Taken together, our study demonstrates a strong infiltration of cytotoxic CD8+ T cells into cerebral lymphoma, which potentially can be disinhibited using checkpoint immunotherapy. Our profiling suggests that PD-1 and TIGIT present appealing targets for such kind of immune disinhibition.

Neuroonkologie V/*Neurooncology V*

V216

Überlebensprognose für Patientinnen mit cerebral metastasierten Mammakarzinom
Prediction of survival in patients with breast cancer brain metastases (BCBM)

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Objective

Breast cancer (BC) brain metastases (BM/BCBM) requiring surgical treatment determine the prognosis in patients with BC. The graded prognostic assessment (GPA) score was described and established as an estimation of the prognosis in BCBM patients, regardless the need for BM surgery. We aimed to develop the scores for the prediction of short (<6 months, STS) and long-term survival (>3 years, LTS) after BCBM surgery.

Methods

All female patients with BCBM who underwent BM surgery in our institution between 2008 and 2019 were included. Various preoperative demographic, clinical and histopathological characteristics of the patients were evaluated as potential STS/LTS score components.

Results

Of 95 BCBM patients in the final analysis (median age: 60.0 years), STS and LTS after BM surgery was observed in 77 (79.4%) and 22 (22.7%) cases respectively. Breast-preserving surgery (1 points), presence of multiple BM (1 point) and age ≥ 65 years at BC diagnosis (1 point) were included in the STS score (0-3 points). In turn, LTS score (0-3 points) consisted of positive HER2 receptor status in BM (1 point), time interval ≥3 years between BC and BM diagnosis (1 point) and KPS≥90% (1 point). The new scores showed higher diagnostic accuracy for STS/LTS prediction (STS-score: AUC: 0.773/ LTS-Score: AUC: 0.775) than the GPA (AUC: 0.498/ AUC: 0.615) and modified-GPA (AUC: 0.642/ AUC: 0.654) scores.

Conclusion

Different factors play the crucial role in the prediction of STS and LTS in BCBM patients selected for microsurgery. These new scores could support the interdisciplinary decision for the selection of proper candidate for the surgical treatment of BCBM.

V217

Die longitudinale Analyse des MRI-T2-Verhaltensmusters wiederspiegelt den klinischen Verlauf der Astrozytome
Longitudinal analysis of T2-imaging pattern reflects clinical course of astrocytoma

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Objective

Therapeutic approaches at recurrence of IDH-mutated astrocytoma still remain unclear. Interpretation of each MRI in follow-up examinations become challenging due to a non-linear growth behavior. Here, we aim to explore growth patterns of IDH-mutated astrocytomas and to predict treatment responses at later stages of the disease.

Methods

Between 2000 and 2018 volumetric diversity of astrocytomas and computed T2-imaging patterns based on segmentation of 7995 follow-up MRI scans of 48 eligible patients diagnosed with IDH-mutated astrocytomas WHO°II and III were analyzed. For tumor segmentation the NORA software tool, a web-based framework for image analysis developed at University of Freiburg has been used. Data analysis was performed by a recently published computational pipeline (by Neurosurgery, University of Freiburg).

Results

The growth patterns of IDH-mutated glioma revealed highly dynamic changes, which were found to be patient-specific and did not directly correlate with clinical parameters or therapeutic interventions. Three major subgroups were identified based on the peak growth maximum at early, middle or late stage of the disease. Frontal tumors were enriched in a subgroup with relatively large tumors at initial diagnosis. Investigations of the optimal timepoint for surgical interventions showed a trend towards a more beneficial effect of resection at initial diagnosis for WHO°III tumors. In WHO°II tumors, no difference between initial surgery or intervention after radio/chemotherapy was found. Surgical resection was found to be beneficial regardless of the WHO grade. In our study an extent of resection above 72.4% of the T2-hyperintense regions was required to show an improvement in overall survival. Multiple resections did not generally improve overall survival, unless greater extent of resection than in previous surgeries was achieved.

Conclusion

Our findings suggest, that in patients suffering from IDH-mutated WHO°II and III astrocytomas show highly dynamic growth behavior that is patient specific (with a large inter-patient variability). In summary, WHO°III IDH-mutated astrocytomas showed improved survival by early surgical intervention while the timepoint of surgical intervention was not crucial for WHO°II tumors. These findings open the possibility for neoadjuvant treatment options at least for IDH-mutated WHO°II astrocytomas in the future

Neurovaskuläre Zentren IV/*Neurovascular centres IV*

V218

Prädiktoren zur langfristigen Prognose von Patienten mit spontaner intrazerebraler Blutung
Predictors of long-term functional outcome in spontaneous intracerebral haemorrhage – a retrospective hospital-based study

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Objective

Spontaneous intracerebral haemorrhage (ICH) accounts for approximately 15% of all strokes and is a leading cause of disability, with a one-month mortality rate of around 40%. Whereas factors predicting short-term mortality are well known, data regarding long-term outcome are scarce and imprecise. We sought to identify possible predictors of poor outcome among patients with spontaneous supratentorial ICH treated in our neurosurgical department over a nine-year period.

Methods

Retrospective evaluation of consecutive patients with primary, spontaneous supratentoriell ICH presenting to and treated by our academic neurosurgical department during the time period 2007-2015. Clinical and CT imaging findings were correlated with functional outcome using the modified Rankin score (mRS) at discharge and as measured at 1 month, 1 year and 2 years follow-up. Outcome was dichotomised according to the mRS (score 0-2, favourable outcome; score 3-6, unfavourable outcome).

Results

309 patients (160 men and 149 women) with primary supratentorial ICH were identified from our clinical record system. The mean age was 67.6 years. The mean baseline Glasgow coma scale (GCS) score on admission was 9. 52.8% of patients bled under anticoagulant therapy. 80.9% of the patients had arterial hypertension. Associated ventricular haemorrhage was present in 50.2% of patients. 186 patients were treated conservatively and 123 of the patients were treated surgically. Operative treatment was performed in all patients within 72 hours of initial haemorhage. At 2 years, 77 patients had died. 90/309 patients (29.13%) had a mRS score of 0 to 2 and at this timepoint, representing a favourable outcome. In 139 patients (45.0%) the mRS score was between 3 and 6 at this interval, representing an unfavourable outcome. Based on a multivariate analysis with unfavorable outcome (mRS 3 to 6) as the dependent variable, poor baseline neurological status (GCS score <11) and large-volume haemorrhage, (>45 ml) were identified as significant predictors of poor outcome at two years.

Conclusion

We demonstrate in a contemporary clinical cohort that baseline neurological findings and bleed volume on initial CT imaging have a significant impact on long-term functional outcome and morbidity. Surgical intervention was associated with lower mortality but had no impact on morbidity or functional status.

V219

Zikulatorische Dipeptidyl Peptidase 3 (cDPP3) als potentieller Biomarker nach aneurysmatischer Subarachnoidalblutung – eine prospektive Evaluation

Prospective assessment of circulatory dipeptidyl peptidase 3 (cDPP3) as a potential biomarker after aneurysmal subarachnoid haemorrhage

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Objective

Delayed cerebral ischemia (DCI) is a common complication after aneurysmal subarachnoid hemorrhage (aSAH) that can culminate in infarction and secondary brain damage. Although DCI-related infarctions are one of the main preventable causes of SAH-related morbidity, there is still a lack of prognostic criteria for identification of patients at risk of developing DCI. Elevated circulatory levels of the cytosolic enzyme dipeptidyl peptidase 3 (DPP3) were recently identified as a promising potential biomarker for prediction of organ failure and outcome in critically ill patients. In the present study, we prospectively determined the temporal profile of circulatory DPP3 (cDPP3) levels in a cohort of aSAH patients and analyzed its relation to the development of DCI, DCI-related infarctions, and long-term outcome.

Methods

cDPP3 levels were quantified in serum samples obtained from 96 confirmed aSAH patients during the early (EP: d1-4), critical (CP: d5-8, d9-12, d13-15) and late (d16-21) phase after aSAH onset. Associations between cDPP3 levels and demographic or clinical parameters were evaluated. The relations between cDPP3 levels and DCI, DCI-related infarctions and long-term clinical outcomes were examined by receiver operating characteristics (ROC) curve analysis and multivariate logistic regression.

Results

Significantly higher cDPP3 levels during CP (d5-8, d9-12, d13-15) were observed in patients with poor clinical ($p<0.001$ to $p=0.033$) or radiological ($p=0.012$ to $p=0.039$) status on admission, DCI ($p<0.001$ to $p=0.001$), DCI-related infarctions ($p=0.002$ to $p=0.007$), and poorer long-term outcome ($p=0.007$ to $p=0.019$). ROC curve analysis showed that higher cDPP3 levels on day 5-8 after aSAH onset were predictive for unfavorable outcome (AUC=0.677, $p=0.007$). In multivariate analysis after adjusting for clinical severity upon admission, there was an independent association between cDPP3 levels on day 5-8 and development of DCI-related infarctions.

Conclusion

Our results provide first evidence that cDPP3 could be a promising biomarker for early diagnosis of DCI-related infarctions in poor grade aSAH patients. These findings and their clinical value should be validated and extended by additional human and animal studies.

Neurovaskuläre Zentren IV/*Neurovascular centres IV*

V220

Chirurgische Behandlung kavernöser Hirnstammfehlbildungen – ein internationaler Delphi-Konsens
Surgical treatment of brainstem cavernous calformations – an international Delphi consensus

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Objective

Indication for surgery in brainstem cavernous malformations (BSCM) is based on many case series, few comparative studies, and no randomised controlled trials. The objective of this trial was to seek consensus about the surgical management of BSCM.

Methods

A total of 29 experts were invited to participate in a multistep Delphi consensus process on the surgical treatment of BSCM.

Results

22/29 (76%) experts participated in the consensus. Qualitative analysis (content analysis) of an initial open-end question survey resulted in 99 statements regarding surgical treatment of BSCM. By a multistep survey with 100% participation in each round, consensus was reached on 52 out of 99 (53%) statements. These were grouped into 4 categories: (1) definitions and reporting standards (7/14, 50%); (2) general and patient-related aspects (11/16, 69%); (3) anatomical-, timing of surgery- and BSCM-related aspects (22/37, 59%); and (4) clinical situation-based decision making (12/32, 38%). Among other things, a consensus was reached for surgical timing, handling of associated developmental venous anomalies, handling of postoperative BSCM remnants, assessment of specific anatomical BSCM localizations and treatment decisions in typical clinical BSCM scenarios.

Conclusion

A summary of typical clinical scenarios and a "catalogue" of various BSCM- and patient-related aspects that influence the surgical treatment decision have been defined and interpreted. Our results provide information that support experts in clinical routine and may serve as a foundation for clinical trial designs and treatment guidelines.

V221

Die Assoziation der Entwicklung eines Arteria Communicas Anterior Aneurysmas zu den umgebenden Gefäßen
The association of parent vessel asymmetry with the formation of an anterior communicating artery aneurysm

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Objective

Although the formation and rupture risk of an anterior communicating artery (ACoA) aneurysm have been the subject of many studies, no previous study has specifically searched for the relationship of the parent vessels and the impact of their ratio on the development and potential rupture risk of an AcoA aneurysm. The objective of this study is to explore this link and to further analyse the surrounding vasculature of the anterior communicating artery aneurysm.

Methods

We conducted a retrospective analysis of 434 patients: 284 patients with an ACoA aneurysm (121 unruptured and 162 ruptured) and of 150 control patients without an ACoA aneurysm. Radiological angiography investigations were used to assess the diameter ratios of the parent vessels in addition to ACoA aneurysm morphology parameters.

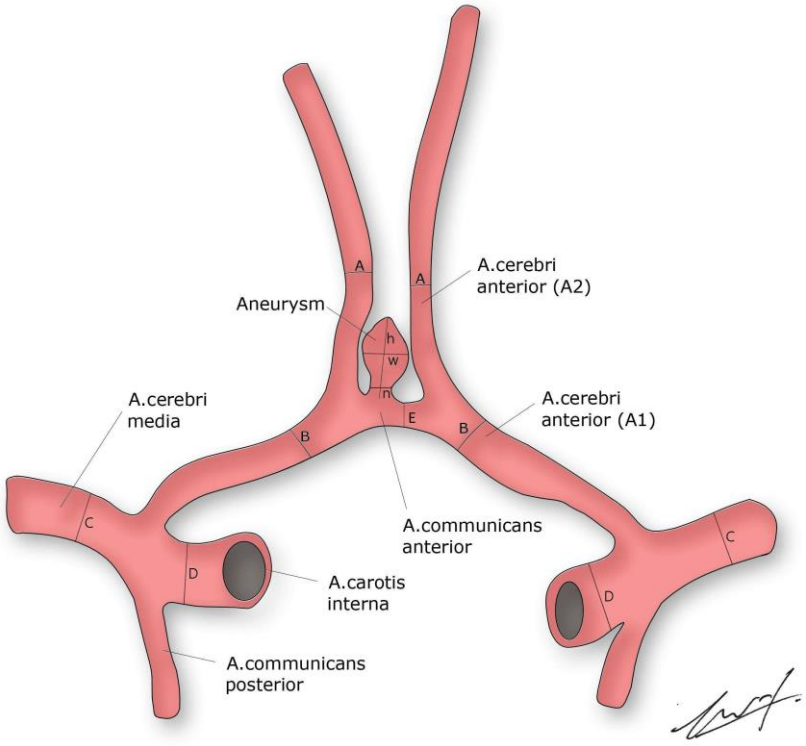
Results

When comparing the ruptured to the unruptured cases, no significant difference was observed in the parent vessel diameter ratios. Younger patient age (OR 0.96, P=0.00) and a higher size ratio (OR 1.10, P=0.02) were of prognostic importance after adjusting for other covariables in the multivariable model (Table 4). The A1 diameter ratio and the A2 diameter were not statistically significant (OR 1.00, P=0.99, and OR 3.38, P=0.25 respectively).

Conclusion

In our study we focussed on asymmetry in the parent vessels together with traditional ACoA aneurysm morphological characteristics. We could label younger patient age and a greater size ratio as independent prognostic factors for ACoA aneurysm rupture. We are unable to label parent vessel asymmetry as prognostic factors. To validate our findings, parent vessels asymmetry should be subjected to future prospective studies.

Fig. 1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posterior

Neurovaskuläre Zentren IV/*Neurovascular centres IV*

V222

Entwicklung der Häufigkeit aneurysmatischer Subarachnoidalblutungen in Deutschland zwischen 2005 und 2018
Trends in the occurrence of aneurysmal subarachnoid haemorrhage in Germany between 2005 and 2018

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Objective

In recent decades, the global incidence of aneurysmal subarachnoid hemorrhage (aSAH) has declined, mainly due to the effects of more widespread medical treatment of arterial hypertension and decreasing smoking habits. However, significant regional differences exist. So far, no evidence has emerged on time trends in the prevalence of aSAH in Germany.

Methods

Data on all patients hospitalized in Germany between 2005 and 2018 with International Classification of Diseases (ICD) codes I60.0 to I60.7 were provided by the German Federal Statistical office and included in the analysis. The prevalence of the main diagnosis aSAH was analyzed on two levels 1) for the entire German population and 2) in relation to all patients hospitalized with any disease during the respective time-period. Mortality for hospitalized patients was assessed based on the number of patients who died due to respective ICD codes in relation to all patients hospitalized with the same ICD codes. Ethical approval was granted by local authorities (EA 1/275/20).

Results

The occurrence of the main diagnosis of aSAH per 100.000 inhabitants remained stable between 2005 (8.9) and 2018 (8.2). In the same period, the overall number of patients hospitalized with any disease increased from 16.1 million to 18.8 million. Therefore, the proportion of aSAH patients per 100.000 patients hospitalized with any disease decreased from 45.8 in 2005 to 36.3 in 2018. There were substantial changes in age distributions over time. Younger patients in 2005 (age group 30-45 years) comprised a higher proportion of patients affected by aSAH (21.1%) than in 2018 (11.7%). On the other hand, the proportion of older patients with aSAH increased over time (for ages 45-60: 39.3 vs. 42.1%; 60-75 years: 26.1 vs. 28.9%; above 75 years: 10.6 vs. 15.3%). In the same period, the duration of hospital stay increased from 19.7 to 24.8 days. Among patients hospitalized with aSAH, mortality rates remained stable (16.2 vs. 16.6%).

Conclusion

The overall occurrence of the main diagnosis SAH in Germany remained stable between 2005 and 2018, as did the corresponding mortality. The observed decrease in the proportion of younger individuals affected by aSAH over time might reflect smoking having become less popular among younger people. The increase in the proportion of older patients with aSAH may explain the observed increase in length of hospital stay and may also reflect the increasing life expectancy in western societies.

Neuroonkologie V/*Neurooncology V*

V225

Resektion von WHO Grad III Gliomen mit geringgradiger Kontrastmittelaffinität – Evaluation von Tumorentitäten, Resektionsausmaß und Outcome in einer konsekutiven Single-Center Kohorte

Resection of WHO grade III gliomas with minor contrast-enhancement – evaluation of tumour entities, extent of resection and outcome in a consecutive single-centre cohort

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Objective

The impact of the extent of resection (EOR) in glioma treatment has been a focus of attention and EOR has repeatedly been shown to correlate with improved survival.However, in gliomas exhibiting contrast enhancing (CE) and non-enhancing (nCE) tumor portions, the role of EOR is less clear. In these cases, we sought to take a closer look at removing different tumor portions and their impact on survival.

Methods

We screened a consecutive retrospective series of WHO Grade III Gliomas (n=178) from 01/2011 to 12/2018 for primary resections that exhibited FLAIR hyperintense nCE tumor portions in combination with minor CE tumor (max. 50% of total tumor volume). Tumor volume was assessed on T1w and FLAIR pre- and postoperatively. Outcome was evaluated including molecular histopathology and EOR. Progression-free survival (PFS) was evaluated by Kaplan-Maier estimates.

Results

This cohort consisted of 27 male and 29 female patients with a median age of 42 years (range 18-80). Integrated histology revealed 34 anaplastic astrocytomas, 21 anaplastic oligodendromas and 1 anaplastic ependymoma. IDH mutations were found in 51 cases (91%). Complete resection (CR) of both tumor portions (CE+nCE) was achieved in 37 patients (66%). 14 patients (25%) underwent CR of CE portions with partial resection (PR) of the nCE portions. 5 patients (9%) underwent PR with residual CE and nCE tumor. Postoperatively, 9 patients (16 %) had transient neurological deterioration (4 patients with speech disorder and 5 with motor deficits). 3 patients (5%) had new persistent neurologic deficits. Overall Karnofsky-Performance-Index was unchanged pre- vs. postoperatively (90 % (range 80-100 %) vs. 90% (range: 20-100%), p=0.42). Kaplan-Maier estimates suggested an increased PFS associated with removal of either CE or nCE portions of tumor. PFS was 48.5m for CR of CE and nCE tumor, 41m for CR of CE and PR of nCE tumor and 23m for PR with residual CE and nCE tumor, respectively. However, these estimates failed to reach statistical significance. Median follow-up was 47 (2-114) months.

Conclusion

Our results suggest an impact on PFS associated with the removal of different tumor portions in WHO grade III gliomas exhibiting nCE with minor CE aspects. An extension of our analysis also including lower and high-grade gliomas exhibiting comparable imaging characteristics is underway to further evaluate the impact of resecting different tumor portions also in conjunction with molecular aspects of histology and survival.

Neuroonkologie V/*Neurooncology V*

V226

Re-Evaluation des Pignatti Risiko-Scores in molekular charakterisierten niedergradigen Gliomen
Revisiting the Pignatti risk score in low-grade glioma patients in the molecular era

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Objective

Until now, the Pignatti risk score has been used to guide treatment decisions after histological diagnosis of diffuse glioma WHO grade II. However, its prognostic value was derived from a historic cohort of gliomas that has been diagnosed by morphologic rather than molecular criteria. Thus, we sought to challenge the Pignatti score in a contemporary, molecularly characterized cohort.

Methods

From our institutional cohort of 422 diffuse gliomas WHO grade II, 202 patients were identified for whom IDH mutation status was known and either 1p/19q co-deletion or loss of ATRX expression unambiguously classified tumours into astrocytoma or oligodendroglioma. Patients with multifocal lesions, brainstem involvement, impossible follow-up or lack of pre-operative MRI were excluded. Potential prognostic factors including the individual items of the Pignatti score (astrocytoma; age ≥40 years; neurologic deficit; maximum tumour diameter ≥6cm; tumour crossing the midline) were correlated with progression-free survival (PFS) by univariate log-rank und multivariate Cox regression analysis.

Results

174 patients with astrocytoma or oligodendroglioma were analysed of whom 114 (66%) had not received adjuvant radio- or chemotherapy. 99 untreated patients with a minimum follow-up of 24 months entered survival analysis. These patients were classified as "high-risk" (Pignatti 3-5) and "low-risk"(Pignatti 0-2) in 15% and 85% of cases and did not differ in terms of potential prognostic factors (sex; resection vs. biopsy; tumour recurrence; IDH mutation status) other than the individual Pignatti score items. Diameter <6 cm ($p<0.0001$), no midline crossing ($p<0.0001$), "low-risk" Pignatti score ($p<0.001$), resection rather than biopsy ($p=0.012$) and presence of IDH mutation ($p=0.003$) significantly prolonged PFS in univariate analysis. Diameter <6 cm (HR 1.86; $p=0.03$), no midline crossing (HR 4.49; $p=0.006$), resection (HR 0.42; $p=0.009$) and IDH mutation (HR 0.36; $p=0.041$) were identified as independent prognostic factors of superior PFS in this cohort. Noteworthy, prognostic factors coincided when all patients (n=153) with a minimum follow-up of 24 months, regardless of adjuvant treatment, were analysed.

Conclusion

In molecularly characterized, untreated diffuse gliomas WHO grade II, the Pignatti risk score as a whole no longer seems to be of prognostic relevance. Instead, outcome seems to be determined by preoperative and postoperative tumour burden and IDH mutation status.

Neuroonkologie V/*Neurooncology V*

V227

Risikofaktor für eine Nachresektion nach der Durchführung von iMRT in der Resektion der Hypophysenadenome Knosp 0-2

Risk factors for additional resection after intraoperative MRI in less invasive pituitary adenomas Knosp 0-2

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Objective

We anticipated that the introduction of endoscopic technique in pituitary surgery might render our standard procedure of performing intraoperative magnetic resonance imaging (iMRI) in pituitary adenoma surgery in cases of non-invasive tumors (Knosp 0-2) redundant.

Methods

We conducted a retrospective monocenter data analysis of patients treated by iMRI assisted transsphenoidal surgery at our department between 2012 and 2020. A total number of 230 consecutive patients (surgeries) with pituitary adenomas graded as Knosp 0-2 were selected for further analysis. Of these 57.8% (N=133) were treated with microscopic 36.5% (N=84) with endoscopic and 4.3% (N=10) with endoscopic assisted technique. Volumetric measurement of preoperative, intraoperative and postoperative tumor extension was performed. Demographic data, tumor characteristics and MRI features as well as endocrine outcome were evaluated.

Results

Median preoperative tumor volume was 3.07 cm3 (ratio 0.01-18.5 cm3). Recurrent adenoma was treated in 12.6% (N=29). Apoplectic adenomas were identified in 9.6% (N=22). A total number of 48 cases (20.9%) needed additional resection after iMRI. Endoscopic approach was used in 8 of these cases. We found a significant association between additional resection and microsurgical technique (p=0.01). Multivariable logistic analysis identified tumor volume (p>0.001, OR 1.2) recurrence (p>0.001, OR 1.8) and microsurgical technique (p=0.026, OR 2.7) as independent risk factors for additional resection. The detailed analysis of adenoma remnants on iMRI after endoscopic surgery revealed the suprasellar location in a diaphragm fold or undetected invasion of cavernous sinus as the main reason for incomplete resection.

Conclusion

Tumor volume, recurrence and microsurgical technique were identified as independent predictor for additional resection in patients with less invasive adenomas Knosp 0-2. Even the endoscopic visualization of the sella turcica did not preclude tumor remnants in iMRI in our series. Tumor remnants in the endoscpic cohort were either large tumors with remnants hidden within the diaphragmic folds or behind the infiltrated wall of cavernous sinus not recognized on preoperative MRI.

Neuroonkologie V/*Neurooncology V*

V228

Risikofaktoren für einen postoperativen Hydrozephalus malresorptivus bei der Resektion von Gliomen
Risk factors for postoperative communicating hydrocephalus in glioma resection surgery

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Objective

Gliomas are the most common primary brain tumors. Maximum extent of tumor resection is one of the most important predictors of overall survival, irrespective of histological or molecular subtype or tumor grade. However, aggressive resection can lead to ventricular opening, potentially increasing the risk for development of communicating hydrocephalus (CH). Complications such as rebleeding and infection may also lead to CH and, eventually, the need for cerebrospinal fluid (CSF) diversion surgery. In this study, we evaluated potential risk factors for the development of postoperative CH in glioma patients.

Methods

1165 patients that underwent glioma resection (WHO grade I: 6,2% of patients; II: 13,1%; III: 17,3%; IV: 63,4%) at our department between 2006 and 2019 were analysed retrospectively. Potential risk factors that were determined for each patient were age, sex, tumor WHO grade, the number of resection surgeries, ventricular opening during resection, postoperative CSF leak, ventriculitis, and rebleeding. Uni- as well as multivariate analyses were performed to identify statistically significant risk factors using the free R software environment.

Results

90 of 1165 (7.7%) patients had CSF diversion surgery (implantation of a ventriculoperitoneal or ventriculoatrial shunt) after glioma resection surgery at, on average, postoperative day 27 (median; mean: 98; range: 0-3531 days). 16 patients had obstructive hydrocephalus and 74 patients had CH. Of these, 66.2% had a grade IV tumor (grade III: 21.6%; II: 5.4%; I: 6.8%). The number of resection surgeries (p=0.005867), ventricular opening (p=0.000162; odds ratio: 5.1), ventriculitis (p=0.000153; OR: 3.1), CSF leak (p=0.0139; OR: 2.2), and rebleeding (p=0.017; OR: 2.3) were identified as significant independent risk factors for development of postoperative CH. Age, sex or WHO grade were not associated with postoperative CH.

Conclusion

Postoperative CH treated by CSF shunting is frequent in glioma surgery. This may be due to the paradigm shift towards intensified treatment regimes in recent years: CH may be a late consequence of the tumor itself that is seen more frequently with more patients surviving longer. On the other hand, it also appears to be influenced by treatment-related factors. If preoperative risk factors (i.e., a high number of resection surgeries, mandatory ventricular opening) are present, one should discuss the possibility of postoperative CH with the patient and maybe even consider pre-emptive shunt implantation.

V229

Operation in und an der Pyramidenbahn mittels prechirurgischem Diffusionstensorimaging und Neuronavigation
Surgery of lesions lying with in or adjacent to the pyramidal tract using preoperative diffusion tensor imaging and FMRI and neuronavigation

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Objective

Surgery within or close to the pyramidal tract demands special attention to avoid permanent plegia. To maximize the extent of resection during surgery within or adjacent to this area, a detailed functional mapping of these areas is necessary.

Methods

DTI was used with 1.9 mm slices and 12 directions to reconstruct the pyramidal tract. Intraoperative MRI was used and registered to the functional images to show the extent of resection, the brain shift and an update of the relation to functional structures. fMRI was used to show the starting area for the pyramidal tract with a 1.5T MR scanner with echo planar imaging (Sonata, Siemens Medical Solutions) and a block paradigm with 120 measurements in 6 blocks (rest alternating with activation, 16 slices, 3mm thickness & resolution TR=1580, TE=60). During the activation intervals patients had to perform movements.

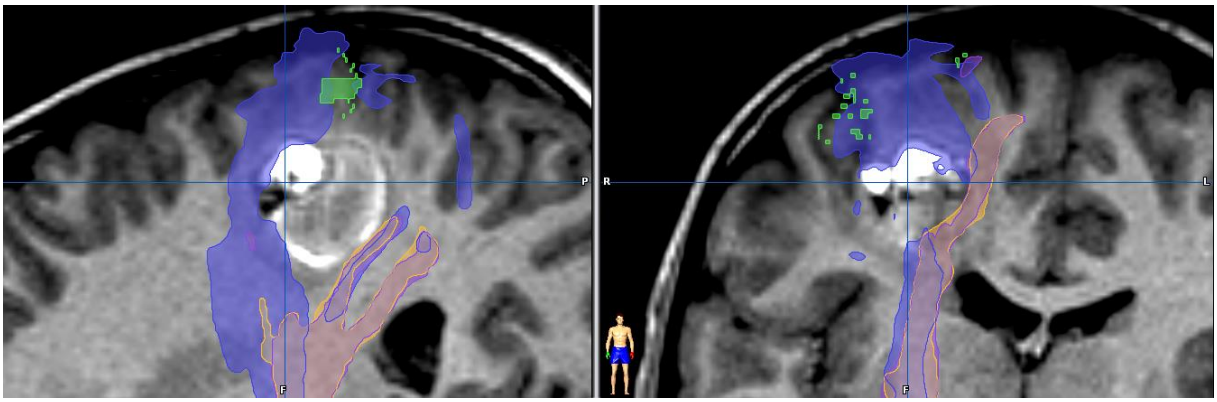
Results

The Pyramidal tract was reconstructed in 470 patients. Surgery in various parts of the pyramidal tracts were accomplished: 1 within the pons (cavernoma), 3 within basal nuclei (2 cavernoma and 1 glioma), the others within the white matter of the telencephalon. There was no worsening of movement abilities of all patients observed due to an injury of the pyramidal tract. Only one patient suffered from an worsening of movement abilities due to an media infarction.

Conclusion

Resection close and even within the pyramidal tract is possible without permanent movement deficit. This demands a detailed reconstruction for the pyramidal tract to several motor areas and an ongoing update of navigation.

Fig. 1



Perspektiven in der Neurochirurgie/*Perspectives in neurosurgery*

V230

Neues Traktographie-basiertes TMS Sprachkartografie-Protokoll
Novel tractography-informed TMS language mapping protocol

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Objective

Navigated repetitive transcranial magnetic stimulation (nTMS) is used for language mapping in patients with tumors of the language system for general preoperative analyses and preoperative planning. The aim of this study was to improve the reliability and reproducibility of language nTMS mapping by using patient-specific cortical ends of language-related fiber bundles as targeted stimulation areas.

Methods

nTMS based language mapping was performed in 44 right-handed female (23) and male (21) patients, age-range 24-78 (*M*=53.3, *SD*=13.9) with left-hemispheric language-eloquent gliomas (WHO grade II (4), III (12), IV (25)) and metastases (3). The patients were further divided into two groups. Group 1 (n=22) received an earlier protocol, in which the entire perisylvian cortex was stimulated, while group 2 (n=22) received the novel tractography-based protocol, which stimulated individual cortical endings of the before delineated arcuate fascicle (AF) and peritumoral areas.

Results

nTMS and delineation of the AF was successful in all 44 patients. We observed a significant increase in error rates between group 2 (*M* = 5.0%, *SD* = 2.8%) and group 1 (*M* = 3.2%, *SD* = 2.1%), $t(42) = 2.4$, $p = 0.02$. Additionally, there was a significantly higher percentage of no response errors in group 2 (*Mdn* = 10%) than in group 1 (*Mdn* = 0%), $U(N_{Group\ 1} = 22, N_{Group2} = 22) = 147$, $z = -2.4$, $p = 0.015$. Our results also showed a significant difference in the distribution between nTMS-induced errors compared to non-errors using Brodmann areas (BA) X^2 (25, $N = 959$) = 54.9, $p = .001$. There was a higher percentage of errors than non-errors intersecting BA 45 (errors: 9.1% vs. non-errors: 3.6%), BA 41 (errors: 4.5% vs. non-errors: 0.7%), BA 37 (errors: 4.5% vs. non-errors: 0.3%), and BA 13 (errors: 2.3% vs. non-errors: 0.0%).

Conclusion

We have demonstrated that by considering the individual anatomy and stimulation of the AF, we were able to improve the efficacy to disrupt object naming via nTMS. Thus, the newly introduced method shows promising results to obtain more reliable non-invasive personalized language maps.

Perspektiven in der Neurochirurgie/*Perspectives in neurosurgery*

V233

Aneurysmavorhersage – ein klinisches Werkzeug
Aneurysm forecast – a tool for clinical use

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Objective

Computational fluid dynamics (CFD) is a powerful tool to simulate flow and derived quantities like wall shear stress, pressure and impingement forces in cerebral aneurysms. It has been shown, that CFD can predict thin-walled and vulnerable aneurysm regions, which can be a valuable information for therapy planning. The aim of our study was to translate this promising method from bench to bedside by developing a reliable, fast and user-friendly tool for neurosurgeons for operative planning as well as for scientific research on aneurysm initiation, growth and rupture.

Methods

We developed a software tool which combines all necessary features to compute the flow field in the aneurysm using 3D rotational angiography data. This includes a semi-automatic workflow for aneurysm segmentation, fully automated numerical mesh generation (open source library cfMesh v1.1.) and flow computation (OpenFOAM) and visualization of streamlines and morphological and hemodynamic parameters often used for rupture risk evaluation, like Size Ratio (SR) and Wall Shear Stress (WSS).

Results

The Aneurysm Forecast tool allows to obtain reliable CFD results in less than thirty minutes for even acute cases. It was rated as user-friendly by practicing neurosurgeons after an initial training. We conducted convergence studies on input parameters like mesh size, optimal length of inlet and outlets and evaluated the influence of flow split on the CFD results. Thus, we defined optimal input parameters to obtain reliable and stable, but also fast results. Nevertheless, the software is open to choose different input parameters for scientific use. The CFD results could be visualized in an in-house developed 3D-viewer in an operative setting, including craniotomy and positioning, allowing patient-specific dissection planning (see Fig. 1 and 2), and also be exported to navigation for intraoperative use.

Conclusion

We present a novel assistance tool for aneurysm surgery which provides fast and reliable predictions about vulnerable aneurysm regions in less than thirty minutes for even emergency cases. Visualization of preoperative CFD simulations helps the surgeon to recognize thin-walled and vulnerable regions correlating to low wall shear stress and high pressure. A CFD-adjusted approach and dissection of the aneurysm can potentially improve surgical tactics to prevent intraoperative rupture. Furthermore, this user-friendly and adjustable tool is suitable for clinical and fundamental research.

Fig. 1

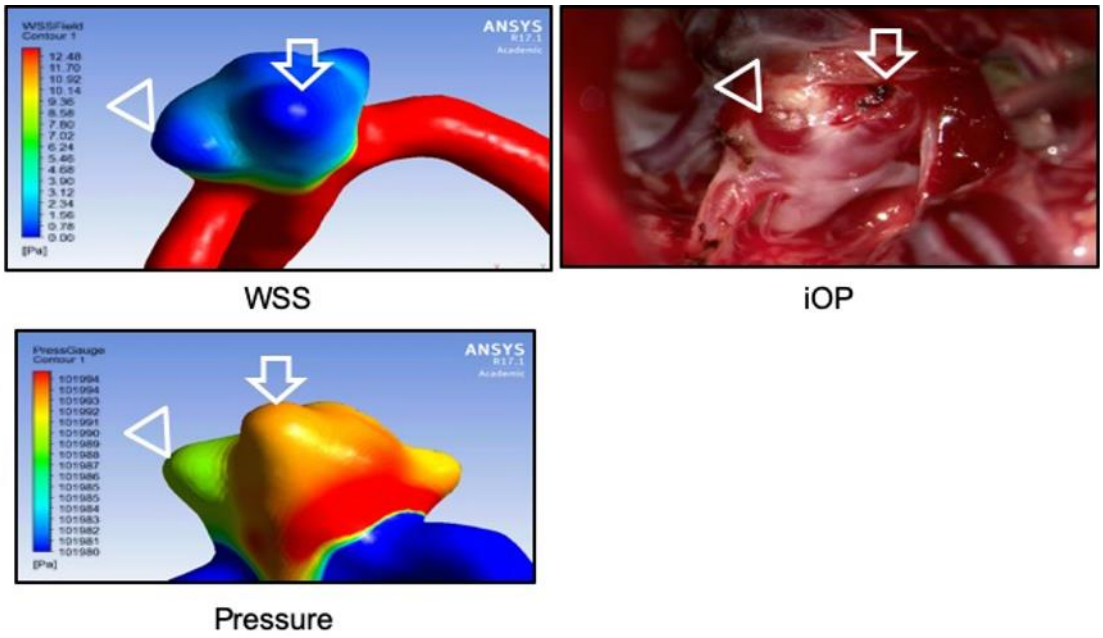
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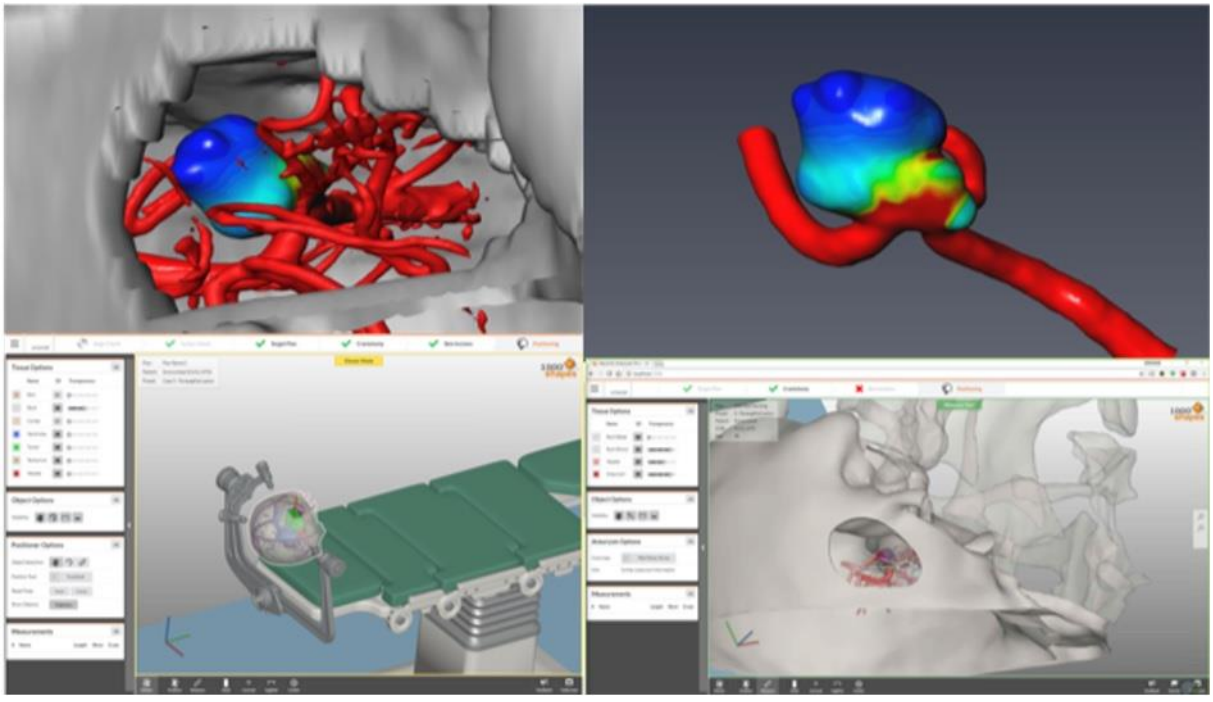
Fig. 2



Qualitätssicherung und Komplikationsmanagement II/*Quality assurance and complication management II*

V234

Qualitätsmessung und spezifische Qualitätsindikatoren für die Akutbehandlung der intrazerebralen Blutung in Hessen

Quality metrics and specific quality indicators for the acute care of intracerebral haemorrhage in Hesse, Gemany

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[3]Johann-Wolfgang Goethe Universität, Klinik für Neurologie, Frankfurt am Main, Germany
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[5]Johann-Wolfgang Goethe Universität, Institut für Neuroradiologie, Frankfurt am Main, Germany
[6]Klinikum Bad Salzhausen, Klinik für Neurologie, Bad Salzhausen, Germany
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Objective

The office of quality assurance in Hesse, Germany was established in 1995 to improve the quality of acute stoke care. Initially, quality indicators (QIs) for hospital-based care for patients with ischemic brain infarctions were developed and measured. In the last years, these QIs were partially transferred for the acute care of intracerebral hemorrhage (ICH) and new specific QIS for ICH were developed.

Methods

In 2019, 105 hospitals participated in the Hessian stroke registry. After completion of a pilot phase in 2018, we agreed on a set of nine QIs for 2019. The QIs measure outcomes (three) and processes (six). Furthermore, two new QIs were developed in 2019: Correcting INR for patients treated with vitamin K antagonists and antidote therapy for patients on new oral anticoagulants. For indicators that measure outcomes additionally ratios of observed (O) and expected rates (E) were calculated.

Results

In 2019 the following results for the QIs of all participating hospitals were observed: Neuroimaging with CT or MRI ≤30 minutes after admission [76.5% (95%CI: 73.4-79.3)], dysphagia screening [87.8% (95% CI: 85.4%-89.8%)], treatment on stroke or intensive care unit [93.8 (95% CI: 92.1%-95.0%)], physical/occupational therapy [93.2% (95% CI: 91.0-94.9)], logopaedic treatment [91.5 (95% CI: 88.7%-93.7%)], and rehabilitation for patients with relevant disabilities [86.7% (95% CI: 83.6%-89.3%)]. The overall pneumonia rate was 16.4% [Ratio O/E: 0.96 (95% CI: 0.85-1.07)]. Overall in-hospital mortality was 23.4% [Ratio O/E: 1.00 (95% CI: 0.91-1.10)]. After excluding patients with palliative settings the observed in-hospital mortality rate was 6.4% [Ratio O/E: 1.02 (95%CI: 0.80-1.28)].

Conclusion

Specific quality indicators for ICH are helpful for the monitoring stroke care quality. They create the basis for quality improvement and prioritization in acute stroke care. QIs must be designed, defined, and implemented based on current guidelines.

Qualitätssicherung und Komplikationsmanagement II/*Quality assurance and complication management II*

V235

Die endoskop-assistierte Technik zur Prävention von Rhinoliquorrhoe nach Vestibularisschwannomoperation über den retrosigmoidalen, transmeatalen Zugang

Reducing the risk of CSF fistulas in vestibular schwannoma surgery via the retrosigmoid transmeatal approach – the endoscope-assisted sealing of the inner auditory canal

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Objective

To analyze risk factors for developing a cerebrospinal fluid (CSF) fistula after vestibular schwannoma (VS) surgery through the retrosigmoid transmeatal approach and to assess the potential role of the endoscope assisted sealing of the drilled inner auditory canal (IAC) in reducing the incidence of CSF leaks.

Methods

238 patients were included in a historical control study. All patients were operated for VS via the retrosigmoid transmeatal approach in our Neurosurgical Department. The patients were divided into two groups. The selection criterion was the point in time of introducing the technique of endoscope assisted closure of the drilled IAC. Patients in group A (n=138) underwent a microscopic closure of the opened IAC with muscle and fibrin glue, while patients in group B (n=100) underwent an endoscope-assisted closure with bone wax, muscle and fibrin glue. Patients" charts, operating reports, imaging studies (MRI, thin slice bone window CT scans) and follow-up records were analyzed. A horizontal line dividing the IAC perpendicular to its longitudinal axis at its midpoint graduated the pneumatization of the IAC in two categories: P1 (solid medial half of the IAC) and P2 (pneumatized medial half of the IAC).

Results

16 CSF fistulas occurred in group A (11,6%), one in group B (1%). The difference is significant ($p < 0.001$). A pneumatization P2 was present in 32% of cases in group A and in 31% of cases in group B. No difference of the extent of pneumatization was noted regarding gender or side of the tumor. In group A the extent of pneumatization P2 was associated with a significantly higher risk of suffering a postoperative rhinoliquorrhea compared to P1 ($p<0.001$). In group B in 96 patients the IAC was opened and in 36 sealed with bone wax, muscle and fibrin glue under endoscopic visualization. Postoperative thin slice bone window CT scan demonstrated opening of air cells at the level of the IAC in 37 cases. All cases were initially treated with a lumbar CSF drainage for 7 days. In 15 patients in group A and in the single case in group B this procedure was successful. One patient in group A needed revision surgery to stop the rhinoliquorrhea (0,7%). No infection occurred.

Conclusion

The extent of pneumatization of the IAC is the determining risk factor for a postoperative CSF fistula in the retrosigmoid transmeatal approach. The endoscope-assisted sealing of the drilled IAC seems to significantly reduce the incidence of rhinoliquorrhea in VS surgery.

Qualitätssicherung und Komplikationsmanagement II/*Quality assurance and complication management II*

V236

Das Syndrom des supplementär motorischen Areals in der Gliomchirurgie – eine Klassifikation basierend auf klinischen und bildgebenden Daten

Supplementary motor area syndrome in glioma surgery – towards a classification system based on clinical and imaging data

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Objective

Surgical resection of gliomas involving the supplementary motor area (SMA) frequently results in a symptom complex described as "SMA syndrome", which is characterized by mostly transient contralateral hemiparesis and speech deficits. As factors potentially influencing the severity and and duration of symptoms remain elusive, we aim to further investigate the clinical outcome and potential predictors in a large, multicentric cohort of patients with diffuse gliomas.

Methods

Forty-five patients with diffuse gliomas located in the superior frontal gyrus were included in this retrospective study. Clinical and neurological status were assessed pre- and postoperatively, at discharge and during follow up. MRI data was obtained pre- and postoperatively. Preoperative tumorous infiltration as well as postoperative injury of cortical and subcortical areas were analyzed using atlas-based parcellation. Associations between clinical and image-based parameters were analyzed using group tests and correlation anlyses.

Results

Incidence of SMA syndrome was 76% (n=36). Main symptoms were hemiparesis, aphasia and mutism. Symptoms resolved within several hours to 42 days (median=1 day). Persistent deficits after 3 months were observed in 27 patients. Duration and severity of symptoms were independant of age, tumor size and extent of resection. Injury of the **SMA proper** was associated with immediate postoperative hemiparesis of the upper (p=0.045; cc=0.425) and lower extremity (p=0.012; cc=0.481). Injury of the **corpus callosum** was associated with longer duration (> 2 days) of motor symptoms (p=0.03; cc=0.317) and with occurrence of mutism (p<0.001; cc=0.519) and aphasia (p=0.041; cc=0.298). Mutism was additionally notably associated with injury of the **pre-SMA** (p=0.048; cc=0.289).

Conclusion

The present study provides novel insights regarding the factors associated with severity and duration of postoperative SMA syndrome in glioma surgery - while further reinforcing current hypotheses of the mechanisms enabling functional recovery after SMA lesion *(interhemispheric connectivity)*. This data will help neurosurgeons in patient consultation and help improve patients´ compliance during recovery period by improved prediction of severity, duration and long-term outcome.

Qualitätssicherung und Komplikationsmanagement II/*Quality assurance and complication management II*

V237

Die Häufigkeit und Art unerwünschter Ereignisse und der Zusammenhang mit menschlichem Versagen in der Neurochirurgie – eine prospektive Beobachtungsstudie

The incidence and nature of adverse events and their association with human error in neurosurgery – a prospective observational study

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Objective

Adverse events (AEs) in neurosurgery are a relevant cause of disability or death. Their incidence is a key quality indicator that plays an important role in the future of health care. The goal of this study was to determine the overall incidence, nature and severity of AEs in neurosurgical care, and to investigate the contribution of human performance deficiencies.

Methods

This was a prospective observation of all in-house AEs at the neurosurgical department of an academic supra-maximum medical care center. A consecutive sample including all 4176 inpatients treated at this institution was obtained between September 2019 and September 2020. AEs were recorded daily. The type of AE according to the American College of Surgeons, the AE severity according to the SAVES-v2 classification and a potential contribution of human error was evaluated weekly by consensus of all senior neurosurgeons of the department. Human errors were classified into one of five categories (Suliburk et al. 2019, JAMA Open): planning, execution, rules violation, communication, or teamwork.

Results

The case mix index of all patients was 3.16. There were 1611 AEs. 1043 (25.0% of all) patients had at least one AE. The most frequent types of AE were urinary and neurological events, followed by unplanned returns to the OR and iatrogenic surgical injuries (Table 1). In 25.9% of these cases, the major AE was associated with human error, mostly with execution (18.3%) or planning (5.6%) deficiencies (Table 2). 48.8% of all cases with AEs were severe (SAVES grade 3 or higher). In the subgroup of patients with AEs related to human error, there were more severe AEs than in the subgroup with spontaneous AEs (69.6% vs. 41.5% with SAVES grade 3 or higher). 361 patients (8.6%) had multiple AEs. This subgroup also had more severe AEs (67.6% SAVES grade 3 or higher). There were more severe AEs in cranial neurosurgery than in spinal neurosurgery (57.6 vs. 39.4%).

Conclusion

Prospective observation revealed that AEs are frequent in neurosurgical care. The high frequency of human performance deficiencies contributing to AEs shows that there is potential to further eliminate avoidable patient harm. These data can serve as benchmarks when discussing quality-based accreditation and reimbursement in upcoming health care reform.

Fig. 1

Type of Adverse Event	Number of pts.	Fraction of all pts.
Urinary event	346	8,3%
Neurological event	221	5,3%
Unplanned return to OR	215	5,1%
Iatrogenic surgical injury	205	4,9%
Venous thrombembolism	145	3,5%
Respiratory event	122	2,9%
Wound event	109	2,6%
Unexpected bleeding or transfusion	95	2,3%
Death	59	1,4%
Cardiac event	30	0,7%
Sepsis or septic shock	18	0,4%
Other	15	0,4%
Diagnostic failure	11	0,3%

Fig. 2

Human Error Class	Number of pts.	Fraction of all pts.	Fraction of pts. with AE
Total	270	6,5%	25,9%
Planning / Problem solving	58	1,4%	5,6%
Execution	191	4,6%	18,3%
Rules violation	18	0,4%	1,7%
Communication	1	0,0%	0,1%
Teamwork	2	0,0%	0,2%

Qualitätssicherung und Komplikationsmanagement II/*Quality assurance and complication management II*

V238

Die Wertigkeit der notfallmäßigen CT-Diagnostik bei shuntversorgten Patienten mit Pseudotumor cerebri Syndrom

To scan or not to scan? The utility of CT in shunted patients with pseudotumour cerebri syndrome presenting to the emergency department

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Objective

Patients with pseudotumor cerebri syndrome (PCS) frequently present to the emergency department (ED) due to disease-related symptoms after ventriculoperitoneal shunting (VPS). Computed tomography (CT) rarely reveals new pathological findings but is frequently performed, mostly considering medicolegal aspects. In this study we evaluated the usefulness of CT in the management of shunted patients with PCS who presented to the ED.

Methods

All adult patients with PCS who were diagnosed and treated with VPS between 2005 and 2019 in our department were included. We excluded patients with PCS initially diagnosed and operated elsewhere but presented postoperatively to our ED. Every CT performed in the ED was compared with previous postoperative CTs and was analysed for pathological findings.

Results

37 patients (29 women / 8 men) were diagnosed with PCS and treated with a VPS. All patients received a programmable valve; 34/37 with an integrated shunt assistant. 20/37 patients presented a total of 72 times in our ED. Most common symptoms were headaches (47 times) and visual disturbances (16 times). An ophthalmological consultation was conducted in 17/72 visits. 40 out of 42 CTs showed no pathognomonic changes when compared to previous available CTs. In 2 patients findings were suggestive for shunt infection and subsequently confirmed by MRI. Out of 42 ED visits with CT no change in the patient management was undertaken in 25 visits (54,3%); in 13 visits (28,2%) the opening pressure (OP) of the valve was altered and in 8 visits (17,4%) the patient was admitted for further treatment. In comparison, when no CT was performed management for the patient remained unchanged in 14 cases (53,8%), the valve OP was altered 5 times and 5 times findings led to admission (19,2%).

Conclusion

Our findings suggest that contrary to shunted hydrocephalus patients CT in shunted PCS patients in general, does not reveal signs of shunt malfunction or subdural hematomas. Therefore management of these patients can rather rely on clinical findings as long as visual deterioration or shunt infection is not concerned. CT should be reserved for after ophthalmological examination confirmed new or worsening of pre-existing findings.

Neurovaskuläre Chirurgie II/*Neurovascular surgery II*

V240

Arteria Meningea Media Embolisation zur Behandlung chronischer Subduralhämatome – eine Fallserie
Middle meningeal artery embolisation for the treatment of chronic subdural haematomas – a case series

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Objective

Chronic subdural hematomas (cSDH) represent a common neurosurgical pathology with an incidence of 1.7-20.6 per 100,000 persons per year. Surgical evacuation shows a significant recurrence rate with the need of reevacuation in up to 10-20%. Endovascular middle meningeal artery embolization (MMAE) was recently proposed as a promising stand-alone or adjunct to surgical treatment. This study aims to evaluate the effectiveness and safety of the endovascular embolization of the middle meningeal artery for the treatment of cSDHs.

Methods

From 06/2019 to 08/2020 a total of 26 patients (19 m / 7f; median age 79 (71-85)) with 35 cSDHs (9 bilateral) were treated with MMA embolization. Patients underwent embolization as stand-alone treatment or as adjunct to surgical evacuation either prior to or after surgery. Patients were assessed clinically and with cCT 2 and 6 weeks after the procedure. Primary outcome was absence of significant recurrence with need for surgery. Complete hematoma resolution or significant reduction of more than 50% of its initial size, periprocedural complications and clinical outcome after the modified Rankin Scale (mRS) were secondary outcome parameters.

Results

MMA embolization was successfully performed in all patient with no serious adverse events. 1 Patient (3.8%) presented a hematoma at the inguinal puncture site without need for further treatment. 13 patients received MMAE without surgery, 18 for recurrence after surgical evacuation and 4 in combination with surgical evacuation. From 21/26 patients (80.7%) with 28 cSDHs (80%) follow-up was available for analysis with a median follow-up of 12 weeks (12-15). During follow-up one patient died due to an unrelated cause. From the 28 sufficiently evaluated cSDHs 2 (7.1%) needed surgery for recurrent cSDH after embolization whereas 26 (92.9%) met the primary outcome with 21 (75%) having a complete resolution. The median mRS on admission was 3 (2-4) with mRS at the last follow-up being 1 (0-1).

Conclusion

Data suggest that endovascular embolization of the middle meningeal artery is an effective and safe treatment method for patients with chronic subdural hematoma as a stand-alone procedure or in combination with surgery. Further randomised controlled studies are warranted.

V242

Die Erholung der Erregbarkeit des motorischen Systems bei Patienten mit chronischer hämodynamischer Ischämie nach Bypassanlage – eine nTMS Studie

Normalisation of motor system excitability after bypass-surgery in patients with chronic cerebrovascular ischemia – a nTMS study

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Objective

Recently we have introduced the concept of the "hibernating brain" in patients suffering from chronic hemodynamic ischemia. In the state of misery perfusion an adaptive reorganization of the cortical motor network consisting of a reduced cortico-cortical excitability, elevated inhibition and enlarged cortical motor area was detected. Surgical revascularization by EC/IC bypass led to a recovery of impaired cortical motor function. The aim this study now was to assess changes of corticospinal excitability and axonal integrity during chronic ischemia and following surgical revascularization.

Methods

In this study 53 Patients were examined before and 3-6 months after EC-IC bypass surgery using navigated transcranial magnetic stimulation (nTMS). We examined the cortical excitability by determining resting motor threshold (RMT) and motor area, corticospinal inhibition by cortical silent period (CSP) and axonal integrity by means of recruitment curve (RC) of both hemispheres.

Results

Hemispheres affected by cerebrovascular impairment presented with a lower cortico-cortical excitability (RMT 41,8 % ± 9,5% compared to 39,5 % ± 7,8 %, p <.05), higher corticospinal inhibition (CSP 172,4ms ± 46,2 compared to 136,7± 47,0, p <.05) and wider motor areas as compared to the unaffected hemispheres (3,3 ± 1,9 cm2 compared to 2,5 ± 1,3 cm2, p <.05). Following bypass surgery an improved corticospinal conductivity (RC 5,5 ± 2,1 compared to 8,9± 2,7, p < .05) and normalization of cortical excitability (RMT 40,7 % ± 7,8 5 compared to 38,8 % ± 8,3 %, p < .05) could be observed.

Conclusion

We demonstrated that the ischemic brain is, after revascularization, capable of reorganizing and restoring neuronal function as shown by a lower resting motor threshold and a change in neuronal recruitment. These findings suggest a "hibernation" of the brain, a condition of impairment capable of preserving functional integrity in chronic ischemia.

Neurovaskuläre Chirurgie II/*Neurovascular surgery II*

V243

Rezidivprädiktion von chronischen subduralen Hämatomen nach operativer Therapie basierend auf der inneren Hämatomarchitektur

Predicting recurrence of chronic subdural haematoma after surgical treatment based on internal haematoma architecture

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Objective

Chronic subdural hematoma (cSDH) constitutes one of the most prevalent intracranial disease entities requiring surgical treatment. A growing incidence is observed due to an aging population and increased use of prophylactic anticoagulant treatment. Although mostly taking a benign course after surgery, recurrence after cSDH treatment is common and associated with additional morbidity and costs. Routine post-operative imaging is brought into disfavor but still common in clinical practice. Aim of this study was to develop hematoma-specific parameters associated with increased risk of recurrence.

Methods

All consecutive cSDH admitted to a single university center between 2015 and 2019 were retrospectively considered for inclusion. Size, volume and midline shift of the initial hematoma was noted alongside relevant patient-specific risk factors. We applied a morphological classification system based on hematoma density, internal architecture and septation consisting of four grades, as a simplification of the Nakaguchi classification focusing on internal hematoma organization rather than stages within the natural healing process (0 = homogenous; 1 = mild compartimentalization, 2 = moderate compartimentalization , 3 = severe compartimentalization). Clinical outcome was assessed by means of the Glasgow outcome scale (GOS) up to 12 months after initial surgery. An odds ordinal logistic regression model was used to assess the score´s performance on predicting hematoma recurrence.

Results

We observed a recurrence rate of 31.6% (125 cases), in a series of 395 patients with a mean age of 75.2 ± 12.0 and a male to female ratio of 250 (63.3%) / 145 (36.7%). Apart from prior anticoagulant treatment (p = 0.012) neither demographic characteristics (age, gender) nor factors related to general patient comorbidity affected hematoma recurrence. Our classification based on internal organization outperformed existing classification systems in predicting hematoma recurrence. A decrease in grade was associated with an increase in the likelihood of developing recurrence, with an odds ratio of 1.944 (95% CI 1.101 to 3.431; p = 0.034) and the highest recurrence risk in the homogenous subtype of 45.7%.

Conclusion

We present a simplified easy to use morphological classification system for cSDH associated with a stepwise increased risk of hematoma recurrence. This provides a tool to identify patients who might still benefit from routine post-operative imaging in order to early identify hematoma recurrence.

Neurovaskuläre Chirurgie II/*Neurovascular surgery II*

V244

Langzeithemmende Wirkung von s-Ketamin auf die Ausbreitung von Depolarisationen in einem KCl-Modell und einem MCA-Okklusionsmodell im gyrencephalen Schweinehirn

Long-term inhibitory effect of s-ketamine on spreading depolarisations in a KCl model and a MCA occlusion model in the gyrencephalic swine brain

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Objective

We investigated the long-term effect of s-ketamine on SD characteristics in two gyrencephalic swine brain models.

Methods

A total of 27 female German landrace swines were used for this study. For this purpose, two gyrencephalic swine brain models were applied. In one model, SDs were elicited through topical application of KCl onto the cerebral cortex (n=15); in the other model (n=12), SDs were spontaneously induced after the occlusion of the middle cerebral artery (MCAo). A total of 15 animals were used in the KCl experimental model. These animals were divided into 3 groups: one control group and two s-ketamine groups. S-ketamine was either perfused at a dose of 2mg/kg BW/h or at a dose of 4mg/kg BW/h for a period of 18h. In the MCAo model 12 animals were used. These animals were divided into two groups of 6 animals, each: a control group and an s-ketamine group. S-ketamine was perfused at a dose of 5mg/kg BW/h for a period of 18h.

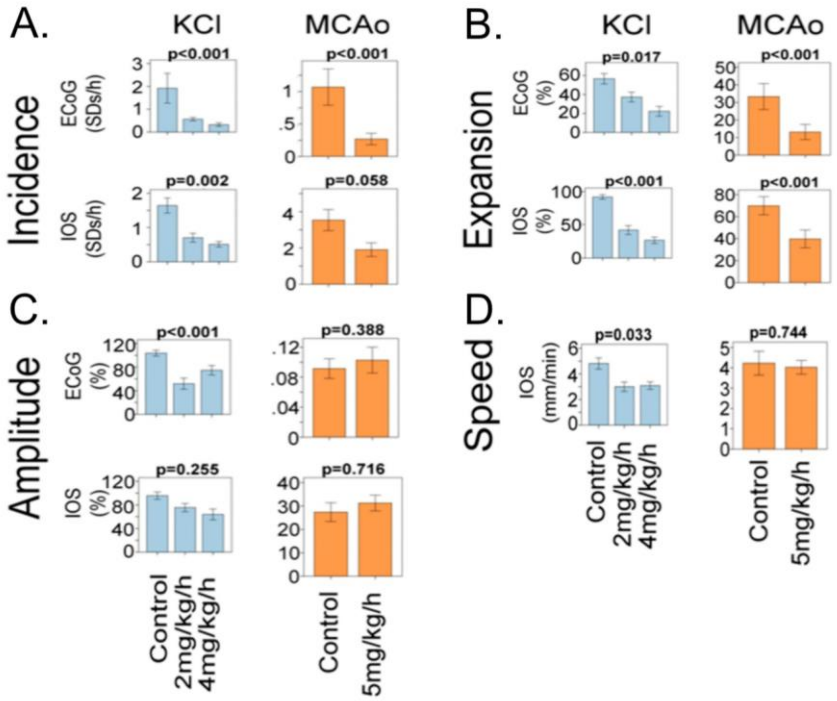
Results

We were able to corroborate that doses of s-ketamine above the therapeutically recommended (2mg/kg /BW/h) are needed to reduce SDs over a prolonged period of time of 18h. In particular, higher doses of s-ketamine are needed for injury-induced SDs than for KCl-induced SDs in order to achieve a similar effect. Our data shows that s-ketamine considerably reduces SD incidence and its expansion during its long-term administration. However, no clear effect on SD amplitude and propagation speed was observed in the stroke model during the same monitoring time, still an effect in these two properties was found in the KCl model. Notably, we did not find clear evidence for the development of tolerance against s-ketamine in the swine brain during the time of administration in either of the models.

Conclusion

Our results indicate that the long-term administration of s-ketamine at human equivalent doses is capable of interfering with SD development in the gyrencepahlic swine brain. Administration of s-ketamine over prolong periods did not lose efficacy against SDs. S-ketamine may be a therapeutically effective option to reduce SDs over prolong periods of time.

Fig. 1


A.
KCl
MCAo
Incidence
ECoG (SDs/h)
IOS (SDs/h)
p<0.001
p<0.001
p=0.002
p=0.058
B.
KCl
MCAo
Expansion
ECoG (%)
IOS (%)
p=0.017
p<0.001
p<0.001
p<0.001
C.
Amplitude
ECoG (%)
IOS (%)
p<0.001
p=0.388
p=0.255
p=0.716
Control
2mg/kg/h
4mg/kg/h
Control
5mg/kg/h
D.
Speed
IOS (mm/min)
p=0.033
p=0.744
Control
2mg/kg/h
4mg/kg/h
Control
5mg/kg/h

Neuroonkologie VI/*Neurooncology VI*

V246

Prädikatoren für prä- und postoperative Anfälle bei Patienten mit einem intrakraniellen Meningeom
Predictors of pre- and postoperative seizures in patients with intracranial meningioma

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Objective

Although pre- and postoperative seizures in patients with intracranial meningiomas are commonly observed, pathogenesis is largely obscure and risk factors for seizure development remain controversial.

Methods

To identify correlations between the occurrence of epileptic seizures and clinical, histopathological and radiological parameters, retrospective uni- and multivariate analyses were performed.

Results

Of 945 included surgically-naïve patients (689 females, 73% and 265 males, 27%; median age: 58 years) being operated between 1991 and 2018, 189 patients (20%) suffered from preoperative seizures. Male gender (OR: 1.91, 95%CI 1.37-2.68; p<.001), grade II/III histology (OR: 2.24, 95%CI 1.46-3.46; p<.001), brain invasion (OR: 2.59, 95%CI 1.45-4.63; p=001), non-skull base tumor location (OR: 3.07, 95%CI 2.13-4.41; p<.001), heterogeneous contrast-enhancement (OR: 1.60, 95%CI 1.04-2.46; p=.031), intratumoral calcifications (OR: 1.91, 95%CI 1.17-3.10; p=.009), an irregular shape (OR: 2.07, 95%CI 1.32-3.26; p=.002) as well as tumor (OR: 1.01 per ccm, 95%CI 1.00-1.02;p=.001) and edema volumes (OR: 1.01 per ccm, 95%CI 1.00-1.01; p<.001) were correlated with seizures in univariate analyses. Multivariate analyses confirmed only non-skull base tumor location (OR: 3.12, 95%CI 1.74-5.59; p<.001) and a rising peritumoral edema volume (OR: 1.01 per ccm, 95%CI 1.00-1.01; p<.001) as independent predictors for preoperative seizures. Furthermore, of 752 preoperatively seizure-naive patients (569 females (76%) and 183 males (24%); median age: 57 years) 69 (9%) presented postoperative seizures. In univariate analyses, a correlation between seizures and the preoperative Karnofsky Score <80 (OR: 1.91, 95%CI 1.01-3.59; p=.045), convexity/ parasagittal tumor location (OR: 1.77, 95%CI 1.06-2.95; p=.030), heterogeneous contrast-enhancement (OR: 2.24, 95%CI 1.14-4.39; p=.019) and intratumoral calcifications (OR: 3.35, 95%CI 1.59-7.05; p=.001) was determined. In multivariate analyses, postoperative seizures correlated with the age at the time of surgery (OR: 1.04, 95%CI 1.01-1.07; p=.009) and intratumoral calcifications on preoperative imaging (OR: 3.70, 95%CI 1.73-7.92; p=.001).

Conclusion

MR imaging contains important information to further asses the risk of pre- and postoperative seizure development in patients with intracranial meningiomas. In contrast, clinical and histological risk factors as well as independent predictors for seizures are sparse.

Neuroonkologie VI/*Neurooncology VI*

V247

Physiologische MR-Bildgebung zur Differenzierung von Glioblastomen und singulären Hirnmetastasen
Physiological MRI biomarkers in the differentiation between glioblastomas and solitary brain metastases

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Objective

Glioblastoma (GB) and solitary brain metastasis (BM) may appear similar in conventional magnetic resonance imaging (cMRI). Management strategies, however, are quite different with significant consequences on clinical outcome. The aim of this study was to evaluate the usefulness of a previously presented physiological MRI approach scoping to obtain quantitative information about microvascular architecture and perfusion, neovascularization activity, and oxygen metabolism to differentiate GB from BM.

Methods

Thirty-three consecutive patients with newly diagnosed, untreated, and histopathologically confirmed GB or BM were preoperatively examined with our physiological MRI approach as part of the cMRI protocol. For the analysis of tissue oxygen metabolism, we used the quantitative blood oxygen level depended (qBOLD) approach and for the neovascularization activity and microvascular architecture the vascular architecture mapping (VAM) approach. From the qBOLD data the oxygen extraction fraction (OEF), the cerebral metabolic rate of oxygen (CMRO2) and the tissue oxygen tension (PO2) were calculated. Likewise, from VAM the microvessel type indicator (MTI) for neovascularisation activity, the vessel size index (VSI) and the microvessel density (MVD) were derived. Furthermore, maps for cerebral blood flow (CBV) and microvascular perfusion (µCBV) were obtained.

Results

Physiological MRI biomarker maps revealed several significant differences in the pathophysiology of GB and BM: Central necrosis was more hypoxic in GB than in BM (30%; P = 0.036), which was associated with higher neovascularization activity (65%; P = 0.043) and metabolic rate of oxygen (48%; P = 0.004) in the adjacent contrast-enhancing viable tumor parts of GB. In peritumoral edema, GB infiltration caused neovascularization activity (93%; P = 0.018) and higher microvascular perfusion (30%; P = 0.022) associated with higher tissue oxygen tension (33%; P = 0.020) and lower oxygen extraction from vasculature (32%; P = 0.040).

Conclusion

Our physiological MRI approach, which requires only 7 minutes of extra data acquisition time, might be helpful to noninvasively distinguish GB and BM based on pathophysiological differences. However, further studies including more patients are required.

Fig. 1

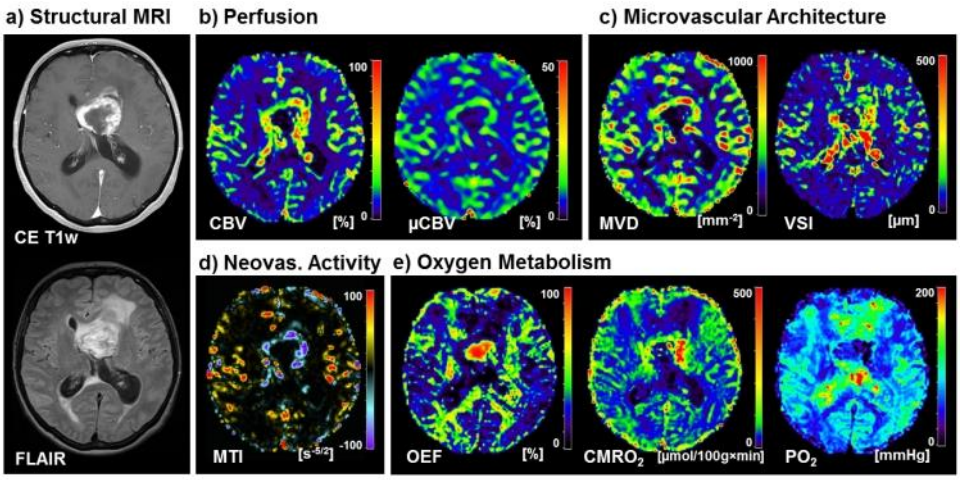

Figure 1. Physiological MR imaging of a patient diagnosed with glioblastoma.

Fig. 2

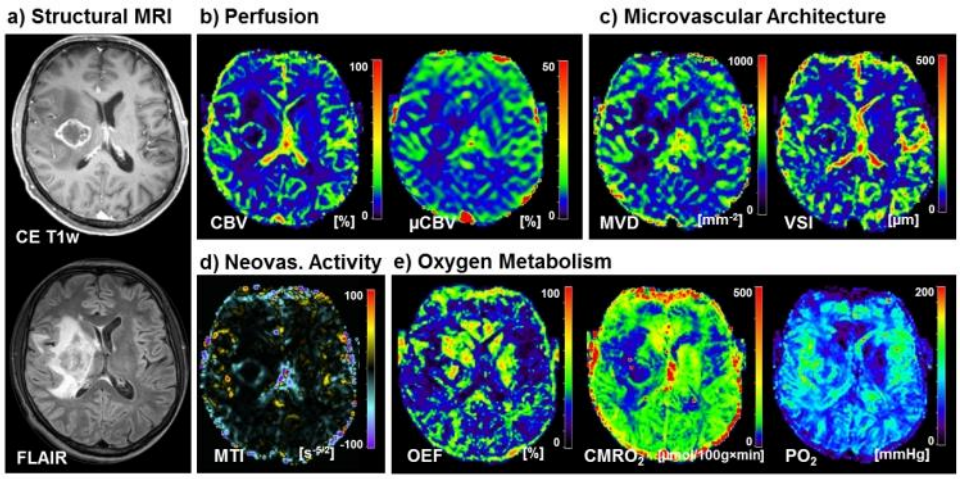

Figure 2. Physiological MR imaging of a patient diagnosed with a brain metastasis originating from bladder cancer.

V248

PSGL-1 auf zirkulierenden und tumor-infiltrierenden T-Lymphozyten bei Patienten mit Glioblastoma multiforme
PSGL-1 expression on circulating and tumour infiltrating lymphocytes in GBM patients

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Objective

We showed previously involvement of P-selectin glycoprotein ligand-1 (PSGL-1) in immune modulatory mechanisms of circulating and intra-tumoral macrophages in patients with *glioblastoma multiforme* (GBM). The aim of the present study was to characterize PSGL-1 expression on circulating and intra-tumoral T cells in GBM patients.

Methods

Surface expression of PSGL-1 and other activation/exhaustion markers was assessed on circulating (CL, n=14) and tumor infiltrating (TIL, n=10) lymphocytes of newly diagnosed GBM patients using flow cytometry. CL of matched healthy persons were used as controls. Arithmetic mean fluorescence intensity was used to determine expression level. CD4+, CD8+ and the subsets of naive, central memory (Tcm), effector memory (Tem) and CD45RA+ effector memory (Temra) T cells were assessed. All GBM patients received dexamethasone (cumulative dose of 70 mg in mean, range from 4 to 120 mg) before taking the blood sample.

Results

PSGL-1 expression was significantly increased on CD4+ naive and Tem CL subsets in patients compared to controls (CD4+ naive: 25.92 vs 25.86, p=0.048; CD4+ Tem: 19.41 vs 16.11, p=0.017). Expression of CD25 on CL was increased on CD4+ (12.37 vs 7.26, p<0,001) and several CD8+ subsets (Tcm: 4.97 vs 2.72, p=0.024; naive: 2.06 vs 1.49, p=0.012; Tem: 2.10 vs 1.42, p=0.021; Temra: 1.21 vs 1.11, p=0.041) in GBM patients compared to controls. PD-1 expression on CD8+ Tem (1.61 vs 1.25, p=0.029) and CD8+ Temra (2.65 vs 1.83, p=0.035) CL was increased compared to controls. No difference of CTLA-4 expression on CL was seen between the groups.

Tumor analysis showed a decrease of PSGL-1 expression on TIL compared to CL in GBM patients both on CD4+ (TIL: 2.47 vs 22.50 on CL, p<0.001) and CD8+ (TIL: 1.88 vs 28.52 on CL, p<0.001) subsets. PD-1 expression was significantly increased on TIL compared to CL on CD4+ (TIL: 7.03 vs 2.08 on CL, p=0.002) and CD8+ (TIL: 5.32 vs 2.04 on CL, p=0.002) populations. TIM-3 expression was increased on CD4+ TIL compared to CD4+ CL (0.51 vs. 0.19, p=0.002).

Conclusion

The decreased PSGL-1 surface expression on TIL in GBM patients is a novel finding in this study. The increased PSGL-1 surface expression on subsets of circulating CD4+ T cells can be a sign of the systemic anti-inflammation in GBM patients. Whether the dexamethasone medication is a confounder needs to be addressed in further studies. PD1 and TIM 3 expression on TIL was as expected in this study.

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Radionekrose nach Behandlung von Patienten mit primären Tumoren und Metastasen
Radionecrosis in patients treated for primary brain tumours and metastases

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Objective

Brain necrosis is a well-known phenomenon that is usually attributed to radiotherapy. It can be difficult to diagnose, to treat and might result in neurologic deterioration and mask tumor recurrences. The aim of this study was to investigate the clinical course of histologically diagnosed brain necrosis regarding symptoms, management, outcome and sampling errors.

Methods

We retrospectively reviewed our histopathological data bank for cases with the diagnosis of radionecrosis in patients who underwent surgery for primary intracranial tumors or metastases at our institution between 2008 and 2020. Analysis included onset and symptoms of radionecrosis, radiological features, correlation with radio- and chemotherapy, rate of sampling errors, management and progression of the necrosis.

Results

Nineteen cases (11 males and 8 females, mean age was 61±13 years) were identified with a histopathological diagnosis of radionecrosis. Ten patients (53%) initially had brain metastases of different primary tumors, seven (37%) had primary brain tumors (oligodendroglioma n=4, glioblastoma n=3), one had a pituitary adenoma and one had an anaplastic meningioma. Five patients (26.3%) presented with symptoms and the remaining patients were asymptomatic. Out of all patients, radionecrosis was radiologically considered only in one case prior to the surgery. At diagnosis of radionecrosis, all patients had underwent radiotherapy. Median interval between radiotherapy and diagnosis of radionecrosis was 9 months (range 1 to 40 months) and median dose of radiotherapy was 52 Gy (range 30 to 60 Gy). Seven cases (36.8%) had received chemotherapy concomitantly during radiotherapy. Radionecrosis was treated in 7 patients with corticosteroids, 4 of which showed regression of the lesion and three were stable. The remaining patients were monitored without further treatment, showed no radiological regression but stayed stable. Subsequently, tumor recurrence was diagnosed through a further surgical intervention in 4 patients, with a median interval between diagnosis of radionecrosis and tumor recurrence of 3 months (range 3 to 5 months), suggesting a sampling error rate of 21%.

Conclusion

Radionecrosis is a rare entity that was mainly associated with radiotherapy of brain metastases and primary brain tumors in our series. It mostly showed a benign clinical course with and without treatment with corticosteroids. Close monitoring is mandatory though, as sampling errors occurred at a rate of 21%.

Neurochirurgie über Sektoren- und Trägergrenzen hinweg/*Neurosurgery crossig health sector and hospital operator boundaries*

V251

Eine Frage der Gebrechlichkeit, nicht des Alters – subdurales Hämatom in geriatrischen Patienten
A matter of frailty, not age – subdural haematoma in the elderly

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Objective

As life expectancy continues to rise in Western countries, neurosurgeons are confronted with an increasing number of geriatric patients suffering from chronic subdural hematoma (CSDH). Studies have determined geriatric patients to be at higher risk for surgical complications, and age has been deemed a risk factor for poor outcome in surgical series of CSDH. In this study, we aimed to determine if frailty, and not age, can better stratify the risk of elderly patients with CSDH for poor outcome and mortality.

Methods

We conducted a matched cohort study of elderly patients undergoing twist-drill craniostomy under local anesthesia for CSDH. We evaluated patients based on traditional predictors of poor outcome, such as Glasgow Coma Scale (GCS) at admission, Markwalder grade, anticoagulant use, and hematoma volume. We assessed their frailty with the Clinical Frailty Scale (CFS) and their outcome based on the Glasgow Outcome Scale (GOS). Good outcome was defined as GOS 4-5. We stratified patients in two groups according to age, ≥85 years, and ≥65<85 years.

Results

A total of 42 patients aged 85 or older were identified and matched to a cohort of 42 patients aged between 65 and 84. In an ANOVA analysis, no statistically significant differences were observed in the baseline characteristics of both groups. Good outcome was observed in n=28/42, 66.7% of younger patients, and n=24/42, 57.1% of older patients, with mortality rates of 9.5% and 4.8%, respectively. These differences were not statistically significant. In a linear regression analysis, GCS and CFS were predictors of outcome and mortality, but not age.

Conclusion

In a continuously aging population, clinical assessment of patients with CSDH based on their premorbid functionality and frailty appears to be more informative than age alone for outcome prognostication.

Neurochirurgie über Sektoren- und Trägergrenzen hinweg/*Neurosurgery crossig health sector and hospital operator boundaries*

V252

Neurochirurgie in Zeiten der Krise – Ergebnisse einer internationalen Umfrage zum Einfluss der Corona-Pandemie auf die Neurochirurgische Tätigkeit

Neurosurgery in times of crisis – results of an international survey regarding the impact of the COVID-19 pandemic on neurosurgical practice

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Objective

Due to international and national political measures dictated by the nature of the pandemic, and the different timescale of diffusion of SARS-CoV-2 throughout the world, neurosurgeons were flooded with a variety of regional regulations, protocols, and timely produced standard operating procedures. Several editorials and articles have been published since. Qualitative studies on how the pandemic affected neurosurgeons personally, with additional focus on their practice, are still scarce. Here we present the results of an international online survey.

Methods

Neurosurgeons were invited to participate in an online survey of 42 questions, endorsed by the European Association of Neurosurgical Societies (EANS). Personal perception and practice relevant information were captured: departmental data, personal feeling of safety, financial security, local precautions, number of surgeries performed, changes in daily routine, and other practice-related information were inquired. Differences among practice types were closely reviewed.

Results

204 neurosurgeons responded (April-May 2020). Most participants were from Germany, followed by Spain, Italy, and the United Kingdom (UK), thus providing a balance between nations initially mildly affected (Germany and the UK) versus those severely affected (Spain and Italy) by the first wave of the pandemic. Neurosurgeons from Lombardy accounted for 5% of total responses. Participants were EANS members (73%), consultants (57.9%), from university hospitals (64.5%). While 65.7% of participants thought their institutions were adequately prepared, lack of testing for SARS-CoV-2, and scarcity of personal protective equipment were still matters of concern. Only 15% continued elective service, whereas 18.7% had already transitioned to COVID-19 and emergency medical services. Overall surgical activity dropped by 68% (cranial by 54%, spine by 71%), and even emergencies decreased by 35%. COVID-19 prompted changes in communication in 74% of departments, 44% increased telemedicine by >50%. While most neurosurgeons had concerns about personal and families" health, financial outlook appeared to be gloomy only for private practitioners.

Conclusion

The lockdown imposed by the COVID-19 outbreak called for drastic change of working routine and resulted in a dramatic decrease of elective surgical procedures. Neurosurgeons share common concerns but were not equally exposed to the personal health and financial dangers of the ongoing pandemic.

Neurochirurgie über Sektoren- und Trägergrenzen hinweg/*Neurosurgery crossig health sector and hospital operator boundaries*

V253

Ambulante parenterale Antibiotika Therapie (APAT) bei neurochirurgischen Patienten
Outpatient antibiotic treatment in neurosurgical patients – a prospective case series

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Objective

Spondylodiscitis and intracranial as well as spinal empyema present challenging cases in the neurosurgical context, and often require a long-term intravenous antibiotic treatment. In order to prevent independent patients from an extensive hospital stay, intravenous antibiotic treatment can be performed in an outpatient setting. Current literature supports its advantages, but lacks data regarding neurosurgical patients. We hereby aim to provide evidence of potential benefits of outpatient antibiotic treatment in neurosurgical patients.

Methods

We prospectively enrolled all patients eligible for outpatient antibiotic treatment in our neurosurgical department. We assessed inflammation markers, the clinical status using the SF-36 and EQ-5D questionnaires and the length of hospital stay and readmittance.

Results

Over a period of 10 months, we included a total of 12 patients. 5 patients suffered from spinal infections (2 patients with spondylodiscitis, 2 spinal empyema, 1 postoperative infection), 7 patients presented with intracranial infections (5 patients with subdural empyema, 1 patient with intracranial abscess, 1 patient with hypophysitis). In 11/12 patients, we identified specific bacteria causing the inflammation (63.6% Staphylococcus species). Median duration of antibiotic treatment was 8 weeks (4 weeks intravenous followed by 4 weeks oral treatment). Mean length of hospital stay was 16 days (range 5-42 days). 2 complications were detected: 1 patient with adverse reaction due to flucloxacillin (leucopenia) and 1 patient with a thrombosis, none of them affected the overall outcome. Patient were satisfied with the outpatient antibiotic treatment.

Conclusion

Outpatient antibiotic treatment provides a satisfying alternative for independent patients requiring long-term intravenous antibiotics. All neurosurgical patients were successfully treated and described a high contentedness with the outpatient treatment.

Neurochirurgie über Sektoren- und Trägergrenzen hinweg/*Neurosurgery crossig health sector and hospital operator boundaries*

V254

Transformation eines städtischen in ein universitäres Krankenhaus in Deutschland – die neurochirurgische Erfahrung

Transformation from municipal to university status of a German hospital – the neurosurgical experience

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Objective

On January 1st, 2019 a high-volume municipal hospital with 1700 bed capacity and a catchment area of 2.5 million inhabitants was transformed into a university hospital. The aim of this study was to identify changes within the department of neurosurgery before and after the conversion.

Methods

We compared two half-year periods, one before (municipal hospital status; August 1st, 2017 – January 31st, 2018) and one after (university hospital status, August 1st, 2019 – January 31st, 2020) the conversion. Time periods were chosen in order to avoid the effects of the first Covid-19 outbreak. Target parameters were hospitalisation rates, number of surgical procedures, length of hospital stay, patient's allocation area (% of patients living > 25 km from the city), as well as number and type of admissions.

Results

There were no differences in baseline patient's demographics between both groups. 52% were female with a median age of 62±17 years. Hospitalization rate increased by 29.4% (655 vs. 506), the increase originated mostly from in-house referrals. Surgical procedures increased by 18.6% (765 vs. 645). Length of hospital stay decreased slightly (8.37 vs. 8.78 days). The referral area did not enlarge (27.1% vs. 26.2% of patients were living > 25 km outside the city; p=0.62). Percentage of referrals from other hospitals (10.1% vs. 9.3%; p=0.69), emergency room admissions (24.8% vs. 27.5%; p=0.3) and elective admissions (65.1% vs 63.2%; p=0.62) did not have a statistically significant change.

Conclusion

Conversation to university status was associated with an increased number of hospitalizations and surgical procedures. Thereby neither referral type nor referral area size changed significantly.

Neurochirurgie über Sektoren- und Trägergrenzen hinweg/*Neurosurgery crossig health sector and hospital operator boundaries*

V255

Neue Klassifikation der postoperativen neurologischen Komplikationen (CPNC) in der Neurochirurgie
Suggestion for a new classification of postoperative neurological complications (CPNC) in neurosurgery

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Objective

The ranking systems are essential for science and quality management. Nowadays, there is a consensus in the neurosurgical field only regarding the use of some simple and less precise classifications such as "intra-/postoperative" and "minor/major" complications. These scales give no possibility to rank and compare the postoperatively occurred neurological disturbances. We aimed to design a classification, that could include all possible, postoperative, neurological disturbances and to prove its validity in terms of comparability and feasibility in the neurosurgical daily practice.

Methods

We designed a Classification with a total of seven grades commencing from grade "0" for no neurological disturbances to grade "6" for coma/vegetative state/demise concentrating on the character and severity of functional restriction. We retrospectively analyzed a period of care between June 2017 and December 2019 in our neurosurgical department. The neurological complications were classified according to the CPNC from two independent raters. The agreement between the raters was statistically analyzed using Cohen's kappa coefficient. The range of complications was also compared with the length of stay and statistically analyzed using two-sided Spearman's rank correlation coefficients.

Results

The study included a total of 1681 operations at 1530 patients. It included 1158 (68,8%) operations on the spine, 46 (2,7%) on the peripheral nervous system, and 477 (28,4%) cases of cerebrovascular surgery. The postoperative neurological disturbances occurred in 7.7% (n=119) of patients, of which 34.45% were classified from both raters as grade 1, 34.45% from one and 32.77% from another rater as grade 2, 12.60% from both raters as grade 3, 7.56% from one rater and 10.08% from another rater as grade 4, 5.04% from one and 4,20% from another rater as grade 5 and 5.88% from both raters as grade 6. The agreement between the raters was statistically "almost perfect," according to Landis and Koch, with K = 0,94. The ranking system was proportional to the length of hospital stay.

Conclusion

The CPNC can be useful in neurosurgery to assess the rates of postoperatively occurred neurological disturbances. We can recommend the CPNC as an easily applicable and comparable instrument in the quality management in neurosurgery.

Fig. 1

Classification of Postoperative Neurological Complications (CPNS)	
Grade 0	No neurological Disturbances
Grade 1	Any remittent neurological disturbances with full improvement spontaneously or as a result of any temporary drug therapy or re-surgery. A single epileptic seizure without the need for anticonvulsant therapy.
Grade 2	Lasting neurological disturbances resulting in no functional restrictions. No epileptic seizures. Need for long-term anticonvulsant therapy.
Grade 3	Lasting neurological disturbances resulting in slight functional restrictions. The patient, with the assistance of some tools, does not need outside help. Rare epileptic seizures despite of anticonvulsant therapy. Slight aphasia
Grade 4	Lasting neurological disturbances resulting in moderate functional restrictions and partial need of outside help. Average frequency of epileptic seizures despite anticonvulsant therapy. Moderate aphasia (e.g., significant restriction of communication).
Grade 5	Lasting neurological disturbances resulting in severe functional restriction and complete need of outside help. High frequency of epileptic seizures despite of anticonvulsant therapy. Severe aphasia (e.g., global aphasia)
Grade 6	Coma/vegetative state/demise
For assessment of long term outcome after medical rehabilitation is the suffix "r" (for rehabilitation) added.	

V256

Der Effekt von Medikamenten auf die kortikale Erregbarkeit gemessen mit transkranieller Magnetstimulation (TMS)

The effect of common neurosurgical medications on cortical excitability measured with transcranial magnetic stimulation (TMS)

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Objective

Preoperative assessment of motor and language function using navigated transcranial magnetic stimulation (nTMS) is becoming increasingly popular in neurosurgical practice. The resting motor threshold (RMT) represents the cortical excitability and has been identified as predictor for the postoperative motor outcome. Thus, a reliable assessment of the RMT is crucial to integrate nTMS results into preoperative planning, but many neurosurgical patients take CNS-effective drugs that can potentially impact the accurate assessment of the RMT. The aim of the present study was to examine the effect of common drugs on the RMT in neurosurgical patients.

Methods

648 patients (age: 53.1 ± 15.7, range 19-85 years; 296 females) were investigated preoperatively using nTMS due to brain tumors affecting the motor cortex and/or the corticospinal tract. Histologies included metastases (n = 167), gliomas (n = 373), meningiomas (n = 34), cavernomas (n = 19), AVMs (n = 17) and other (n = 38). The RMTs for both hands were recorded resulting in a sample size of 1298 observations. Linear mixed models were used to analyse the effect of drug intake on the RMT in a between-subjects design. Besides medication (antiepileptic drugs, benzodiazepines, corticoids or antidepressants), age, gender, hemisphere (tumor or healthy) and histology of the tumor were included in the analyses.

Results

There was considerable variation in the RMT across subjects (mean 35.7 ± 9.0, range 15-97%). There was no difference in RMTs between patients that took antiepileptic drugs compared to those that did not ($p = 0.149$), but RMTs increased when more than one antiepileptic drug was taken ($p = 0.034$). When looking at the specific drugs, only Carbamazepine led to a significant increase in the RMT ($p < 0.001$) and this effect was dependent on the dose ($p = 0.027$). Further, increased RMTs were observed under benzodiazepine intake ($p < 0.001$) and this effect did not vary between different benzodiazepines ($p = 0.175$). Corticoids ($p = 0.245$) or antidepressants ($p = 0.235$) did not influence the RMT. None of the previous effects was influenced by the histology.

Conclusion

Our results contrast with previous studies showing an effect of antiepileptic drugs on cortical excitability measured by the RMT. Only intake of Carbamazepine and benzodiazepines was associated with higher RMT values, while no other drug influenced the RMT. These results are strengthened by the large sample size of the present study.

V257

Die psychoonkologische Belastung von Patienten mit aggressiven Meningeomen – Ergebnisse einer retrospektiven Querschnittstudie

The psycho-oncological burden of patients with aggressive meningioma – results from a retrospective cross-sectional study

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Objective

Despite the overall perception of meningioma as a benign disease, 20-35% of patients experience a clinically aggressive course with debilitating treatment and poor outcome. In contrast to the growing interest in novel therapeutic strategies, the impact on health-related quality of life (QoL) is still understudied. Here, we analysed the psycho-oncological burden of patients with aggressive meningioma.

Methods

Our institutional cohort was searched for patients with surgery as the first intervention for intracranial meningioma and health-related QoL was assessed retrospectively at one time point with standardized self-assessment questionnaires (HADS-D, EORTC-QLQ-C30). Aggressive meningioma was defined as WHO grade II or III histology or recurrence of a WHO grade I meningioma within 5 years after index surgery. Results were correlated with demographic, tumour- and treatment-related factors by univariate und multivariate linear regression and were compared to internal control patients (WHO grade I meningioma, no recurrence within the first 5 years).

Results

400 out of 653 meningioma patients addressed returned the questionnaires (62%). Of those, 95 patients (24%) were classified as aggressive meningioma (recurrent WHO grade I: n=45; WHO grade II: n=49; WHO grade III: n=1) while 305 patients served as internal control. Patients with and without aggressive meningioma differed with regard to sex (p=0.019), age (p=0.015), extent of resection (p<0.0001) and adjuvant radiotherapy (p<0.0001) at index surgery and KPS at 1st follow-up (p=0.037). 34% and 24% of aggressive meningioma patients were screened positive on the anxiety and depression subscales of HADS-D as opposed to 33% and 27% of internal controls (not significant). Aggressive meningioma patients fared significantly worse on most of the function scales of QLQ-C30 (QL: p=0.004; PF: p=0.049; RF: p=0.003; CF: p=0.01; SF: p=0.018) and reported more financial difficulties (FI: p=0.015). In multivariate regression analysis of the complete cohort, female sex, KPS at 1st follow-up <70 and aggressive meningioma were independent factors of impaired QoL.

Conclusion

In this cross-sectional analysis, QoL was significantly impaired in aggressive meningioma patients, in line with a higher treatment intensity and lower postoperative functional status. Knowing that, patients with aggressive meningioma should be screened and treated for their psycho-oncological needs and QoL should be assessed longitudinally.

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Tumor-assoziierte Makrophagen sind ein unabhängiger prognostischer Marker in Meningeomen
Tumour-associated macrophages are independent prognostic markers in meningiomas

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Objective

Tumour-associated macrophages (TAMs) play an emerging role in tumour progression by creating an immunosuppressive tumour microenvironment. Therefore, we investigated TAM numbers and their activation (M1/2) in primary (p-) and recurrent (r-) meningiomas and evaluated their impact on survival.

Methods

Presence of TAMs was analysed in 195 clinically well-annotated cases (WHO°I *n* = 43, WHO°II *n* = 95, WHO°III *n* = 57; pMGM *n* = 120, rMGM *n* = 75). TAMs were quantified by a semiautomated analysis on whole tissue sections stained by multicolour immunofluorescence for CD68 as general TAM marker, and for CD163 and CD204 as M2 marker. CD68+ macrophages positive for either CD163 or CD204 were regarded as M2-polarized TAMs. Furthermore, concentration of 27 immune-relevant cytokines and chemokines from meningioma tissue samples (*n* = 46) were assessed by Luminex analysis.

Results

Median TAM infiltration accounted for 2.47% per total cell count in pMGM and 3.22% in rMGMs. Although no significant WHO°-dependent changes regarding TAM numbers were observed, high numbers of TAMs were associated with shorter progression-free survival (PFS) independent of prognostic confounding variables such as WHO, sex and age. In pMGMs, proportion of M2-polarized TAMs was significantly increased in WHO°II and WHO°III tumours compared to WHO°I (*P* = 0.009 and *P* = 0.003, respectively). Luminex data revealed a WHO°-dependent increase of several cytokines including IL-8, IL-10, and IL-12p70. Tissue samples containing higher numbers of TAMs demonstrated significant elevated concentrations of interleukin-1 family members (IL-1β, IL-1ra), IL-2, IL-4 IL-6, Eotaxin, G-CSF, and IFNγ. Furthermore, upregulation of IL-1β and IL-1ra resulted in shorter overall survival of patients (*P* = 0.049, *P* = 0.006, respectively). Correlation matrix clustering resulted in three distinct clusters, including two cytokine and one cellular cluster.

Conclusion

Taken together, we identified higher numbers of TAMs as an independent prognostic factor for shorter progression-free survival in meningioma patients. This was associated with increased levels of the interleukin-1 family members IL-1β and IL-1Ra and a shorter overall survival, indicating an important tumour promoting function in the tumour microenvironment, and thus might serve as therapeutic target.

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JM-PSN-04

Valproinsäure verändert den gesamten DNA-Methylierungsgrad und schwächt den Temozolomid-Effekt ab in Glioblastomzelllinien

Valproic acid modifies total DNA methylation level and attenuates temozolomide effect in glioblastoma cell lines

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Objective

Valproic acid (VPA) is a first-line antiepileptic drug for glioblastoma patients. There is also some evidence that it improves the clinical outcome in those patients. However, the exact mechanism of VPA action is vague. Therefore, we decided to look more precisely at a mode of VPA action. Epigenetics provides a new explanatory area for many pathological processes. It offers a connection between genetic and environmental factors that influence the development of the disease. Epigenetic regulation of gene expression is a dynamic, responsive, and reversible process. The best-characterized epigenetic mark is 5-methylcytosine (m^5C) in DNA. Temozolomide (TMZ) is a gold standard chemotherapeutic in glioblastoma. The aim of that project is to show the effects of VPA administration, alone and in combination with TMZ, on the total DNA methylation level.

Methods

Using the nucleotide post-labeling method, we analyzed the total amount of 5-methylcytosine, the main DNA epigenetic mark, in DNA of glioblastoma (T98G, U118, U138), cancer (HeLa) and normal (HaCaT) cell lines treated with VPA, and a combination of VPA and with TMZ.

Results

We adjusted the VPA doses used in the study to the ones virtually achieved in the central nervous system during treatment. We observed dose-dependent changes in the total DNA methylation in neoplastic cell lines and the lack of such effect in a normal cell line. VPA alone produced a clear dose-dependent increase in total DNA methylation in glioblastoma cell lines and scarce in the non-neoplastic cell line. In GBM cell lines, TMZ decreased the level of m^5C. However, the exposition of glioblastoma cells to the combination of VPA and TMZ caused an adverse synergistic effect resulting in DNA demethylation. The highest loss of m5C was observed at the highest concentration of TMZ (100 µM) and VPA (350 µM), after 3 h of incubation in the T98G cell line.

Conclusion

Total DNA methylation changes in glioma cell lines under VPA treatment suggest the new mechanism of that drug action and promote clinical implications for adjusting VPA and TMZ therapy in glioblastoma patients. The results of our study show the potential and possible obstacles of the combined therapy of temozolomide with valproic acid. Our experiments show that combined therapy with both drugs leads to total DNA hypomethylation. Therefore the conclusion would be to stop VPA administration during TMZ chemotherapy temporarily.

V259

Intraoperative Indocyaningrün (ICG)-Videoangiografie in der Hämangioblastomchirurgie
Intraoperative indocyanine green (ICG) videoangiography in haemangioblastoma surgery

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Objective

Hemangioblastomas are highly vascularized tumors and can cause an extensive architecture of surrounding pathological vessels. During microsurgical en-bloc tumor resection, it is crucial to first ligate tumor-feeding vessels. However, the distinction between these tumor-feeding vessels and draining veins is usually not obvious even under microscopic view. Indocyanine green (ICG) videoangiography is an intraoperative procedure that enables time-resolved fluorescence-based imaging of vessels (Figure 1). The aim of this investigation is to provide recommendations in which hemangioblastoma cases this technique might be beneficial for safe en-bloc tumor resection.

Methods

We reviewed all resected CNS hemangioblastomas over a period of 28 months (Aug 2018 - Nov 2020) in our VHL center to identify surgeries in which ICG angiography was used. Analyzing these cases, we qualitatively evaluated the benefit of intraoperative ICG angiography to identify possible tumor-feeding vessels and draining veins. Identified advantages and limitations of this technique were collected.

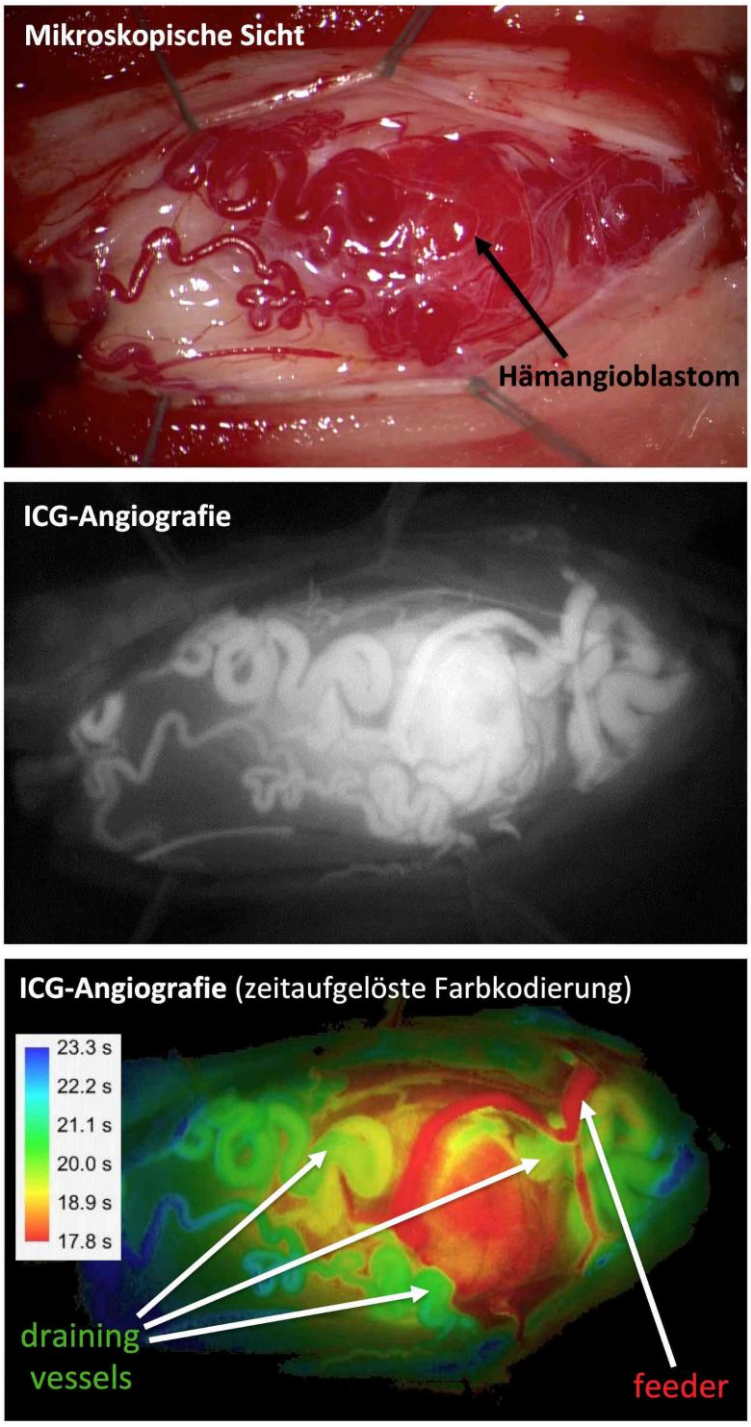
Results

In total, 48 patients had surgery for removal of up to six hemangioblastomas. Intraoperative ICG videoangiography was performed for 13 spinal and two intracranial hemangioblastoma in 15 surgeries (31 %). In 13 of the selected cases, the applied intraoperative ICG videoangiography provided useful information about the vascularization of the tumor and was therefore considered helpful (Figure 1). In two cases, the pathological vessels could not be clearly defined as tumor-feeding or draining vessels. Complete tumor removal was achieved in all patients. One patient experienced facial nerve palsy (House-Brackmann grade III) after removal of a tumor at the cerebellopontine angle.

Conclusion

ICG videoangiography offers real-time intraoperative imaging of the tumor vasculature and thus improves surgical decision-making. It should be noted that ICG videoangiography requires direct microscopic visualization of the structures to be assessed. For structures that are located deeper in or covered by the parenchyma, the information gain from ICG videoangiography is clearly limited.

Fig. 1


Mikroskopische Sicht
Hämangioblastom
ICG-Angiografie
ICG-Angiografie (zeitaufgelöste Farbkodierung)
23.3 s
22.2 s
21.1 s
20.0 s
18.9 s
17.8 s
draining vessels
feeder

Seltene Erkrankungen III/*Rare diseases III*

V260

Ein integriertes Behandlungskonzept mit limitierter Chirurgie und medikamentöser Wachstumshemmung bei NF2 assoziierten Vestibularisschwannomen bei Jugendlichen und jungen Erwachsenen verringert die Tumorwachstumsraten und ermöglicht einen längerfristigen funktionellen Hörerhalt

Effects of integrated operative and medical management of vestibular schwannomas in adolescents and young adults with NF2 on tumour growth rates and long-term preservation of hearing quality

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Objective

We reviewed our institutional experience in managing of NF2-associated vestibular schwannoma (NF2-VS) aiming at long-term hearing preservation in adolescents and young adults. Our focus was on effects of limited surgery and - if indicated - bevacizumab treatment in the further course of disease .

Methods

A total of 579 MRI based tumor volumetric measurements and hearing data sets were analyzed over time including all clinical follow-up data. The effect of surgery on tumor volume and growth rate was investigated in 46 tumors and on hearing function in 39 tumors. Long-term hearing follow-up behavior was compared with 20 non-operated ears in additional 15 patients. 16 operated NF2-VS were treated with bevacizumab in due course. Mutation analysis of the NF2 gene was performed in 25 patients.

Results

Limited surgery aiming at hearing preservation significantly slowed down NF2-VS growth rate. Factors associated with a higher growth rate were increasing patient age, tumor volume, and constitutional truncating mutations. Immediately after surgery, functional hearing was maintained in 82% of ears. Peri-operative deterioration of hearing was associated with initial hearing quality, larger tumor volumes, and larger resection amounts. Average hearing scores were initially better in the group of non-operated NF2-VS. Over time, hearing scores in both groups worsened with a similar dynamic. During bevacizumab treatment of residual tumors, four different patterns of growth were observed.

Conclusion

Decompression of the internal auditory canal with various degrees of tumor resection decreases postoperative tumor growth rates. Carefully tailored BAEP-guided surgery does not cause additional hearing deterioration. Secondary bevacizumab treatment showed heterogenous effects both regarding tumor size and hearing preservation. Overall, the integrated surgical and medical management of NF2-VS enables hearing preservation for years to enable these young patients in a vulnerable period of life to finish school and professional education with sufficient functional hearing in the majority of cases. In NF2-VS there is no place for initial surgery aiming at tumor removal.

Seltene Erkrankungen III/*Rare diseases III*

V261

Etablierung eines nationalen Register-basierten Netzwerkes für Neurofibromatose Typ 2 (NF2-Netzwerk)
German nation-wide registry-based neurofibromatosis type 2 service (NF2-Netzwerk)

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Objective

Neurofibromatosis type 2 (NF2) is a rare autosomal-dominant genetic disease with a prevalence of 1:60,000. Patients typically develop various tumours in the central and peripheral nervous systems and other disorders leading to a wide range of deficits. Due to the complexity of the disease, multidisciplinary teams in a specialised centers are required for optimal treatment of these patients. Despite the existence of such specialized centers, there is no systematic nationally coordinated approach to the treatment of NF2 in Germany.

Methods

Analogous to the UK national NF2 service delivery, we plan to implement a coordinated network of specialized NF2 centers[RS1] in Germany. These specialized centers will share an online-accessible registry that will capture prospective data from all patients treated at those centers and associated health care facilities. In addition to clinical data, patient reported outcome measures (PROMs), including quality of life and psychological questionnaires, will be collected digitally from patients via smart app. Data storage and handling is based strictly regulated according to current EU legislation and GCP standards.

Results

The aim of this approach is to improve the quality of patient care, resulting in higher and longer lasting quality of life as well as lower morbidity and mortality. Patient data will be accessible online for all participating medical professionals resulting in lower workload, a more complete medical profile of patients, timely notification for diagnostic follow-up, interventions and rehabilitation, and avoidance of unnecessary and duplicated investigations. Additionally, prospective data from a large multicenter cohort will be collected, which will improve the basis for high-quality research studies. The layout of the registry with the first 100 patients entered will be presented.

Conclusion

A nationally-coordinated approach of NF2 care in Germany is expected to improve the treatment and patient-based outcomes in this rare disease.

Seltene Erkrankungen III/*Rare diseases III*

V262

Lebensbedrohliche Meningeome bei Neurofibromatose Typ II – Eine Indikation für eine Peptid-Rezeptor-Radionuklid-Therapie?

Life threatening meningiomas in neurofibromatosis type 2 – An indication for peptide receptor radionuclide therapy?

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Objective

Multifocal progressive meningiomas in Neurofibromatosis type 2 (NF2) may become life threatening by increased intracranial pressure and severe neurological deficits, especially in reduced state from chronic NF disease. This analysis was designed to assess feasibility and safety in somatostatin receptor (SSTR)-targeted peptide receptor radionuclide therapy (PRRT).

Methods

Out of a cohort of 105 NF2 patients, eleven patients (7 females and 4 males; mean age, 39 (SD 12 y) with multifocal, progressive meningiomas underwent a median of 4 cycles of PRRT (range, 2 – 6 cycles). Therapy monitoring consisted of clinical and neurological examinations, laboratory tests, treatment response by MRI at 6 months intervals applying Neuro-Oncology response criteria for meningiomas (RANO) and for any acute or chronic adverse events according to NIH Common Toxicity Criteria (CTC) version 5.0.

Results

All patients tolerated PRRT without any acute adverse effects. Temporary hematologic toxicity (CTC °3) occurred in 2 patients. In 6 out of 11 patients (54.5%), NF disease was stabilized with a median progression-free survival (PFS) of this sub-cohort of 39 months (range 32-55 months). The remaining 5 patients without any sustained effect had only 4 months PFS. The median PFS of the entire cohort was 12 months (range, 1 – 55 months) and overall survival was 37 months (range, 5 – 61 months), respectively.

Conclusion

This pilot study showed PRRT to be feasible and well-tolerated in NF2 patients at advanced disease stages. In multiple, recurrent or treatment-refractory meningiomas with life threatening impact, PRRT might become a suitable treatment option.

Seltene Erkrankungen III/*Rare diseases III*

V263

Multizentrische retrospektive Mortalitätsstudie in Neurofibromatose Typ 2
Mortality in neurofibromatosis type 2 – a multi-centre retrospective study

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Objective

Neurofibromatosis type 2 (NF2) is an autosomal-dominant hereditary disease characterized by multiple tumours of the central and peripheral nervous system. NF2 is associated with a considerable morbidity and mortality. However, little data is available on life-expectancy, negative prognostic factors and causes of death in patients with this genetic variation.

Methods

In this multi-center retrospective study, we screened patient records from three dedicated NF2 centers and identified deceased individuals. We evaluated these patients" records with regard to age at death, cause of death, location of death and clinical presentation at last hospital/out-patient visit. Approval from the local ethics committees was granted.

Results

55 deceased patients were identified (n=27 female, n=28 male). Deaths were recorded between 1997 and 2019. The median age at diagnosis was 26 years (range 0.5 – 64 years). The median age at death was 40 years (range 1.5 – 86 years). 89% of patients had a high intracranial and spinal tumor load with bilateral vestibular schwannomas, > 3 further intracranial tumours and multiple spinal tumours. Caudal cranial nerves were affected by tumours in 27% of cases. Cachexia was recorded in 18% of patients. 23% of patients had hydrocephalus. Considerable vision impairment was recorded in 51% of cases, considerable hearing impairment was recorded in 87% of cases. Depression was recorded in 30% of patients. 2 patients developed malignancies: 1 of them had high-grade meningiomas, 1 had a basalioma. The cause of death was recorded in 19 cases: 8 patients died due to direct effects of brain tumors, while 2 patients died in the postoperative phase after brain tumor surgery. Pulmonary infections were the cause of death in 3 cases. Another 3 patients committed suicide. 3 patients died of cardiac insufficiency and 2 fell victim to road traffic accidents (RTA). The location of death was recorded in 13 cases: 5 patients died at home, 5 died in a hospital, the 2 RTA victims died on-scene and 1 patient died in a hospice.

Conclusion

This study shows that not only the direct effects of brain tumors such as raised ICP and strokes may be lethal for NF2 patients, but also indirect effects such as lower cranial nerve defects and the psychological strain associated with the disease can be life-threatening. Therefore, a tightly-woven interdisciplinary approach is key to the treatment of NF2 patients.

Seltene Erkrankungen III/*Rare diseases III*

V264

Neuropathie bei Neurofibromatose Typ I, II und III – ein Studienprotokoll zur Behandlung eines vernachlässigten Symptoms

Neuropathy in neurofibromatosis types 1, 2 and 3 – a study protocol to address a neglected feature

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Objective

Neurofibromatosis (NF) is associated with multiple nerve tumors mostly presenting at young or even adolescent age. Neuropathy is a further frequent symptom in NF and may be related to schwannoma / neurofibroma formation or may occur independently. This study is designed to identify factors triggering the development and resolution of neuropathy and pain, and is being supported by a Grant by the German Research Council (DFG).

Methods

A cohort of 200 patients with NF types 1, 2, or 3 will be included into the study for baseline and longitudinal characterization of neuropathy and pain by validated questionnaires and standardized worksheets. Further, in-depth clinical phenotyping of NF subtypes will be combined with extensive electrophysiological investigation of the large and small caliber nerve fibers, in-vitro testing of patient-derived individual sensory neurons, and differences in Schwann cell activities. Besides standard MRI investigations for all participants, selected patients will additionally undergo dorsal root ganglion perfusion and permeability analysis.

Results

To date, preliminary results are available. Most severe disease manifestation with high tumor load and neuropathy is present in about 25% of NF patients. NF-associated neuropathy occurs and develops in a disease-specific manner across the spectrum of NF disorders with a prevalence of neuropathic pain in subtypes NF1 and NF3, while tumor-independent neuropathic deficits are more frequent in NF2.

Conclusion

Neuropathy and pain in NF1, NF2, and NF3 are of great importance with regard to diagnostic measures, decision taking for therapy, and their impact on quality of life. A standardized test battery may be developed along with this study and serve for better identification of patients at risk.

Seltene Erkrankungen III/*Rare diseases III*

V265

Patienten mit Neurofibromatose in Deutschland – Prävalenz der in Krankenhäusern behandelten Patenten und klinische Merkmale zwischen 2007 und 2017

Patients with neurofibromatosis in Germany – prevalence of hospitalised patients and clinical characteristics between 2007 and 2017

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Objective

Neurofibromatoses (NF) I-III are rare genetic diseases which affect the nervous system and in case of NF I and II other organ systems. Despite fundamental differences between the diseases, the German Disease Related Group (DRG) classification system summarizes the three NF entities with one DRG code (Q.85.0). So far, no nationwide evidence on clinical characteristics of NF in Germany as well as prevalence over time exists.

Methods

Data on all patients hospitalized in Germany between 2007 and 2017 with International Classification of Diseases (ICD) code Q85.0 were provided by the German Federal Statistical Office and included in the analyses. We examined the prevalence of NF as main and concomitant diagnosis, age groups, overall mortality as well as Operation and Procedure Classification (OPS) codes for NF main diagnosis. Ethical approval was granted by local authorities (EA1/275/20). Data is presented as means per year ± SD.

Results

Between 2007 and 2017, 43.453 patients with NF (7.736 main diagnosis, 35.717 concomitant diagnosis) were treated in German hospitals. There were no relevant changes in NF prevalence between 2007 (n=4.148, main diagnosis n=762) and 2017 (n=3845, main diagnosis n=691). Most frequent concomitant diagnosis include benign and malignant neoplasms, arterial hypertension, café au lait spots, facial paresis, and headache. The mean mortality rate was 0.32% (±0.31) for NF as main diagnosis and 0.02% (±0.004) for NF as concomitant diagnosis. In patients with NF as main diagnosis, the most prevalent age group treated in a hospital was age 5 to 10 (16.5 %±1.4). The mean duration of hospital stay for NF patients showed a slight decrease over time (2007: 5.5 days; 2017: 3.7 days). Between 2007 and 2017, the most frequent diagnostic in-hospital procedures per year were MRI (610 ± 32), EEG (123±21), computed tomography (72 ± 21), neurophysiological (61±9) and audiometric (19±11) examinations. Most frequent therapeutic procedures was excision of diseased tissue of the skin (radical: 244 ± 133, local: 97 ±27) as well as neurosurgical interventions including surgery for benign neoplasms (46 ± 6) and rare (n<10) other procedures such as craniotomy, orbitotomy, functional nerve decompression and nerve excision.

Conclusion

Between 2007 and 2017, the prevalence of NF remained unchanged. The duration of hospital stay showed a slight decrease over time. Most frequent therapeutic procedures included dermatological and neurosurgical interventions

Ökonomie und Qualität/*Economics and quality*

JM-PSN-05

Kosten, Behandlungsschema und Auswirkungen der analgetischen Pharmakotherapie auf die postoperative Schmerzfunktion

Analgesic pharmacotherapy costs, regimen, and impact on postoperative pain-related functioning

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Objective

To analyze the impact of analgesic pharmacotherapy used after spine surgery on subjective quality of life and pain relief of patients with lumbar degenerative vertebral disc disease.

Methods

Fifty patients with LDVDD in L5/S1 and L4/L5 spine section who were qualified for spine surgery were recruited into this study.

The outcomes of postoperative pain and functional outcomes were recorded using standarised questionnaires.

Results

The greatest improvement in functioning between baseline and follow-up measurements was observed in the group of patients treated with non-opioids. Total average pharmacotherapy cost amounted to EUR 453.42 (±49.09).

Conclusion

This study supports the notion that pain pharmacotherapies could potentially be differentiated in terms of overall impact on quality of life, and that pain-related distress might be the most relevant driver of quality of life in this setting.

Ökonomie und Qualität/*Economics and quality*

V266

Über die Sella hinaus – Hypophysenadenome und die Effekte der transnasalen endoskopischen Mikrochirurgie auf Nasengesundheit und Lebensqualität

Beyond the sella region – transnasal endoscopic surgery for pituitary adenoma and its effects on nasal health and patients' quality of life

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Objective

The preferred neurosurgical route to resect lesions of the skull base, such as pituitary adenomas, is the transnasal endoscopic approach. Though commonly accepted as a gentle treatment, it has been reported that nasal health may be diminished after surgery. A systematic pre-/postoperative comparison is required to assess the amount of nasal distress after transnasal surgery and provide a basis for prophylactic supportive treatment to minimise side effects.

Methods

In this prospective single-centre observational study, we collected data with signed informed consent from a total of 77 patients operated between August 2016 and June 2020 with initial assessment and three months follow-up. All patients were diagnosed with pituitary adenoma operated at our institution via the endoscopic transnasal binostril transsphenoidal approach. We evaluated the quality of life with the standardised short form-36 inventory (SF-36) and nasal health with the sino-nasal outcome test for neurosurgery (SNOT-NC).

Results

The SF36 score, including its independent subcategories, was not significantly changed through endoscopic surgery. Also, SNOT-NC aggregate value did not change from pre- to postoperative (χ^2 p=0.520). However, patients reported a significant decrease in the ability to smell (χ^2 p=0.003), increase in nasal dryness (χ^2 p=0.001) and a weird nasal smell (χ^2 p<0.001). On the other hand, auricular pain decreased (χ^2 p<0.001) as well as orbital pain (χ^2 p=0.003) and dryness (χ^2 p=0.01). We observed a tendency towards improved nasal symptoms when nose drops were regularly used after surgery (χ^2 p=0.052). These observations were independent of the hormonal activity.

Conclusion

We could show that in patients with pituitary adenoma neither quality of life nor nasal health appeared to be significantly altered by endoscopic transsphenoidal resection. Furthermore, decreased auricular and orbital pain, as well as orbital dryness, proved an additional treatment success. Prophylactic symptomatic therapy of occurring symptoms like nasal dryness or impairment of smell by nose drops may reduce long-term side effects and improve patients' outcome.

Ökonomie und Qualität/*Economics and quality*

V267

Beeinflusst die Dauer der Kryokonservierung die Knochenstruktur von Knochendeckeln – computertomographische Analyse der Dichte von 158 Knochendeckeln mittels Densitometrie

Does the duration of cryopreservation impact the morphology of the bone flaps – computed tomography densitometry analysis of bone flap density in 158 patients

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Objective

Decompressive craniectomy (DCE) is a well-established surgical treatment for refractory intracranial hypertension, usually followed by autologous cranioplasty. Autologous bone flaps therefore are stored with cryoconservation (CC) for several months until cranioplasty can be performed. Bone flap resorption is a common problem after cranioplasty leading to disfigurement and protection loss of the brain, requiring further surgical treament. Here, we investigate the density of cryoconserved bone flaps by CT scanning after different periods of CC to identify the impact of storage duration on bone structure.

Methods

Over a 7-year period, bone flaps from 158 patients were preserved postmortem via CC. We performed thin slice CT densitometry and measured the bone mineral density (BMD) in Hounsfield units (HU) at multiple locations of cortical bone and spongiosa.

Results

According to the duration of CC 7 groups (from 1 year to 7 years of CC) were defined. There were no significant differences in BMD values of cortical bone or spongiosa among or within the groups. Both bone structures showed a physiological density, the mean density of the bone flaps was as followes (in HU): 1801,8 cortical/ 365,4 spongiosa (1 year); 1632/ 613 (2 years); 1632/ 522 (3 years); 1473,3/ 772,1 (4 years); 1303/606,3 (5 years); 1605/ 562,5 (6 years); 1640,9/ 510,5 (7 years).

Conclusion

In this series, there was no significant difference in the density of the bone groups associated with duration of CP. CT densitometry therefore cannot predict bone resorption after cranioplasty.

V268

Einfluss von Zertifizierungen und Digitalisierung auf die Patientensicherheit
Impact of accreditation and digitalisation on patients' safety

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Objective

Accreditation and digitalization are common tools to improve the efficacy of processes in clinical routine. The aim of this study was to elucidate, whether measures for quality management and digitalization have the ability to reduce treatment risks of patients in a surgical clinic.

Methods

All involved employees in patient treatment were asked for a systematic, process orientated and anonym survey to assess the probability of occurrence of 69 treatment risks during the stationary treatment of patients. Those possible risks were defined by a project team consisting of representatives of every occupation group involved in patient care. This survey was done before a quality management and digitalization were introduced in 2006 and latest, after various accreditations were performed and the digitalization was completed.

Results

Regarding the results of this survey, although the number of surgeries was increased by 1.8fold, while the number of employees increased only by 1.2fold to 1.4fold, the probability of occurrence of 20 treatment risks could be significantly reduced. The pronounced risk reduction was described for mistaken identity of patients, while complex process risks like deficient postoperative aftercare or dissatisfaction of patients due to deficient communication were unchanged.

Conclusion

Possibly increased process risks due to increased workload can be compensated with measures for quality management and digitalization. This requires a quality and risk management that is organized by the administration and carried by responsible and risk-aware employees without compulsion. Digitalization and measures of quality management have the ability to reduce patients" treatment risk and to compensate an increased workload. Particularly, accreditations are helpful to sustain and push measures for quality management.

Ökonomie und Qualität/*Economics and quality*

V269

Die Effekte der L4 Ganglionstimulation auf das molekular-inflammatorische und sensorische Profil von neuropathischen Schmerzpatienten

Molecular inflammatory and sensory phenotyping in CRPS patients treated with unilateral L4-dorsal root ganglion stimulation

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Objective

Complex regional pain syndrome have been associated with a pro-inflammatory state driven by different circulating mediators. Dorsal root ganglion stimulation (DRGSTIM) suppressed pain levels and improved functional capacity in intractable CRPS in observational and randomized-controlled studies. However, in-human studies evaluating the effects of selective DRG stimulation using objective outcome measures remains under-investigated.

Methods

This pilot study performed molecular inflammatory phenotyping (saliva/serum), gene expression assay of neuroinflammatory genes (PantherTM pathway enrichment analysis), quantitative sensory profiling and score-based assessment of pain, mood and sleep in 24 subjects (12 CRPS patients - 12 healthy controls) before and after 3 months of selective L4-DRGSTIM.

Results

After L4-DRGSTIM CRPS pain significantly decreased with improved sleep and mood. Elevated levels were found pre- and post L4-DRGSTIM for high-mobility group box 1, tumor-necrosis factor α, IL-6 and leptin indicating a pro-inflammatory state in CRPS patients. IL-1β was elevated pre-L4 DRGSTIM, but not post-treatment. IL-10 decreased after 3 months in serum, while saliva oxytocin increased after L4-DRGSTIM (Fig.1). Gene expression analysis demonstrated down-regulated *TLR1*, *FFAR2*, *IL1RAP*, *ILRN*, *C5*, *PKB* and *IL18* and upregulated *CXCL2, CCL11, IL36G, CRP, SCGB1A1, IL-17F, TNFRSF4, PLA2G2A, CREB3L3, ADAMTS12, IL1F10, NOX1, CHIA* and *BDKRB1*. CRPS subjects showed significantly increased thresholds for warmth, tactile and vibration detection (WDT, MDT and VDT) and exaggerated pain summation (WUR). After 3 months of unilateral L4-DRGSTIM all pain parameters exhibited trends towards normalization of sensitivity accumulating to a significant overall normalization for pain sensitivity (effect size: 0.91, $p<0.01$). Reduction of pain summation (WUR) correlated significantly with pain reduction after 3 months of L4-DRGSTIM.

Conclusion

L4-DRGSTIM promoted pain relief and improved functional impairment in CRPS patients revealing a pro-inflammatory molecular pattern. Serum IL-10 significantly declined, while saliva oxytocin increased after L4-DRGSTIM. Sub-group analysis demonstrated either upregulated or downregulated genes involved in immune host response and neural pain circuits and evoked significant normalization in the pain domain of the somatosensory profile. Thermoreception and mechanoreception remained unchanged.

Fig. 1

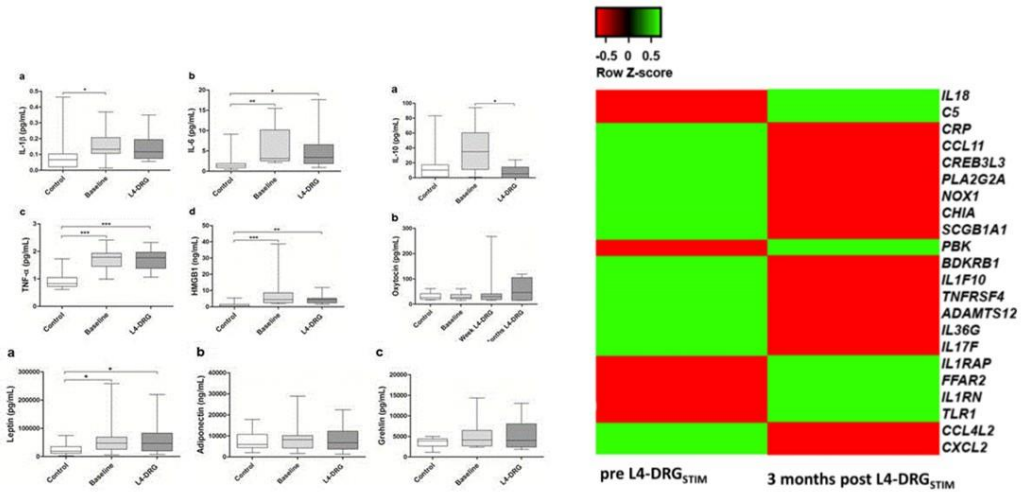
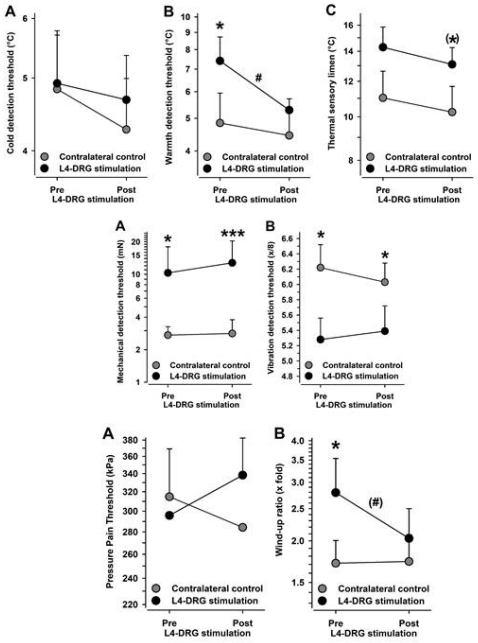

-0.5 0 0.5
Row Z-score
IL18
C5
CRP
CCL11
CREB3L3
PLA2G2A
NOX1
CHIA
SCGB1A1
PBK
BDKRB1
IL1F10
TNFRSF4
ADAMTS12
IL36G
IL17F
IL1RAP
FFAR2
IL1RN
TLR1
CCL4L2
CXCL2
pre L4-DRG$_{STIM}$
3 months post L4-DRG$_{STIM}$

Fig. 2


Cold detection threshold (°C)
Warmth detection threshold (°C)
Thermal sensory limen (°C)
Mechanical detection threshold (mN)
Vibration detection threshold (x8)
Pressure Pain Threshold (kPa)
Wind-up ratio (x fold)
Contralateral control
L4-DRG stimulation
Pre
Post
L4-DRG stimulation

Neurovaskuläre Chirurgie III/*Neurovascular surgery III*

V271

Mikrochirurgische Behandlung von unrupturierten Arteria cerebri media Bifurkationsaneurysmen – eine retrospektive monozentrische Langzeitstudie

Surgical treatment of unruptured middle cerebral artery bifurcation aneurysms – long-term retrospective single-centre study

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Objective

Microsurgical clipping of middle cerebral artery aneurysms (MCA) has traditionally been regarded as a standard treatment. Recently, a caseload reduction related to improved endovascular treatment options has occurred in cerebrovascular neurosurgery. Therefore, studies reporting the clinical and radiological long-term outcomes after clipping are highly warranted.

Methods

Patients with an unruptured MCA bifurcation aneurysm, who were surgically treated between 2002-October 2019, were included. In each patient the surgical strategy and clinical as well as radiological outcome was retrospectively determined. Logistic regression analyses were conducted in order to identify possible effects of clinical and demographic variables on several main and secondary target criteria related to complication.

Results

Overall 272 consecutive patients were included (mean age at operation 55 years, range 18-79 years). 270 patients were successfully clipped (mean aneurysm diameter: 5.8mm, range 2-25mm; 1-8 clips per patient) with an additional wrapping performed in six patients. Complete aneurysm occlusion was demonstrated in 252 patients (92.7%) using postoperative digital subtraction angiography in 254 patients (93.4%). Intraoperative rupture occurred in eight patients. In six patients (2.2%) a permanent neurological deficit persisted after treatment. At the last follow up only two of these six patients had an unfavorable outcome (modified ranking scale 3-5). In logistic regression analysis a significant effect of intraoperative rupture (p=0.049) on a permanent neurological deficit was estimated. Further, the risk of neurological deficits decreased significantly over time meaning that patients who were operated at a later time point suffered less often from a permanent neurologic deficit (p=0.009). Two patients died (0.7%) perioperatively (fatal fulminant sepsis versus pulmonary embolism). Two patients were retreated approximately 6 and 14 years after initial clipping surgery, of whom one patient presented with subarachnoid hemorrhage.

Conclusion

In this long-term retrospective study the morbidity and mortality rates were estimated to be very low when microsurgical clipping was performed. Especially retreatment rates were found to be low. Therefore, mircrosurgical clipping remains an adequate treatment strategy in patients with unruptured MCA aneurysms.

Neurovaskuläre Chirurgie III/*Neurovascular surgery III*

V272

Symptomatisches chronisches Subduralhämatom – Warum sind BNP-Werte bei Aufnahme erhöht?
Symptomatic chronic subdural hematoma – Why are brain natriuretic peptide serum levels at admission high?

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Objective

Brain natriuretic peptide serum levels (BNP) on admission are frequently elevated in patients with symptomatic chronic subdural hematoma (cSDH). However, the reasons for these elevated levels remain unclear. In patients with traumatic brain injuries, elevated BNP was associated with increased intracranial pressure (ICP), but cSDH exhibits unsteady expansion due to intermittent neomembrane microhemorrhages and fluid exudation, making ICP increases inconsistently. In addition, recent histopathological studies have demonstrated that immature cSDH neomembranes with increased microbleedings result in both the rapid expansion of small hematomas and worse clinical presentations. Therefore, the purpose of this study was to identify predictors of elevated BNP in symptomatic cSDH.

Methods

Patients with unilateral symptomatic cSDH who were surgically treated in our department between November 2016 and May 2020 and had a head trauma event for >3 weeks were enrolled in this study. BNP was measured on admission, and patients' neurological conditions and symptoms were prospectively assessed using a study questionnaire. Preoperative hematoma volumes (Hem-Vol) and midline shifts were measured on initial computer tomography to assess the degree of brain compression. BNP values were log10-transformed for a normal distribution to assess linearity with Hem-Vol values. These clinical and radiographic cSDH findings were then compared to a cohort of patients with isolated unilateral traumatic acute SDH (aSDH), characterized by a rapid hematoma expansion, who were admitted during the same period with head-trauma events within 24 hours of admission.

Results

In total, 212 patients were analyzed (cSDH: n=100; aSDH n=112). A linear regression analysis showed that higher log10BNP values were significantly associated with smaller Hem-Vol values in cSDH patients (p=0.003); but in aSDH patients with larger values (p=0.014). A multivariate analysis revealed that the presence of a neurological deficit (p=0.041), Hem-Vol <140 ml (p=0.047), advanced age (p=0.023), and a head trauma <24 hours were all independent predictors of elevated BNP in cSDH patients.

Conclusion

Elevated BNP in symptomatic cSDH patients is not related to a higher degree of brain compression as in aSDH, but instead, amongst others, to smaller hematoma volumes and the presence of neurological deficits. These represent two arguments in favor of cSDH immaturity prompting hematoma expansion. Further histopathological prospective studies are needed to validate our findings.

Neurovaskuläre Chirurgie III/*Neurovascular surgery III*

V273

Agatroban führt zu einer Reduktion des Sekundärschadens im ICB Mausmodell
Systemic administration of argatroban reduces secondary brain damage in a mouse model of intracerebral haemorrhage

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Objective

Spontaneous intracerebral hemorrhage (ICH) is a leading cause of disability and mortality. Perihematomal thrombin expression plays a pivotal role in edema formation and neuronal death. It is hypothesized that direct thrombin inhibitors (DTI) such as Argatroban mitigate secondary injury development after ICH. In our study we analyze the effects of systemic Argatroban treatment on neuronal injury and neurological outcome in an ICH mouse model.

Methods

We established a stereotaxic ICH model using C57BL/6 mice. 30 µl autologous blood was injected into the right basal ganglia. Intra-operative monitoring included intracranial pressure (ICP), cerebral blood flow (CBF) and blood pressure (BP) measurment. Argatroban (9mg/kg bodyweight) was injected 1 hour after surgery. Neuroscore and Rotarod testing were performed to detect neurological deficits. Mice were euthanized 24h and 72h after ICH. Frozen sections were stained with hematoxylin and eosin to evaluate size and localization of ICH. Immunohistochemistry was used to detect perihematomal thrombin. Immunofluorescence staining for NeuN and GFAP were used to evaluate parenchymal damage.

Results

The ICP increased during ICH induction with peak values of 54.0+-10 mmHg in the blood group and remained at 8.1+-0.6 mmHG in sham operated animals. CBF dropped to 32.0%+-8.1% of baseline in blood- and remained unaltered in sham animals. ICP and CBF returned to baseline values within 30 min after ICH. Perilesional thrombin expression increased by 4.24+-0.50-fold ($p < 0.05$) 24h after ICH. Perihematomal NeuN immunoreactivity was decreased in animals injected with DTI (3.79+-1.34-fold, 34.4+-0.21% area ($p=0.001$)) and those injected with saline (4.32+-2.26-fold, 31.8+-0.11 % area ($p=0.001$)). After 72h, mice receiving the DTI showed significantly lower neuronal loss, compared to mock injected animals (56+-19.2% area vs 107+-24.5%; $p=0.0013$). GFAP expression was increased in animals receiving the DTI 72h after ICH (0.99+-0.55% area vs 1.88+-0.83%; $p < 0.005$). Both groups performed similar using the rotarod performance test (saline: 92.5+-5s; DTI: 95+-3s; $p < .0001$). Likewise, no statistically significant disparities were detected using the neuroscore.

Conclusion

Systemic administration of Argatroban starting 1 hours after ICH significantly reduced neuronal damage 3 days after ICH. At the same time, GFAP expression increased indicating developing astrogliosis as potential protective mechanism to restrict the focus of neuronal damage.

Neurovaskuläre Chirurgie III/*Neurovascular surgery III*

V275

SEBES-Score vorhersagt die Notwendigkeit der konservativen Hirndrucktherapie und dekompressiven Kraniektomie nach Subarachnoidalblutung

The SEBES score predicts the need for conservative ICP treatment and decompressive craniectomy after subarachnoid haemorrhage

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Objective

The severity of early brain edema after aneurysm rupture was reported to be strongly associated with the risk of cerebral infarction and unfavorable outcome in patients with aneurysmal subarachnoid hemorrhage (SAH). Using the recently developed Subarachnoid Hemorrhage Early Brain Edema Score (SEBES), we analyzed the predictors of early brain edema and its impact on the complications related to intracranial pressure (ICP) increase after SAH.

Methods

All consecutive cases with SAH treated between 01/2003 and 06/2016 with available pre-treatment imaging (<72h after ictus) enabling the SEBES assessment were included (n=698). The data on demographic characteristics, previous medical history, common features of SAH, need for conservative ICP treatment and decompressive craniectomy, cerebral infarcts, in-hospital mortality and unfavorable outcome at 6 months (mRS>3) were collected from the institutional database.

Results

The mean SEBES value of the cohort was 2.51 points (±1.4). Of eleven pre-SAH parameters with significant results in the univariate analysis, only higher age (UC=-0.04 per-year-of-age-increase, p<0.0001) and presence of hyperuricemia (UC=-0.68, p=0.038) were inversely associated with the SEBES in the final multivariate analysis. In turn, the SEBES was independently associated with the need for conservative ICP treatment (aOR=1.38 per point-increase, p<0.0001) and decompressive craniectomy (aOR=1.68, p<0.0001) during SAH, as well as with the risk of cerebral infarcts (aOR=1.26, p=0.001), in-hospital mortality (aOR=1.25, p=0.02) and unfavorable outcome at 6 months (aOR=1.33, p=0.001). According to the receiver operating characteristic analysis, the clinically relevant cutoff for the SEBES for the association with the study endpoints was ³3 points.

Conclusion

Early brain edema on the admission computed tomography scan is a reliable marker of further ICP-related complications and poor outcome of SAH. Older individuals and those with hyperuricemia seem to be less prone to severe early brain edema after SAH.

Neurovaskuläre Chirurgie III/*Neurovascular surgery III*

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Zeit ist Hirn unter neuem Licht – Einfluss der Zeit bis zur dekompressiven Hemikraniektomie im malignen Schlaganfall

Time is brain revisited – the influence of timing for decompressive craniectomy in malignant stroke

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Objective

Decompressive craniectomy (DC) is an established life-saving surgical measure for malignant cerebral infarction (MCI), with randomized controlled trials showing case fatality reduction by 50-75% compared to best medical therapy. Timing of surgery is considered to be crucial, with studies advocating to perform DC within the first 48 hours after ictus. In this study, we aim to elucidate whether early (within the first 24 hours) and ultra-early (within the first 12 hours) DC can reduce mortality and improve outcomes in MCI.

Methods

We conducted a retrospective study of patients undergoing DC for MCI at our institution from 01/2011-03/2019, and stratified them into three groups according to the interval between ictus and DC: (a) ≤12 hours, (b) >12≤24 hours, (c) >24 hours, and compared them through a one-way ANOVA test in terms of mortality and outcome, as objectivized with the modified Rankin scale (mRS) at discharge.

Results

A total of 111 patients were included. Of these, 26, 23% underwent ultra-early DC, 34, 31% early DC, and 51, 46% late DC. Mortality in the ultra-early group was 50% (13/26), 32% (11/34) in the early group, and 29% (15/51) in the late group. In the ultra-early group, 6, 23% achieved mRS ≤3; in the early and late group, good outcome was achieved by 6, 17%, and 10, 20%, respectively. No statistically significant difference was observed in terms of mortality (p=.189) or outcome (p=.874) between the groups.

Conclusion

Our study suggests no additional benefit in terms of mortality and outcome from performing ultra-early (within 12 hours) and early (within 24 hours) DC in MCI. Further studies are needed to determine the best timing for DC in MCI.

Neuroonkologie VII/*Neurooncology VII*

V277

Herstellung von transformierten humanen induzierten pluripotenten Stammzellen zur Erzeugung von synthethischen *in vitro* Modellen für molekulare Subtypen von Hirntumoren

The generation of transformed human induced pluripotent stem cells – towards the generation of synthetic in vitro models for molecular subtypes of brain tumours

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Objective

Glioblastoma (GBM) and medulloblastoma (MB) are the most common malignant brain cancer in adults and children, respectively. Patient-derived brain cancer models have been used over the last years for oncological research but show limitations in genetic stability. Further, some subgroups cannot be cultured under laboratory conditions. We recreated GBM and MB subgroups with human induced pluripotent stem cells (hiPSC) through genetic manipulation. Generated models were used for OMICs analysis and a drug screen to identify new treatment approaches.

Methods

Lentiviral transduction was used to generate the subgroup specific GBM and MB models. Known genes to be involved in the malignant transformation were used for model generation: TP53, EGFRvIII, c-Myc and Gli1. Cell lines were antibiotic selected and protein over-expression was confirmed by western blot. Stem cell marker expression of hiPSC models was verified with FACS and immunocytochemistry (ICC) staining. hiPSC models were utilized for a semi-automated drug screen with 167 FDA approved compounds. Candidates were chosen to validate their treatment potency in a smaller set-up. RNA and DNA of all lines was collected for transcriptome and methylome analysis, respectively.

Results

The development of GBM and MB models was achieved for the classical GBM (EGFRvIII), SHH MB (Gli1) and Group 3 MB (c-Myc) subgroup. Overexpression of the marker genes was confirmed in comparison to the wild type and empty vector control. Stem cell expression of Nanog, Sox2 and Oct3/4 could be verified. All markers showed an expression of over 70%. ICC staining with Tra-1-60 and Oct3/4 was positive for all generated models. The drug screen identified compounds effective on the generated models and one compound that is only effective in MB models. Methylome analysis showed a demethylation for all genes expect for EGFR.

Conclusion

We could successfully generate hiPSC models with gene activation similar to GBM and MB subgroups. These models can be used for cancer research. Neural differentiation of hiPSC allows the usage of the cells for further screenings. GBM subgroup specific neurospheres are currently under investigation for the implementation into embryonic chicken brain to verify the tumour forming potential.

Neuroonkologie VII/*Neurooncology VII*

V278

Die Metinfilt Studie – molekulare Biopsie der Hirnmetastasen-Infiltrationszone
The Metinfilt study – molecular biopsy of the macro metastasis/brain parenchyma interface

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Objective

Brain metastases (BM) are considered to be circumscript lesions with very little infiltration of the adjacent brain. However, recent studies demonstrated extensive colonization of the macro metastasis / brain parenchyma interface (MMBPI). Importantly, these studies showed a correlation between higher degree of MMBPI infiltration and poor prognosis. Several molecular pathways responsible for MMPI invasion have been identified in vitro, but no in vivo validation of these signals has been performed. One challenge of such experiments is the aspect of precise and reproducible tissue sampling from the exact area of MMBPI. We therefore designed a prospective study design in which we combined imaging - based identification of the MMBPI, intraoperative neuronavigation, and fluorescence supported tissue acquisition to ensure reproducible sampling from the MMBPI.

Methods

On the day of surgery, the study team consisting of the neuroradiologist, the neurosurgeon and the basic scientists, identified the MMBPI based on the preoperative, contrast enhanced T1 weighted MRI. Subsequent to craniotomy and durotomy, neuronavigation was employed to re – identify the MMBPI, carefully preventing any csf draninage to avoid significant brain shift. Subsequently, MMBPI defined as the transition zone between tissue areas with either absent or low to moderate fluorescence signal was visualized with a YELLOW 560 nm filter integrated into the surgical microscope. At least four wedge – shaped samples representing the MMBPI were acquired, and divided into two groups, one for histological confirmation of MMBPI and one for molecular analyses.

Results

The study has recruited 24 patients (9 female, 15 male; mean age 59.8 years). The most frequent primary tumor was lung cancer (n= 8), frontal lobe was the most frequent site (n = 11). No additional morbidity was induced, surgery time was not significantly prolonged. Histological analysis revealed an excellent representation of the MMBPI in all cases including the detection of infiltrating tumor cells, as well as microglial and astroglial activation. The samples prepared for molecular analysis showed high yields of high quality RNA, DNA and proteins.

Conclusion

The results of this ongoing study demonstrate the successful tissue acquisition from the MMBPI with high precision and reproducibility by combining presurgical imaging analysis, intraoperative neuronavigation, and fluorescence supported tissue sampling.

Neuroonkologie VII/*Neurooncology VII*

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Risiko score für das Outcome nach mikrochirurgischer Resektion von intraspinalen Ependymomen (SOURCE score)
Risk score for outcome prediction after microsurgery for spinal ependymoma (SOURSE score)

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Objective

Microsurgical resection of spinal ependymomas is associated with considerable risk of postoperative neurological deterioration. Several factors were reported to be related to the risk of postoperative outcome. We aimed at developing a risk score for the prediction of functional outcome after microsurgery for spinal ependymoma.

Methods

All patients who underwent surgical resection of spinal ependymoma in our institution between 1990 and 2015 were eligible for this study. Different preoperative and early postoperative parameters were collected for the score construction. The study endpoint was the risk of functional dependence at 6 months after surgery defined as the modified McCormick Scale. Clinically relevant cutoffs were defined using the receiver operating characteristics analysis.

Results

Of 131 individuals (mean age: 45.6 [±16.7] years; 64 [48.9%] females) included in the final analysis, 38 cases (29%) showed poor outcome at 6 months after surgery. Based on the results of the univariate analysis, preoperative MMS, subtotal tumor resection, cranial tumor level on the spinal cord, tumor extension, intramedullary location, and WHO grading were included in the multivariate analysis. The final risk score consisted of the following independent predictors of poor outcome: preoperative MMS >1 (1 point), proximal tumor level at Th 10 and higher (1 point), and tumor extending over ≥3 vertebrae (1 point). The constructed score (0-3 points; **S**core for **OU**tcome **R**isk in **S**pinal **E**pendymoma [**SOURSE**]) showed high diagnostic accuracy for the prediction of functional dependency at 6 months after surgery (area under the curve [AUC]=0.883), which was superior as compared to preoperative MMS (AUC=0.798) and KPS (AUC=0.794). In particular, the patients scoring 0, 1, 2 and 3 points of the score showed poor outcome in 0%, 12.9%, 54.6% and 76.2% of the cases respectively.

Conclusion

The presented **SOURSE** score based on preoperative neurologic condition, tumor location and extension showed a high predictive value for early prognostication of postoperative outcome in patients undergoing microsurgery for spinal ependymoma. We recommend external validation of the proposed outcome score.

Neuroonkologie VII/*Neurooncology VII*

V280

Umfassende szientometrische Analyse von Tumour Treating Fields in Gliomen
Scientometric field-wide survey of tumour treating fields and glioma

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Objective

Over the past decade, tumour treating fields (TTF) has moved from novel to established part of the therapeutic armamentarium for high-grade glioma. As of 2020, the Joint Federal Committee (G-BA) broadly approved the use of TTF in newly diagnosed glioblastoma (GBM). However, there is a wide range of further applications of TTF that still need to be explored and validated in clinical trials. This study aims to give an overview of published research and ongoing trials in this field.

Methods

Data regarding published studies, clinical trials and grants was obtained through the meta-research platform Dimensions, which harvests data from sources such as CrossRef, PubMed, the Directory of Open Access Journals, Open Citation Data, clinical trial registries, patent offices, and over 100 publishers. The search terms [("tumor treating fields" OR "tumour treating fields" OR Optune OR NovoTAL) AND (glioblastoma OR GBM OR astrocytoma OR oligodendroglioms OR oligoastrocytoma)] was used.

Results

Since 2009, 482 studies on TTF in glioma have been published. The number of publications increased exponentially until 2019 when 140 studies were published and decreased in 2020 with 67 studies published by the end of November. The most common journals were Neuro-Oncology (IF 10.9; n=167), Journal of Clinical Oncology (IF 32.9; n=26) and International Journal of Radiation Biology (IF 2.3; n=23). 173 of the publications originated from the USA, followed by Germany (n=37) and Israel (n=22). In total, 51 clinical trials on TTF in glioma were identified, 14 of which are completed and 37 ongoing. 13 of these trials were phase 1, 24 were phase 2, 11 were phase 3, and 3 were phase 4. 28/37 ongoing trials are being conducted in the USA. Ongoing trials mainly evaluate the effect of TTF on newly diagnosed or recurrent GBM in combination with a variety of radiotherapy, chemotherapy and immunotherapy approaches. Another topic of interest appears to be the role of radiographic imaging in glioma treatment with TTF. 39 completed studies and 10 ongoing studies have been funded, most commonly by the American National Cancer Institute (n=20). 35 of the ongoing clinical trials are sponsored by Novocure.

Conclusion

There is rapidly growing research interest in TTF in glioma treatment, mainly for GBM. Ongoing clinical trials also appear to focus on this subcategory of gliomas. Most of the research appears to be conducted in the USA, where most of the research funding is provided.

Neuroonkologie VII/*Neurooncology VII*

V281

Wirbelsäulenmetastasen – Studie zur Inzidenz neurologischer Defizite mit und ohne vorbekannten Primärtumor
Spinal metastases – study about the incidence of neurological deficits with and without known primary tumour

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Objective

Spinal metastases are present in a sizeable proportion of patients with malignant neoplasia. Once neurologic deficits are present, life quality and prognosis decrease. This work is based on the assumption that patients with known malignant disease more frequently obtain medical care and screening. It is also assumed that unspecific back pain in these patients quicker leads in further diagnostic measures. Our aim is to evaluate the hypothesis that the incidence of neurologic deficits is higher in patients without previously known malignant neoplasia.

Methods

We analyzed a consecutive dataset of patients with spinal metastases. Besides demographic and clinical baseline characteristics, we assessed whether neurological deficits were present at admission. Furthermore, we evaluated whether a primary tumor was already known at first admission for spinal symptoms. Uni- and multivariate analyses were performed to assess potential associations of known primary and tumor type with neurological deficits.

Results

N=731 patients were included in the present analysis. Mean age was 63+-13 years. In 182 cases (25%) a motor deficit led to initial presentation. In 549 cases (75%), other symptoms or routine imaging led to the diagnosis of the spinal metastases. 539 patients (74%) already had a previously known primary tumor. In 192 patients (26%) the primary was unknown. In the patient group with known primary, neurologic deficits led to initial presentation in 119/539 cases (22%). In the patient group without known primary this rate was 63/192 (32%; p=0.003).

Conclusion

The likelihood of a symptomatic spinal metastasis to present with a motor deficit is markedly higher in patients without a known primary. However, one in five patients with a known primary tumor suffer from motor deficits at admission. This knowledge should prompt a discussion about the efficacy of current screening intervals and contribute to the prevention of neurological deficits in patients with known malignancies.

Neuroonkologie VII/*Neurooncology VII*

V282

Operation einzelner Hirnmetastasen – eine im frühpostoperativen MRT bestätigte Komplettresektion verlängert das Patientenüberleben

Surgery for single brain metastases – a complete resection proven by early postoperative MR imaging prolongs patient survival

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Objective

To evaluate the potential impact of the degree of resection on survival after surgery for single brain metastases. Brain metastases are believed to be circumscribed, well-delineated tumors and therefore easy to resect completely.Nevertheless, postoperative MR imaging reveals residual tumor in a substantial number of cases.

Methods

We retrospectively identified all 257 cases undergoing surgery between March 2016 and March 2020 for the removal of brain metastases in our departmental electronic database. 85 cases were operated for a single metastasis and had early postoperative MR imaging. We recorded all pertinent clinical data. Follow-up information was obtained through our outpatient department. All postoperative MR studies were reviewed and assessed for residual tumor (RANO 2015 criteria): complete resection vs. nonmeasurable (contrast enhancing lesion < 10 mm in one dimension) vs. measurable tumour. Standard statistical analyses including Kaplan Meier estimates, logistic and Cox regression analysis using a commercially available software (SSPS 25, IBM) were performed.

Results

The series comprised 47 (55.3%) females and 38 (44.7%) males. Median age was 60.9 (25-75% IQR: 54.3-70.1) years. 22 (25.9%) tumors were located in the posterior fossa. The most frequent primary tumor locations were lung (44.7%), breast (18.8%) and the GI tract (16.5%). The median preoperative KPI was 90 (25-75% IQR: 80-90) and the median postoperative KPI was also 90 (25-75% IQR: 80-90). 95% of cases had postoperative radio- and/or chemotherapy. Median postoperative survival was 22.5 months. Residual tumor was predictive of survival: complete resection (N=63) vs. non-measurable (N=13) vs. measurable residual disease (N=9) - median overall survival not reached vs. 15.1. vs. 13.8 months; p=0.021). Extracerebral metastases had a borderline negative prognostic impact (p=0.051). Infratentorial location, age and preoperative KPI did not correlate significantly with survival.

Conclusion

Our data point to a very significant correlation between degree of resection and survival after surgery for single brain metastases. This supports routine early postoperative MR imaging after brain metastases removal and also points to a potential role of repeat surgery for residual metastatic disease if safely possible.

Wirbelsäulenchirurgie II/*Spinal surgery II*

V283

Bedeutung von Röntgenfunktionsaufnahmen im Vergleich zur Schnittbildgebung mittels CT und MRT in der Detektion einer Instabilität bei Spondylolisthesis der Lendenwirbelsäule

Intermodal comparison of supine magnetic resonance imaging (MRI) and computed tomography (CT) versus functional radiographs to determine dynamic instability in patients with lumbar degenerative spondylolisthesis

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Objective

Spondylolisthesis is defined as anterior displacement of one vertebra relative to the subjacent vertebra. Spondylolisthesis is most common on level L4/L5 or, less commonly, L5/S1 or L3/L4. Symptoms arise through a combination of the degenerative changes, segmental instability and consecutive stenosis. In this study, we sought to identify the proportion of patients with dynamic instability using single functional radiographs compared to supine CT or MRI.

Methods

Data acquisition was conducted as a single-center retrospective analysis. Patients presenting with spondylolisthesis from June 1st, 2018, to May 30th, 2020 with functional radiographs and either CT or MRI were included in our analysis. The amount of translation, in millimeters, was calculated on supine MRI, CT and radiographs of inclination while sitting, -standing reclination and prone using the Meyerding technique. The amount of translation was compared between CT and MRI and each radiograph to either CT or MRI.

Results

One hundred and thirteen patients with spondylolisthesis on one hundred twenty-five vertebral levels were included in this study. The mean patient age was 73.52+-12.59 years. 69 (60.5%) patients were female, 45 (39.5%) male. The most commonly affected level was L4-5 (62.4%). Levels L3-4 (16%) and L5-S1 (13.6%) were affected equally. The average translations measured on supine CT was 4.13+-5.93mm and 4.417+-3.492mm on MRI. The difference of inclination while sitting radiographs to slice imaging was 3.373+-3.642mm, inclination while standing to slice imaging was 2.665+-3.031mm, reclination while standing to slice imaging was 1.596+-3.148mm and prone to slice imaging was 2.189+-3.020mm. While no statistically significant difference was detected between CT and MRI, both were statically significant different to all radiographic modalities. The largest differences were detected between inclination while sitting and CT/MRI.

Conclusion

In this study, we analyzed the meaning of different functional radiograph modalities versus CT and MRI for detection of dynamic instability in lumbar spondylolisthesis. We showed that radiograph modality (inclination, reclination or prone) in comparison to CT or MRI is sufficient to detect lumbar instability. Therefore, putting patients through different positions during functional radiographic imaging causes avoidable radiation exposure, discomfort and costs to our health care system.

Wirbelsäulenchirurgie II/*Spinal surgery II*

V284

Spontane Verknöcherung des Iliosakralgelenks – Prävalenz und Risikofaktoren
Spontaneous ossification of the sacroiliac joint – prevalence and risk factors

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Objective

Sacroiliac joint (SIJ) degeneration is common in middle aged and elderly patients. In some cases, spontaneous intraarticular ossification can occur, even in the absence of prior spinal fusion surgery or any symptoms. Why some patients exhibit spontaneous SIJ ossification while others do not, remains unclear. We aimed to assess the prevalence of spontaneous SIJ ossification and to describe different ossification patterns. We also examined factors associated with spontaneous SIJ ossification.

Methods

Using pelvic CT imaging, we examined ossification patterns across the SIJ in 200 subjects: 100 subjects after transforaminal lumbar interbody fusion (TLIF) and 100 control subjects, which underwent CT as part of tumor staging diagnostics unrelated to the SIJ or the spine. Cases were categorized according to the following patterns of spontaneous SIJ ossification: anterior, entheseal or posterior (Figure 1). Patient characteristics were derived from the electronic medical records.

FIGURE 1: Ossification patterns a. anterior, b. entheseal, c. posterior

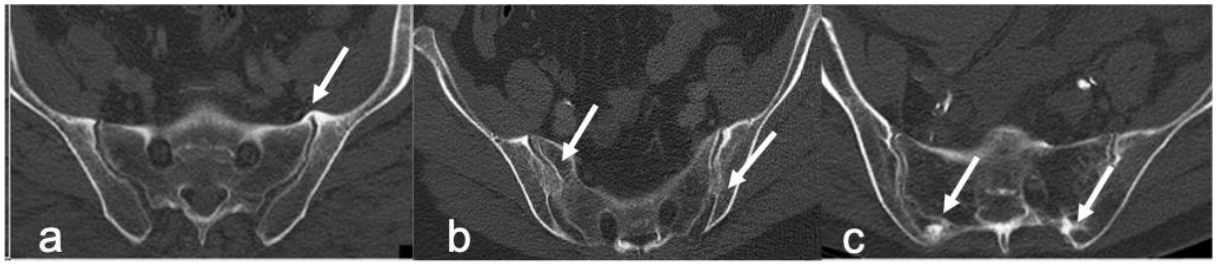
Results

Pelvic CT examinations of 116 men and 84 women between 2019 and 2020 were evaluated. Subjects in the control group were significantly older (mean 70.4y, SD 11.3) compared to those after TLIF (mean 65.2y, SD 14.3; p=0.006). The overall prevalence of spontaneous SIJ ossification was 64.0%, 62% in the control group and 66% in the TLIF group. We observed a trend towards a predominance of the anterior type SIJ ossification in both groups (control group: 28/62 [45.2%] vs. TLIF group: 43/66 [65.2%]) followed by posterior type (20/62 [32.3%] vs. 11/66 [16.6%]) and entheseal (14/62 [22.5%] vs. 12/66 [18.2%]). Factors associated with the occurrence of spontaneous SIJ ossification were age (OR 1.03; 95% CI: 1.01-1.06; p=0.005) and previous spinal fusion surgery (OR 0.46, 95% CI (0.25-0.85); p=0.013).

Conclusion

Our findings highlight that spontaneous SIJ ossification is a frequent phenomenon, both in non-spine patients and in patients with previous spinal fusion surgery. The fact that most commonly the anterior SIJ section displayed ossification may reflect higher load bearing in this location. Since patients in the control group were at higher risk of displaying SIJ ossification, previous spinal fusion surgery may be less of a deciding factor in SIJ degeneration than frequently assumed.

Fig. 1



Wirbelsäulenchirurgie II/*Spinal surgery II*

V285

Vergleichende Langzeitstudie der Schmerzreduktion und Komplikationsrate zwischen Radiofrequenzdenervierung und endoskopischer Rhizotomie bei Facettengelenksarthropathie

Superior long-term pain reduction and lower complication rates upon radiofrequency vs. endoscopic neurotomy for facet joint arthropathy

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Objective

Radiofrequency neurotomy (RFN) of the lumbar medial branch has been considered as the standard of care for facet joint arthropathy related chronic low back pain. However, during the last decade, an upsurge of interest for endoscopic procedures was seen in spine surgery. Endoscopic neurotomy (EN) has been adopted recently as a treatment option for facet joint arthropathy. The long-term outcome of both therapies has not been compared in a standardized setting yet. We hypothesized that radiofrequency neurotomy is associated with superior long-term outcomes compared with endoscopic neurotomy.

Methods

Data from patients with facet joint arthropathy were collected prospectively between 01.01.2016 and 31.12.2019. Spinal imaging was performed in all patients to rule out other pathologies. Patients were grouped based on treatment modality into radiofrequency neurotomy group (Gr.RFN (n=36)) and endoscopic neurotomy group (GR. EN (n=29)). We compared the following parameters over time (1 year) and between groups: Core Outcome Measures Index for the back (COMI), VAS (Visual Analog Scale)-scores, complications and financial costs

Results

65 patients (35 female) with a median (IQR) age of 62 (54-72) years were included. Pre-interventionally, patients had a median (IQR) COMI-Score of 8.6 (7.7-9.0) and a median (IQR) VAS of 8.0 (7.0-9.0). No statistically significant differences in baseline parameters were encountered. After intervention, a significant drop in VAS occured in both conditions. Thereafter, pain-scores rose gradually within the first 12 months in the EN group, whereas VAS-levels in the RFN group remained unaltered. Complication rates were significantly lower in the RFN group, compared with EN-patients ($p<0.007$). Total costs were significantly lower in RFN-procedures ($p<0.05$), and earlier return to work was documented in patients treated by RFN than those individuals treated by EN ($p<0.05$).

Conclusion

The current comparative study reveals that radiofrequency neurotomy of the lumbar medial branch is associated with enhanced long-term pain relief, lower complication rates and lower costs than endoscopic neurotomy for facet joint arthropathy related chronic low back pain.

Wirbelsäulenchirurgie II/*Spinal surgery II*

V286

Die Kortikospinale Reserve – die Wiederherstellung der Erregbarkeit und Funktionalität des Motorkortex nach operativer Dekompression bei Patienten mit moderater cervikaler Myelopathie

The corticospinal reserve – surgical decompression restores cortical motor excitability and function in cases of mildly symptomatic degenerative cervical myelopathy

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Objective

We have recently shown an adaptive reorganization of the corticospinal network in patients with degenerative cervical myelopathy (DCM) which led to the concept of the "corticospinal reserve capacity". In patients suffering from mild symptoms (JOA>12) and preserved reserve an increased neuronal recruitment and disinhibition with enlarged motor area was observed. In contrast, severely symptomatic patients (JOA≤12) with an exhausted reserve presented with a restricted motor area, reduced corticospinal conductivity and increased inhibition. The current prospective multicenter trial has been designed to validate the new pathophysiological concept.

Methods

120 patients with DCM from four spine centers in Germany and Switzerland. were examined preoperatively and 9 months after surgical decompression with navigated transcranial magnetic stimulation (nTMS). On the basis of the initial Japanese Orthopedic Association (JOA) Score three patient groups were established (JOA≤12, 13-15, >15). Corticospinal excitability was determined by navigated transcranial magnetic stimulation (nTMS) with the following parameters: Resting motor threshold (RMT), recruitment curve (RC), cortical silent period (CSP) and motor area.

Results

In patients with moderate symptoms (JOA 13-15) we encountered a compensatory increased motor cortex activation (motor area: p.± 213,3 vs. JOA ≤12: 225,7 ± 159,5). Surgical decompression led to a recovery of corticospinal excitability expressed by an increased RC (p.± 5,0 vs. follow up 11,72 ± 5,4 p±1,1 vs. JOA follow up 14,5+1,5). In contrast, patients with severe symptoms (JOA≤12) presented a reduced excitability of cortico-cortical axons reflected by an elevated RMT (p≤12: 43,8 ± 11,4 vs. JOA >15: 39,2 ± 8,4) and a reduced RC slope (p≤12: 8,4± 4,8 vs. JOA 15-17: 11,1± 5,2). The diminished cortical motor area (p± 4,8 vs. RC follow up 10,0 ± 4.3) after surgical decompression which was further reflected in a lack of significant clinical recovery of symptoms (JOA preop 10±1,3 vs. JOA follow up 11,4+2,7).

Conclusion

In summary our prospective multicenter trial confirmed our concept for functional reorganization in patients suffering from DCM, i.e. the "corticospinal reserve capacity". It became apparent that the individual pattern of compensation is a sensitive marker to objectify the state of the disease and functional reserve and may therefore indicate imminent non-reversible clinical deterioration. This innovative approach to evaluate patients suffering from DCM might improve current concepts of clinical diagnostics and impact future treatment strategie

Wirbelsäulenchirurgie II/*Spinal surgery II*

V287

Die Nützlichkeit des "Spinal Instability Score" für Patienten mit Wirbelkörpermetastasen – eine monozentrische Studie mit 332 Patienten

Utility of the spinal instability score in patients with spinal metastases – a single-centre study with 332 patients

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Objective

Spinal metastases may cause spinal instability. The Spinal Instability Neoplastic Score (SINS) was developed to assess spinal neoplastic-related instability. Aim of this study was to determine the utility of SINS in predicting progression of a pathologic fracture due to spinal metastases.

Methods

A retrospective analysis of patients with a pathologic fracture due to a spinal metastases between January 2018 and December 2018 was performed. We selected patients with a minimum follow-up of 12 months and analysed them according to the SINS criteria. The primary endpoint was the progression of vertebral body fracture following radiotherapy.

Results

332 Patients were identified. Median age was 68 SD +/- 10,3. 38% were female. Median follow-up was 26 months (range 12-29). 30, 283 and 19 patients presented with low (0-6), moderate (7-12) and high (13-18) SINS, respectively. Fracture progression following radiotherapy was seen in 9 (30%), 84 (30%) and 8 (42%) in cases with low, moderate, or high SINS (P = 0.522), respectively. During follow-up, 44% of patients with low SINS showed a progression to moderate SINS without neurological deficits. In the originally moderate group, 17% had progression with neurological deficits needing surgery. None had functional recovery postoperatively. 83% of the progression cases in the moderate group did not develop neurological deficits and 4 underwent surgery for pain management. 63% of all progressions in the high group developed neurological deficits, however none of them recovered postoperatively (P < 0.001).

Conclusion

SINS is a very useful tool for assess stability of a pathologic fracture due to spinal metastases after radiotherapy for spinal metastases. Moderate or high SINS are associated with a high risk of fracture progression as well as risk for neurological deterioration, therefore surgical instrumentation in these groups may be advised prior to radiotherapy.

Wirbelsäulenchirurgie II/*Spinal surgery II*

V288

Alignementverschiebung zwischen prä- und intraoperativer CT Bildgebung bei navigierter spinaler Instrumentierung
Alignment shift between pre- and intraoperative CT imaging during navigated spinal instrumentation

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Objective

The precision of machine learning algorithms and surface matching and for planning and execution of spinal navigation based on preoperative imaging may be hampered by spinal alignment shifts caused by the intraoperative shift to prone position. In this study, we determined the spinal alignment shift between pre- and intraoperative CT data sets in patients undergoing navigated posterior instrumentation.

Methods

All patients that underwent navigated posterior instrumentation with intraoperative CT imaging between 2014 and 2017 and in whom an additional, preoperative CT was available were included. The alignment shift between the preoperative (supine) and intraoperative (prone) CT before screw insertion was determined using sagittal alignment parameters defined as "modified cobb angle" (CA), "plumb line" (PL) and "translation" (T). Alignment parameters were analyzed according to the anatomic region and the indication for surgery. Also, an explorative risk factor analysis for prediction of an increased likelihood of shift was performed.

Results

We identified 104 patients with a median age of 66 (IQR 56-75). Spinal pathologies were identified as degenerative (35/104; 34%), tumor (35/104; 34%), trauma (21/104; 20%) and infection (13/104; 12%). Pre- and intraoperative alignment parameters differed frequently (in 98% for CA, 92% for PL and in 29% for T) and across all regions of the spine. Region-based analysis showed that shifts in the cervical and thoracic spine were most reliably detected by CA (*$p<0.05$), whereas shifts in the thoraco-lumbar spine were better identified with PL (*$p<0.05$). Although the likelihood of an alignment shift was not significantly affected by the presence of an instability risk factor, the need for a long-segment instrumentation (>5 segments) was associated with a significantly higher likelihood of shift (*$p<0.05$).

Conclusion

Spinal alignment shifts between pre- and intraoperative CT imaging occur frequently and across all regions of the spine, which needs to be considered as a source of inaccuracy for machine learning algorithms and spinal navigation based on preoperative CT imaging alone.

V289

Systematische anatomische Vergleichstudie von Mittellinien-, paramedianen supracerebellären infratentoriellen und okzipitalen transtentoriellen Zugängen zum hinteren Tentoriumschlitz und Fallillustrationen anhand von zweizeitig resezierten komplexen falco-tentoriellen Meningeomen

A systematic anatomical comparison of midline, paramedian supracerebellar infratentorial and occipital transtentorial approaches to the posterior incisural space and case illustrations by two staged surgeries for complex falcotentorial meningiomas

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Objective

The posterior incisural space (PIS) represent a neurosurgical challenge given its depth and complex anatomy. To access the PIS, the midline supracerebellar infratentorial approach (MSIA) has been traditionally applied, but several neurosurgeons propose that a paramedian supracerebellar infratentorial (PSIA) or interhemispheric occipital transtentorial approach (IOTA) might enable a better accessibility. We systematically compared these 3 approaches in cadaver specimens and present the application of PSIA/IOTA as staged surgery for resection of complex falcotentorial meningeomas.

Methods

We performed 8 cadaver dissections assessing morphometrical features related to exposure, operability, brain retraction and obstacles to the PIS during MSIA, PSIA and IOTA. Additionally, we operated two patients presenting supra-infratentorial growing falcotentorial meningiomas through a two-staged endoscopic assisted PSIA combined with IOTA.

Results

Superficial vermian draining veins at an average depth of 11.38±1.5 mm and the superior vermian vein at a depth of 54.13±4.12mm limited the access to the PIS during MSIA. MSIA required sacrifice of these veins and retraction of the vermian culmen of 20.88±2.03mm to obtain comparable operability indexes (as described by Salma et al.) to PSIA and IOTA[1]. Cerebellar and occipital lobe retraction averaged 14.31±1.014mm and 14.81±1.17mm during PSIA and IOTA respectively, which was significantly lower than during MSIA (both $p<0.001$). Only few tiny veins were encountered along the access through PSIA and IOTA. The application of PSIA provided high operability scores around the pineal gland, the ipsilateral colliculus and splenium, and acceptable scores on contralateral structures. The main advantage of the IOTA was improving surgical manoeuvres along the ipsilateral splenium. Staged PSIA and IOTA enabled successful resection of both falcotentorial meningiomas. Postoperative course was uneventful and patients recovered without new neurological deficits.

Conclusion

Although IOTA and PSIA may render some difficulties related to tentorial incision and spatial orientation, these approaches may provide advantages in terms of brain retraction, vein sacrifice and operability. Their application can be effective for staged surgery of complex falcotentorial meningiomas.

[1] Salma A, et al. Extradural endoscope-assisted subtemporal posterior clinoidectomy: a cadaver investigation study. Operative Neurosurgery (2010) 67:ons43-ons48

Neuroonkologie VII/*Neurooncology VII*

V290

AKT1 E17K-Mutationen sind häufige genomische Ereignisse bei zervikalen spinalen Meningeomen
AKT1 E17K mutations are frequent genomic events in cervical spinal meningiomas

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Objective

Spinal meningiomas represent about one third of all spine tumors. To date, few is known about the molecular profile of spinal meningiomas and its clinical impact. In this study, we correlate clinical parameters with targeted sequencing findings in a well-characterized cohort of 42 patients.

Methods

Samples from 42 spinal meningiomas (31 females and 11 males) were collected. Targeted sequencing for *AKT1 E17K* hot spot mutations was performed. Furthermore, clinical and imaging data were collected and correlated with the *AKT1* mutation status.

Results

Gross total resection (Simpson grade I /II) was achieved in all patients. The mean follow-up period was 60 months (6 –288 months). None of the patients demonstrated a tumor recurrence. *AKT1E17K* mutations were detected in 8 patients (19%), in five male and three female patients (p= 0.019). Although the majority of resected meningiomas (n= 28, 66.6%) were located in the thoracic spine, meningiomas originating in the cervical spine harbored significantly more *AKT1 E17K* mutations (6 out of 14, p= 0.010). Notably, all *AKT1* mutated meningiomas arose ventrally or ventrolaterally to the spinal cord. The histological examination revealed a WHO Grade 1 in 36 meningiomas (85.7%): 21 meningothelial, 8 psammomatous, 5 transitional, 2 fibrous. The remaining six meningiomas were classified as atypical WHO grade 2. Remarkably, *AKT1 E17K* mutations were significantly related to a meningothelial subtype (p= 0.044).

Conclusion

Our molecular study demonstrates that *AKT1* E17K mutations are a frequent genomic event in spinal meningiomas. The majority of *AKT1* mutated meningiomas occurred in male patients, originate in the cervical spine and exhibit a meningothelial histology.

V291

Allogene NKG2C-positive NK-Zellen zur Immuntherapie des Glioblastoma multiforme
Allogeneic NKG2C-positive NK cells for immunotherapy of glioblastoma multiforme

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Objective

NKG2C-positive natural killer (NK) cells represents a small NK cell subset, which is found in higher frequency in human cytomegalovirus (HCMV) seropositive patients. NKG2C+ NK cells can recognize target cells displaying HLA-E loaded with intracellularly processed ER signal peptides (sp) derived from classical HLA-A,B,C alleles and from HLA-G. Of note, HLA-E and HLA-G is frequently expressed in glioblastoma multiforme (GBM). Consequently, the NKG2C+ NK subset might have an increased intrinsic capacity to recognize and kill GBM cells. This study investigated, whether allogeneic NKG2C+ NK cells have an anti-tumor effect against HLA-E+/G+ GBM cells.

Methods

GBM patients and NK donors were HLA genotyped for HLA:KIR match/mismatch analysis. HCMV IgG and IgM titers from NK cell donors were analyzed using ELISA. HLA-E+/G+ GBM cells were prepared by enzymatic/mechanic tumor dissociation and were cultivated in standard DMEM medium. Untouched NK cells were generated using negative NK cell isolation technique. The NKG2C+ NK cell fraction was expanded for 14 days using NK feeder cells, designated, PC3-PSCA-IL-2-mIL-15d-HLA-E^{spG}, expressing an activating B2M-HLA-E^{spG} trimeric fusion protein, IL-2 and membrane-bound IL-15. Enrichment of expanded NKG2C+/A- NK cells was accomplished by MACS-assisted depletion of NKG2A+ NK cells. For control, NK cells from same donors were expanded using a feeder cell line only expressing IL-2 and mIL-15d known to augment outgrowth of NKG2A+/C- NK cells. Freshly prepared and expanded NK cells were characterized using antibodies for CD56, NKG2A, NKG2C and KIRs. Cytotoxicity of NK cells towards GBM cells was investigated by chromium release assay.

Results

PC3-PSCA-IL-2-mIL-15d-HLA-E^{spG} feeder cells induced a 32-fold increase in NKG2C+ NK cell numbers. Likewise, the mean frequency of NKG2C+ NK cells in the NK cell population increased from in the mean 9% to 33%. MACS-assisted depletion of NKG2A+ NK cells resulted in NKG2C+ NK cell purity >90%. In cytotoxicity assays, only NKG2C+ NK cells showed lytic activity towards HLA-E/G-positive GBM cells. Of note, NKG2C+ NK cells were reactive against C2/Bw4-mismatched but also towards KIR:HLA-matched allogeneic GBM cells.

Conclusion

Our results demonstrate the feasibility of allogeneic NKG2C+ NK cells for immunotherapy of GBM, which operates independently from KIR/HLA-setting. Further preclinical studies are required to confirm the potential of NKG2C+ NK cells for immunotherapy of glioblastoma.

Neuroonkologie VII/*Neurooncology VII*

V292

Der CMV Serostatus correliert mit einem verkürzten Überleben bei Patienten mit Glioblastom
Anti-CMV serostatus correlates with shortened progression free- and overall survival in patients with glioblastoma

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Objective

Cytomegalovirus (CMV) has been linked to glioblastoma for over a decade,while its oncomodulatory role is poorly understood.Despite ample evidence, CMV remains notoriously hard to detect in glioblastoma samples, rendering the field an ongoing a matter of debate. Here we found evidence that serostatus, staining and mRNA expression concur and correlate with the clinical outcome in patients with glioblastoma.

Methods

25 patients with glioblastoma (16 male, 9 females; mean age 67.2+-12.27 years) and 10 controls (5 male, 5 females; mean age 60.3+-11.63 years) were included in our study. All patients were treatment as inpatients at our department and received adjuvant therapy in our outpatient clinic. All patients were followed up every 3 months until time of death. Polymerase chain reaction was used to detect CMV (PCR). Anti-CMV IgM and IgG were measured using Enzyme linked immunosorbent assays (ELISA). Tumor samples were stained via immunofluorescence using an anti-CMV polyclonal- and anti-pp65 monoclonal antibody. CMV immediate early gene (IE1) and envelope glycoprotein B (gB) mRNA expression in tumor specimen was analyzed using RT-PCR.

Results

Anti-CMV IgG were detected in 17 (68%) patients and 6 (60%) controls. Anti-CMV IgM or viral DNA were not detected. Thus, there was no higher prevalence of seropositivity in patients with glioblastoma compared to controls. CMV IgG antibody levels ranged from levels 1.1 to >250 U (131.1+-84.92 U). CMV antigens were detect in tumor specimen of all seropositive patients and were absent from those who were seronegative. Using RT-PCR, IE1 and gB were only detected in tumors from seropositive patients while it was not detectable in total RNA from normal cerebral cortex of healthy individuals. In oour cohort, mean progression free survival (PFS) was significantly shorter in seropositive glioblastoma patients (187.8+-125.7) compared to CMV naïve patients (361.9+-212.6 days; p=0.037). Higher Serum IgG levels correlated with longer PFS (r=0.6; p=0.021) and weaker fluorescence staining. Mean overall survival was shorter in patients with past CMV infection (322 days) compared to CMV negative patients (487.5 days).

Conclusion

Our findings ad proof that CMV latency does lead to tumoritropic infection and strengthen the importance of an oncomodulatory role of CMV in glioblastoma. Seropositivity does correlate with shortened PFS and OS.

Neuroonkologie VIII/Neurooncology VIII

V293

Tumor-assoziierte Anfallsereignisse bei Patienten mit kranialen Metastasen – die Nekrose-Tumor Ratio als prognostisches Tool der postoperativen Anfallsfreiheit

Tumour-associated epilepsy in patients with brain metastases – necrosis-to-tumour ratio forecasts postoperative seizure freedom

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Objective

Tumor-related epilepsy (TRE) has an excellent outcome in patients with brain metastases (BM) after surgical treatment. Nevertheless, persistent epilepsy has a significant negative impact on the health-related quality of life. Therefore, early identification of potential patients with unfavorable seizure outcome after BM resection seems of utmost importance.

Methods

In a retrospective cohort study, patients with surgically treated BM and TRE were examined at the authors' institution with regard to preoperatively identifiable risk factors for unfavorable seizure outcome. According to the classification of the International League Against Epilepsy (ILAE), seizure outcome was categorized as favorable (ILAE 1) and unfavorable (ILAE 2 - 6) after 3 months in order to avoid potential interference with adjuvant cancer treatment.

Results

Among all 38 patients undergoing neurosurgical treatment for BM with concomitant TRE, 34 patients achieved a favorable seizure outcome (90%). Unfavorable seizure outcome was significantly associated with tumor volume ($p=0.012$), a midline shift > 7 mm ($p=0.025$), and a necrosis/tumor volume ratio > 0.2 ($p=0.047$).

Conclusion

Neurosurgical treatment of brain metastases might yield favorable seizure outcomes in the majority of patients suffering from tumor-associated epilepsy. The present study identifies preoperatively identifiable risk factors for unfavorable seizure outcome in patients with BM and TRE. Subsequently, patients with persistent postoperative epilepsy might benefit from additional neuro-oncological expertise accompanying their further systemic therapy.

Neuroonkologie VIII/*Neurooncology VIII*

V294

Der klinische Verlauf von IDH1/2-Wildtyp Astrozytomen
The clinical course of IDH1/2-wildtype astrocytomas

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Objective

DH1/2-wildtype (wt) astrocytomas have a high recurrence rate. Since the cIMPACT-NOW update 3, the subgroup of diffuse tumors with certain molecular markers are categorized as WHO IV tumors. Treatment recommendation has shifted to a more aggressive strategy. In this study, we aimed to evaluate the treatment related clinical course of IDH1/2-wt astrocytomas graded as II or III without inclusion of molecular markers.

Methods

The medical records of all patients who underwent surgery (2016-2019 in 4 neurosurgical departments) for a histologically diagnosed IDH1/2-wt astrocytoma WHO II-III according to light microscopy were reviewed to assess the progression-free survival (PFS), overall survival (OS) and prognostic factors.

Results

This multicenter retrospective study included 90 patients (median age 57 years; 44.4% female). Mean follow-up was 16.2 months (SD 12.1). The predominant histology was anaplastic astrocytoma WHO III (76.7%), followed by diffuse astrocytoma WHO II (22.2%) and diffuse glioma with molecular markers of a glioblastoma WHO IV (7.8%). Gross total resection (GTR) was achieved in 46.6% of patients, subtotal resection in 34.2% and biopsy was performed in 19.2%. Mean PFS (18.4; SD 9.6 months) and OS (32.2; SD 7.2 months) did not differ among the WHO grades. Independent from WHO grade, GTR lead to a significant increase of PFS in comparison to STR (P=0.012) and biopsy (P=0.002). 81.1% of patients were treated by the Stupp regimen, while 7.8% underwent radiotherapy alone, 4.4% received chemotherapy alone and 6.7% had no treatment due to unknown reasons. The loss of nuclear ATRX expression resulted in a significant longer PFS (HR:0.56 95% CI 0.34-0.91; P=0.017), while strong amplification of EGFR shortened the PFS (HR:3.08 95% CI 1.06-8.96; P=0.001). No influence of the TERT-promotor mutation or MGMT-promotor methylation on PFS and OS could be detected. Younger age, GTR and low ECOG-score were associated with a significantly prolonged PFS (age: HR:1.02 95% CI 1.003-1.04; P=0.022; ECOG: HR:0.55 95% CI 1.14-2.10; P=0.024; GTR: HR:0.30 95% CI 0.14-0.63; P=0.002).

Conclusion

In the present study no difference in PFS of IDH1/2-wt astrocytomas WHO II-IV undergoing same treatment regimen could be detected. Retained nuclear ATRX expression and a high EGFR amplification were associated with a poorer prognosis. Similar to glioblastoma the most important prognostic factors remained the extent of resection, age and clinical status.

Neuroonkologie VIII/*Neurooncology VIII*

V295

Anwendung von Tumor Treating Fields (TTFields) bei Tumorzelllinien erhöht die Membranpermeabilität
Tumor Treating Fields (TTFields) application to cancerous cell lines elevates membrane permeability

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Objective

Tumor Treating Fields (TTFields), encompassing intermediate frequency, alternating electric fields, are an anticancer treatment delivered loco-regionally and non-invasively, through transducer arrays placed on the skin, to the tumor region. TTFields therapy has demonstrated efficacy and safety and is CE certified for treatment of patients with glioblastoma (GBM). Recently, TTFields were reported to alter the cellular membrane structure of GBM cells, rendering them more permeable. The objective of this study was to characterize the effect of TTFields treatment on cancer cell permeability and to assess functional significance in combination with other anticancer agents.

Methods

TTFields were applied for 72 h to GBM, uterine sarcoma, and breast adenocarcinoma cell lines across a range of frequencies (50-500 kHz). Cell membrane permeability was assessed by flow cytometry quantification of 7-aminoactinomycin D (7-AAD) intracellular accumulation, and TTFields-elicited cytotoxicity was examined by cell counts. Process kinetics was evaluated by exposing the cells to 7-AAD during the final minutes of treatment versus later time frames following treatment cessation. The potential facilitation of TTFields for enhanced accumulation of anthracycline chemotherapeutics in cancer cells was evaluated in chemotherapy-sensitive and chemotherapy-resistant cells.

Results

TTFields induced increased cellular permeability in all examined cancer cell lines, as evident from elevated 7-AAD accumulation. The highest potency was observed at an optimal frequency that differed from the optimal cytotoxic frequency. TTFields-induced cell membrane permeability was shown to be transient (effective only during delivery), reversible (to normal pretreatment conditions), and able to improve intracellular uptake of chemotherapeutic agents. Moreover, co-application of TTFields allowed accumulation of chemotherapeutic agents in chemotherapy-resistant cancer cells to the same extent as in chemotherapy-sensitive cancer cells.

Conclusion

TTFields treatment increased cancer cell permeability across multiple cancer types, facilitating accumulation of chemotherapeutic drugs, even in chemotherapy-resistant cells. Maximal membrane permeability was obtained at a frequency different from the optimal frequency for inducing cytotoxicity. Of note, enhanced TTFields-induced permeability was transient and reversible, with treatment cessation restoring normal conditions.

Neuroonkologie VIII/*Neurooncology VIII*

V297

Die Rolle von altersbedingten Veränderungen in der Mikroumgebung beim Glioblastom
The role of aging induced environmental alterations in glioblastoma

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Objective

Aging of the human brain is a multifactorial process that is only partially explored. One major finding is that brain samples acquired from an elderly cohort are enriched with glial cells in comparison to a younger cohort and exhibit inflammatory activation. Due to the fact that glioblastomas mostly arise in older patients, we aimed to explore similarities between the GBM microenvironment and healthy age-related transcriptional alterations.

Methods

We performed spatial transcriptomics using Visium 10X Genomics technology, on 24 specimens and performed meta-module analysis of weighed networks to extract correlations between gene expression modules and clinical characteristics. We used a human neocortical model with different age groups and injected a "young" (45y) or an "old" (86y) patient-derived tumor cell line. We performed single-cell RNA-sequencing of the extracted cell lines to trace back transcriptional dynamics within age-related environments.

Results

We identified a transcriptional signature significantly correlated to age which was shared in non-malignant and tumor samples. This signature was marked by complement activation and expression of typical astrocytic inflammatory genes (GFAP, C3, C1S, C1R, SERPING1, CXCL9), confirmed by immunostainings. Age-related signatures were highly enriched in cells of the reactive subtype (hypoxic or immune reactive subtype) and not expressed in cells of differentiated lineages (NPC-like, OPC-like). In our neocortical slice model, we showed that primary GBM cells from "old" (86y) specimen did not grow in younger tissue microenvironment (2y), altered their morphology in "mid-age" tissue (38y) and proliferate the most in age-matched tissue environment. On the contrary, primary GBM cells from "young" (45y) old specimen showed a similar behavior with the maximum growth-rate in elderly tissue. Single-cell RNA-sequencing confirmed the enrichment of reactive states in elderly tissues.

Conclusion

Our analyses suggest that age-related differences in the human brain are also reflected in glioblastoma. The aging environment is responsible for reactive transcriptional subtypes of glioblastoma and support tumor growth. Our findings support the essential demand for personalized therapy for glioblastoma.

V298

Prognostische Bedeutung des Methylierungsgrades des MGMT-Promotors für das Gesamtüberleben bei Patienten mit Erstrezidiv eines Glioblastoms, welche eine lokale Carmustin-Applikation unterlaufen – Zwischenergebnisse der CARENTA Studie

Clinical and oncological course of patients with recurrent glioblastoma multiforme treated with local carmustine wafers in relation to the methylation status of the MGMT promotor – preliminary results of CARENTA – a prospective multicentre observational study

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Objective

The methylation of O6-methylguanine-DNA-methyltransferase (MGMT) is an established biomarker in IDH-wildtype glioblastoma (GBM) patients. It enhances the effectiveness of alkylating chemotherapy and by such affects the progression free survival (PFS) and overall survival (OS). Standardized therapy modalities regarding of recurrent GBM are yet to be established. The goal of this study was to investigate a beneficial use of carmustine wafers in recurrent glioblastoma in relation to the MGMT methylation promotor status.

Methods

Adult patients with the first recurrence of a GBM were included in this study. Only patients were included who underwent prior gross total resection and adjuvant chemoradiotherapy following the "Stupp"protocol. The methylation status of the MGMT promotor was evaluated by pyrosequencing of the tumor tissue after the primary resection. Study documentation resembles clinical practice. Follow-ups were performed at 3, 6 and 12 months postoperatively. Clinical parameters, quality of life data and MRI results were gathered. The primary outcome measure was the OS (measured after the date of recurrent resection and carmustine wafer implantation) in relation to the grade of methylation of the MGMT promoter. Secondary outcome measures obtained PFS after recurrent resection, the quality of life (using the Short-Form [SF] 36 health survey) and complication rates. A monitor regularly visited the study sites to ensure the quality of the data.

Results

Patient enrollment began in 2015. Four study centers participated. The target number of 60 participants was reached in 2020. The median patient age was 57 years. In 60% of the patients, histological analysis revealed an unmethylated MGMT promotor status. The mean OS after recurrent resection was 213 days (7.1 months). The mean OS of patients after carmustine wafer implantation with an unmethylated MGMT promotor status and a methylated MGMT promotor status were 207 days and 222 days, respectively. The OS showed no significant difference in the groups (Log Rank test; p=0.729). An increased rate of complications associated with the use of carmustine wafers has not been observed.

Conclusion

The therapy of recurrent GBM remains challenging. The preliminary results of our study suggest that the use of carmustine wafers might counterweigh the shorter OS in patients with unmethylated MGMT promotor.

Neurovaskuläre Chirurgie IV/Neurovascular surgery IV

V299

Troponin (Trop I) als Marker für vaskuläre Komplikationen bei Subarachnoidalblutungen (SAB)
Troponin I (Trop I) as a marker of vascular complications in subarachnoid haemorrhage (SAH)

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Objective

Trop I has been stated to be a marker of poor prognosis in patients with SAH. As a metabolic substrate released from cardiac tissue during myocardial functional insufficiency. In case of functional failure of the heart-brain axis with its origin in the diencephalon Trop I may increase without primary cardiac failure. This might occur in the presence of vasospasm (VS) after SAH followed by cerebral ischemia. It is unknown whether VS correlate to Trop I as an indicator of damage to the cerebro-cardiac axis and as a marker of the clinical condition.

Methods

Prospective monocentric ongoing protocol with so far 29 consecutive patients (16 f, 13 m; mean age 55,1 yrs) with SAH between March 2020 and October 2020.

Measurements of Trop I (normal value below 26,4 (ng/l) from day 1 for 10 days, in case of proven VS on digital subtraction angiography (DSA) till day 21. Routinely measurements of blood flow velocity (BFV - as mean flow in cm/s) by transcranial Doppler sonography (TCD) in the middle cerebral arteries (MCA) of both sides were performed. Documentation of Glascow Coma Scale at ictus, Hunt & Hess and Fisher grade, brain infarcts (CCT), delayed ischemic neurological deficit (DIND) by daily neurologic evaluation. Primary myocardial malfunction as the main cause of Trop I elevation were excluded by ECG and in some cases by cardiac sonography. Additionally cardiac co-morbidities were documented by pts. history.

Results

Half of the pts. (15/29) presented with elevated Trop I during their course on the intensive care unit (day 1 till day 14) (36 till 3333 ng/L.). 7 (25%) of these pts. developed after initial normal values during their stay an elevated Trop I (max. 3333ng/L), which in the majority started suddenly and with a very short interval to its highest value. On average these pts presented a higher Hunt & Hess (>3) and Fisher Grade (IV) on admission with a GCS Score of 11 points.

Within averaged 2,4 days vascular complications could be seen (i.e. increasing of BFV, events of CCT infarcts, VS in DSA). 3 pts. (10%) with Trop I elevation died within 7 days after initial bleeding and could not be followed up. Only one patient out of 29 had a history of cardiac comorbidity (tachyarrhytmia absoluta).

Conclusion

Daily estimation of Trop I can be a marker of delayed vascular complications in pts. during the first two weeks after initial subarachnoid bleeding. Trop I elevation may indicate risky cerebrovascular situations and can contribute to the better estimation of a poor prognosis.

Neurovaskuläre Chirurgie IV/*Neurovascular surgery IV*

V300

Ultraschall-induzierte Medikamentenfreisetzung von mit Nimodipin geladenen Nanopartikel – *in vivo* Analysen am CAM-Modell

Ultrasound-induced drug release from nimodipine-loaded nanoparticles – in-vivo analysis using the chicken chorioallantoic membrane model

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Objective

Nimodipine has been demonstrated to reduce ischemic complications following subarachnoid hemorrhage (SAH). In order to overcome the fist-pass effect of nimodipine, nanocarrier systems with sustained local drug delivery have gained increasing interest. The aim of this study is to produce nimodipine-loaded polymers and to evaluate the possibility of controlled drug release by applying ultrasound in the chicken chorioallantoic membrane (CAM) model.

Methods

Nimodipine-loaded nanoparticles were produced with Pluronic® F127 by the direct dissolution method. Vasospasm was induced by direct ultrasound-application (Physioson, 3 MHz, 1.0 W/cm^2) for 60 seconds. The drug release from was performed by means of ultrasound (1 MHz, 1.7 W/cm²). The effect on the vessels was evaluated with the CAM-model. Nimodipine-loaded nanoparticles were applied in the control group without and in the treatment group with ultrasound application. The vessel diameter before and after treatment was visualized and measured using ImageJ.

Results

The ultrasound-induced nimodipine-release was evaluated on 20 embryo eggs (10 treatment group, 10 control). We found no change in the vessel diameter over time in the control group. The mean relative reduction in vessel diameter after vasospasm induction was 46% (range 44-56%). Eight minutes after ultrasound-induced nimodipine-release in the treatment group the mean vessel diameter of spastic vessels increased again to 90% (range 83-91%) of the initial diameter, which was statistically significant (t-test, p=0.0002).

Conclusion

A controlled drug release from nimodipine-loaded nanoparticles could be reliably induced by applying low frequency continuous wave ultrasound, which resulted in a significant vasospasm reduction in the CAM-model. These results are encouraging further evaluation of this treatment concept with intrathecal application of nimodipine-loaded nanoparticles in an animal SAH-model for controlled vasospasm resolution.

Neurovaskuläre Chirurgie IV/*Neurovascular surgery IV*

V301

Cerebrale Kavernome – Entwicklung der Lebensqualität im longitudinalen Ein-Jahresverlauf
Untreated cerebral cavernous malformations (CCM) – quality of life in one-year longitudinal follow up

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Objective

To estimate quality of life (QoL) during the natural course of patients with untreated cerebral cavernous malformations (CCM) using a one-year longitudinal follow up.

Methods

246 consecutive cases of CCM were included in a prospective longitudinal study assessing QoL and neurological/psychiatric constitution over the past two years in our institution. QoL was assessed by SF 36 survey (2 sum scores (physical sum score PCS/mental sum score MCS) and 8 subdomains (physical function PF, role bodily BR, bodily pain BP, general health GH, vitality VIT, social functioning SF, role emotional ER, mental health MH)), psychiatric constitution by HADS-A/D and functional condition by modified Rankin score. Longitudinal follow-up was achieved within 12 months ± 2 months. Pairwise comparison of data was performed by Wilcoxon test.

Results

So far, 73 patients of the whole cohort were re-assessed at the one year follow up, 4 were excluded as they underwent surgical treatment of the CCM in between the surveys. Therefore, n= 69 cases were included in a preliminary analysis. In these, CCM were located supratentorial (71%), in the brainstem (26%) and cerebellar (3%). Five patients showed multiple CCM, 10 suffered from cavernoma related epilepsy (CRE) and 33 were asymptomatic. Twenty-eight patients (40%) had an initial symptomatic hemorrhage. Two patients suffered from a bleeding event in between the 2 surveys. Comparing longitudinal QoL values, no significant improvement or deterioration was found. Longitudinal HADS-A scores improved significantly (p= 0.047). Subgroup analysis revealed that patients with CRE showed deterioration in most QOL subdomains and component scores.

Conclusion

It is known that diagnosis of CCM effects QoL and mental state (anxiety and depression). Our data reveals that at untreated one-year follow up, QOL does not significantly change, but anxiety levels improve (HADS-A). The latter may reflect an improvement in coping with the diagnosis. Suffering from CRE leads to decrease of QOL reflecting the specific burden of epilepsy.

Neurovaskuläre Chirurgie IV/*Neurovascular surgery IV*

V302

Validierung hämodynamischer CFD-Simulationen intrakranieller Aneurysmata mittels optischer Kohärenztomographie

Validation of haemodynamic CFD-simulations of intracranial aneurysms using intraoperative optical coherence tomography

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Objective

Computation Fluid Dynamics (CFD) is a well established tool to investigate hemodynamics in vascular geometries. Various authors found correlations between specific CFD-parameters and intraoperatively thin-appearing aneurysm wall regions. Optical Coherence Tomography (OCT), providing tissue images of high local resolution, was already successfully used in cardiology for local intravascular analysis of vessel wall layer composition. The aim of our study was to assess feasibility of intraoperative OCT performed during aneurysm surgery for validation of local wall thicknesses predicted by hemodynamic patterns from CFD simulations.

Methods

We prospectively investigated a series of 4 patients electively undergoing aneurysm surgery. For CFD-simulations, we built patient-specific 3D-volume-meshes based on 3D rotational angiographies using AMIRA 5.6 (FEI Visualization Sciences, France), ANSYS ICEM and CFX (ANSYS Inc., USA). We assumed rigid walls, pulsatile flow and modelled blood as a non-Newtonian fluid with a shear-dependent dynamic viscosity following a Power Law model. Intraoperatively, OCT scans were performed with a ZEISS LUMERA 700 OCT microscope. For postprocessing, ImageJ (imagej.nih.gov) and AMIRA were used. Comparison of local hemodynamic patterns, distribution of parameters like Wall Shear Stress (WSS) and local wall thicknesses were performed in overlay with the intraoperative situs using AVIZO Wind 7.1 (FEI Visualization Sciences).

Results

In all patients, good OCT results were obtained. Thin-appearing translucent areas correlated well with OCT scans. Hemodynamically, low WSS, high pressure and high OSI could be found in these areas. Quantitative measurement of wall thickness was possible and validated intraoperatively using pre-defined plastic sheets. We visualized walls as 3D thickness maps in overlay with the intraoperative view through the microscope. Operating neurosurgeons subjectively profited well from hemodynamic simulations of the individual cases.

Conclusion

We present a novel tool to validate predictions on the local biology of the aneurysm wall derived from hemodynamic CFD-simulations in vivo. CFD-simulations can provide valuable information regarding local thin-walled areas susceptible of rupture serving as a base for a reliable prediction tool for patient-specific aneurysm wall properties and rupture risk. The operating neurosurgeon could concretely benefit from these hemodynamic data to adopt individual dissection strategy to avoid intraoperative rupture.

Neurovaskuläre Chirurgie IV/*Neurovascular surgery IV*

V303

Virtual reality und Aneurysmata der Arteria communicans anterior
Virtual reality and arteria communicans anterior aneurysms

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Objective

Anterior communicating artery (ACoA) aneurysms are known to have diverse configurations, vascular relationships, and anatomical variations. Evaluation and operative treatment of these aneurysms necessitate perfect surgical strategy based on review of three-dimensional (3D) angioarchitecture using several radiologic cranial imaging methods. We retrospectively analyzed the potential influence of 3D virtual reality (VR) reconstructions compared to conventional computed tomography angiography (CTA) scans on the identification of vascular anatomy and neighboring structures, and on the surgical planning in patients with unruptured ACoA aneurysms.

Methods

Medical files were retrospectively analyzed regarding patient- and disease-related data. Preoperative CTA scans were retrospectively reconstructed to 3D-VR images and visualized via VR software to detect the characteristics of unruptured ACoA aneurysms. A questionnaire of experienced neurosurgeons evaluated the influence of VR visualization technique on identification of aneurysm morphology and relevant arterial anatomy and on surgical strategy.

Results

Twenty-six patients were included and 520 answer sheets were evaluated. Image presentation using 3D-VR modality significantly influenced the detection of the aneurysm-related vascular structures ($p = 0.0001$), as well as the recommended head positioning ($p = 0.005$) and surgical approach ($p = 0.001$) in the planning of microsurgical clipping.

Conclusion

In patients with unruptured ACoA aneurysms, the reconstruction of conventional preoperative CTA scans into 3D images and the spatial and anatomical presentation in VR models enable greater understanding of the anatomy and pathology, provide realistic haptic feedback for aneurysm surgery, and thus influence operation planning and strategy.

Neurovaskuläre Chirurgie IV/*Neurovascular surgery IV*

V304

Visual evoked potentials (VEP) and transcranial Doppler sonography (TCD) of the cerebral posterior circulation in patients with subarachnoid haemorrhage (SAH)

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Objective

In patients (pts) with SAH vasospasms (VS) are the most threatening complication in the first 3 weeks. In daily practice of patients with reduced consciousness the red flag for VS is the increase of blood blow velocity (BFV) in TCD. However, VS of the posterior cerebral artery (PCA) distal to the P1 segment are often insufficiently identified by TCD, due to the angel between the PCA blood stream axis and the sonographic beam. BFV does not inform about functional capacity. However, VEP are depending on the cerebral oxygen metabolism. Recording of prolonged latency (La) and reduced amplitude (Am) might suggest an insufficient metabolism. There is no report in the literature using VEP and TCD as combined techniques in SAH with VS of the basilar artery branches.

Methods

In comatose pts with SAH daily TCD including the PCA was performed from day 3 till days 21. As soon as mean BFV increased above 110cm/s repeated VEP measurements were added. 2 plastic pads (diameter 14 mm), one per eye, equipped with 19 stimulating white LED lights (each diameter 1,5 mm) were connected to an IOM machine (Eclipse MedtronicR), placed on the closed eye lid and covered with black cotton eye patches. Flicker frequency was 2 Hz, intensity was increased till occurrence of peak N1/P1. Stimulation was performed with bilateral alternating light and mono-ocular stimulation. VEP were recorded by needle electrodes at Oz, O1, O2 and Cz. This allowed calculation of VEP La and Am for each occipital lobe.

Results

TCD identified P1 in all pts on both sides, P2 in 4/6 on at least 5 days and in 4 pts on 4 days. In 3 pts mean BFV and VEP (N1 68,5 - 78,4) and P1 (100,4 – 108,3) were normal. CCT did not show infarcts. In 3 other pts (2 with a. basilaris aneurysms, 1 with ACA aneurysm) mean BFV was increased in MCA/ACA and in 2 of these pts also in PCA (above 120 cm/s). DSA confirmed VS. CCT identified Infarcts in the PCA territory in these 3 pts. In these 3 pts VEP La (P1 above 115 ms) after VEP stimulation of one or both eyes was due to the development of an unilateral PCA infarct. In 2 pts VEP La increased before CT-visualization of infarcts.

Conclusion

This is to our knowledge the 1st report on measurements of both TCD and VEP in SAH during the acute state. VEP may indicate an insufficient oxygen metabolism despite increased BFV due to VS. It seems possible that the reliability of TCD in the posterior circulation is supplemented by VEP measurements.

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