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Conference Report

Abstracts of the 2023 Joint Annual Meeting of the Swiss Neurological Society and Swiss Society of Neurosurgery Guest Society: Swiss Society of Behavioural Neurology, Kongresshaus Zurich, Switzerland, November 23–24, 2023 †

Swiss Neurological Society (SNS) [1,*] and Swiss Society of Neurosurgery (SSNS) [2]

[1] Swiss Neurological Society (SNS), c/o, IMK Institute for Medicine and Communication Ltd., Münsterberg 1, CH-4001 Basel, Switzerland
[2] Swiss Society of Neurosurgery (SSNS), c/o, IMK Institute for Medicine and Communication Ltd., Münsterberg 1, CH-4001 Basel, Switzerland; sgnc@imk.ch
* Correspondence: swissneuro@imk.ch
† Abstracts of the Joint Annual Meeting 2023: Swiss Neurological Society (SNS)|Swiss Society of Neurosurgery (SSNS), Guest Society: Swiss Society of Behavioural Neurology (SSBN), Kongresshaus Zurich, Switzerland, November 23–24, 2023. Main Topic: Therapeutic Revolutions.

Abstract: On behalf of the SNS and SSNS, we are pleased to present the abstracts of the Joint Annual Meeting to be held in Zurich, Switzerland, on 23–24 November, 2023. In total, 119 abstracts have been selected: 4 abstracts for the Plenary Sessions, 12 abstracts for Free Communications, 18 abstracts for Poster flash presentations, 6 abstracts for the SAYN GemSession, and 79 abstracts as ePosters. We congratulate all the presenters on their research work and contributions.

Keywords: neurosurgery; neurology; stroke; cerebrovascular; movement disorders; neurodegenerative; neurotrauma; neuroimmunology; neuro-oncology; spine and pain; biological psychiatry; epilepsy and sleep disorders; neuropsychology; behavioral neurology; clinical neurophysiology; headache; neuropathology; neurorehabilitation

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O01

Myd88-TLR4-Dependent Choroid Plexus Activation Precedes Perilesional Inflammation and Secondary Brain Edema in a Mouse Model of Intracerebral Hemorrhage

K Akeret [1], RM Buzzi [2], BR Thomson [1], N Schwendinger [1], J Klohs [3], N Schulthess [2], L Baselgia [2], K Hansen [2], L Regli [1], F Vallelian [2], M Hugelshofer [1] and D Schaer [2]

[1] Department of Neurosurgery, Clinical Neuroscience Center, Universitätsspital and University of Zurich, Zurich, Switzerland;
[2] Division of Internal Medicine, Universitätsspital and University of Zurich, Zurich, Switzerland;
[3] Institute for Biomedical Engineering, University of Zurich and ETH Zurich, Zurich, Switzerland

Background: The functional neurological outcome of patients with intracerebral hemorrhage (ICH) strongly relates to the degree of secondary brain injury (ICH-SBI) evolving within days after the initial bleeding. Different mechanisms including the incitement of inflammatory pathways, dysfunction of the blood–brain barrier (BBB), activation of resident microglia, and an influx of blood-borne immune cells, have been hypothesized to contribute to ICH-SBI. Yet, the spatiotemporal interplay of specific inflammatory processes within different brain compartments has not been sufficiently characterized, limiting potential therapeutic interventions to prevent and treat ICH-SBI.
Methods: We used a whole-blood injection model in mice, to systematically characterized the spatial and temporal dynamics of inflammatory processes after ICH using 7-Tesla

magnetic resonance imaging (MRI), spatial RNA sequencing (spRNAseq), functional BBB assessment, and immunofluorescence average-intensity-mapping.
Results: We identified a pronounced early response of the choroid plexus (CP) peaking at 12 to 24 h, that was characterized by inflammatory cytokine expression, epithelial and endothelial expression of leukocyte adhesion molecules, and the accumulation of leukocytes. In contrast, we observed a delayed secondary reaction pattern at the injection site (striatum) peaking at 96 h, defined by gene expression corresponding to perilesional leukocyte infiltration and correlating to the delayed signal alteration seen on MRI. Pathway analysis revealed a dependence of the early inflammatory reaction in the CP on toll-like receptor 4 (TLR4) signaling via myeloid differentiation factor 88 (MyD88). TLR4 and MyD88 knockout mice corroborated this observation, lacking the early upregulation of adhesion molecules and leukocyte infiltration within the CP 24 h after whole-blood injection.
Conclusions: We report a biphasic brain reaction pattern after ICH with a MyD88-TLR4-dependent early inflammatory response of the CP, preceding inflammation, edema and leukocyte infiltration at the lesion site. Pharmacological targeting of the early CP-activation might harbor the potential to modulate the development of ICH-SBI.

O02

From Conservative to Interventional Management in Treating Unruptured Intracerebral Aneurysms

B Bandhauer [1], P Gruber [2], L Andereggen [1], J Berberat [2], S Wanderer [1], M Cattaneo [3], G Schubert [1], L Remonda [2], S Marbacher [1] and B Grüter [2]

[1] Department of Neurosurgery, Cantonal Hospital Aarau, Switzerland;
[2] Department of Neuroradiology, Cantonal Hospital Aarau, Switzerland;
[3] Clinical Trial Unit, Department of Clinical Research, University of Basel, Switzerland

Objectives: This study aims to identify characteristic patterns and potential predictors of unruptured intracranial aneurysms (UIA) that request revision of an initially conservative management strategy.
Background: Indication for treatment of UIAs depends on several factors, such as patient's age, previous medical history, UIA location and size. For some patients harboring UIAs initially managed noninvasively, treatment strategy may change to surgical or endovascular intervention during follow-up.
Methods: Out of n = 1041 intracerebral aneurysms diagnosed between 2006–2022 in our institution, n = 144 patients were identified initially aligned to conservative management. These cases were retrospectively reviewed for patient and UIA characteristics at diagnosis (such as patient age, comorbidities, previous medical history, potential risk factors, as well as UIA angioarchitecture, location, and size), and for a change in their treatment strategy (reason for change, time to intervention, modality of intervention).
Results: In n = 10 out of 144 initially conservatively managed patients (6.9%) indication changed to microsurgical clipping (n = 6) or endovascular embolization (n = 4) after a median follow-up of 26 months (interquartile range, 8.5–64.5 months). Out of the n = 10 patients with change of treatment strategy, indication for intervention was given by aneurysm growth (n = 7), change in its configuration (n = 2) or both (n = 1). Overall median follow-up for the entire population was 24.5 months (interquartile range, 7.75–55.75 months).
Conclusions: The likelihood of later change to invasive UIA treatment is relatively low if initially a conservative treatment strategy was established and remains unpredictable. However, if it comes to a change in the treatment strategy, this is most often due to UIA growth over time. Therefore, conservatively managed UIA patients need to be followed with regular radiographical monitoring of the UIA.

O03

Flow Capacity of a Superficial Temporal Artery as a Donor in a Consecutive Series of 85 STA-MCA Bypasses

M Sebök, LM Höbner, J Fierstra, T Schubert, Z Kulcsar, A Luft, L Regli and G Esposito

UniversitätsSpital & Universität Zürich, Switzerland

Objective: A superficial temporal artery to middle cerebral artery (STA-MCA) bypass is an extra-to-intracranial (EC-IC) direct bypass that consist of a direct microvascular anastomosis between an extracranial donor artery (the superficial temporal artery—STA) and an intracranial recipient artery. Direct bypass procedures can be further categorized according to the amount of flow (capacity) provided into: low, medium or high flow. The flow in the flow-augmentation STA-MCA bypass is influenced by flow demand of the revascularized territory. We report our intraoperative flow measurement data in a consecutive series of 85 performed STA-MCA bypasses. Moreover, in the subanalysis, we show the postoperative bypass flow measured with quantitative non-invasive optimal vessel analysis (NOVA) MRA.
Methods: Between May 2019 and January 2023, 85 patients with acute large vessel occlusion (LVO), chronic LVO or Moyamoya disease underwent a flow-augmentation STA-MCA bypass revascularization at our department. A consecutive subgroup of 31 patients underwent a postoperative (before discharge) bypass flow measurement with qMRA-NOVA imaging tool.
Results: The mean ± SD intra-operative bypass flow in our consecutive series of 85 STA-MCA bypasses was 57.6 ± 28.3 mL/min (range: 15–154 mL). In the subanalysis, there was no difference in the intraoperative flow capacity of a donor STA artery between the acute, chronic and Moyamoya group (acute group (n = 19): 59.8 ± 31.4 mL/min, chronic group (n = 35): 54.3 ± 26.8 mL/min and Moyamoya group (n = 31): 59.0 ± 28.9 mL/min). In a consecutive 31 STA-MCA bypass cases, where a postoperative flow measurement was performed using qMRA-NOVA, a trend of flow increase after surgery was seen (intra-OP flow in 31 cases: mean ± SD bypass flow: 71.1 ± 29.3 mL/min (range: 30–154 mL); post-OP flow in 31 cases: mean ± SD bypass flow: 99.5 ± 45.1 mL/min (range: 24–236 mL)).
Conclusions: Using intra-operative and post-operative quantitative flow capacity measurement of a superficial temporal artery, our data confirm that the flow in the flow-augmentation STA-MCA bypass is influenced by flow demand of the revascularized territory and can reach high values if needed.

O04

Impact of Acute Hydrocephalus after Aneurysmal SAH on Longitudinal Neuropsychological Outcome

S Maschke [1], M Germans [2], P Bijlenga [3], R Maduri [4], R Thomas Daniel [5], A Chiappini [6], T Robert [6], A Zeitlberger [7], J Goldberg [8], D Bervini [8], O Bozinov [7], E Keller [9], L Regli [2], M Stienen [7] and IC Hostettler [10]

[1] Kantonsspital St. Gallen KSSG, Switzerland;
[2] University Hospital Zurich, Zurich, Switzerland;
[3] University Hospital Geneva, Geneva, Switzerland;
[4] Swiss Medical Network, Clinique de Genolier, Genolier, Switzerland;
[5] University Hospital Lausanne, Lausanne, Switzerland;
[6] Cantonal Hospital Lugano, Lugano, Switzerland;
[7] Kantonsspital St. Gallen, Switzerland;
[8] University Hospital Berne, Berne, Switzerland;
[9] University of Zurich, Zurich, Switzerland;
[10] Kantonsspital St. Gallen, Switzerland

Aims: Hydrocephalus occurs in up to 67% of patients with aneurysmal subarachnoid hemorrhage (aSAH). It is associated with increased morbidity and mortality. While a deletrious effect of acute hydrocephalus on short-term cognitive functions is known, its longitudinal effect, especially in lower-grade aSAH patients, is poorly understood. The aim of this study was to evaluate its effect on longer-term cognitive outcome after aSAH.

Methods: Prospective, observational multicenter study (8 Swiss centers) including patients from all cultural and linguistic Swiss areas. Alert patients (Glasgow Coma Scale $\geq$ 13 points 48 h–72 h after aSAH) underwent serial neuropsychological assessments (Montreal Cognitive Assessment [MoCA]) by a trained, independent neuropsychologist getting baseline (first assessment <72 h after aSAH), short- (14–28 days [discharge]) and longterm assessment (3 months). We compared standardized MoCA scores (adjusted for normed Swiss age and sex) and determined the likelihood for a clinically meaningful decline of $\geq$2 points from baseline in patients with and without hydrocephalus.
Results: We included 112 patients (87.5%). Mean age was 53.9 years (13.9 SD), 66.1% were female. Forty patients (35.7%) developed acute hydrocephalus, ten (25%) needed a permanent ventriculo-peritoneal shunt. MoCA z-score was significantly lower in the hydrocephalus group both at baseline (-2.84 vs. -1.12, $p < 0.001$) and at discharge (0.53 vs. -3.35, $p < 0.001$). Patients with hydrocephalus were more likely to experience a decline of $\geq$2 points at discharge (OR 2.76, 95% CI 1.16–6.53; $p = 0.02$). However, this effect was not evident at the 3 month follow-up (OR 1.22, 95% CI 0.32–4.62; $p = 0.77$).
Conclusions: Lower-grade aSAH patients with hydrocephalus have worse short-term cognitive function compared to those without. However, its effect is no longer detectable at the 3 months follow-up, likely indicating the beneficial effect of restored cerebro-spinal fluid flow or its permanent diversion. Hydrocephalus is an independent risk factor for a temporary, but clinically meaningful decline in neurocognitive function.

O05

Bleeding Risk of Cerebral Cavernous Malformations in Patients on Statin and Antiplatelet Medication: A Cohort Study

L Marques [1], C Jaeggi [2], M Branca[3], A Raabe [4], D Bervini [4] and J Goldberg [4]

[1] Universitätsspital Basel, Switzerland;
[2] Kantonspital Olten, Switzerland;
[3] Universität Bern—Inselgruppe, Switzerland;
[4] Inselspital—Universitätsspital Bern, Switzerland

Background: Statin medication has been identified as a potential therapeutic target for stabilizing cerebral cavernous malformations (CCMs). While increasing evidence suggests that antiplatelet medication decreases the risk of CCM-hemorrhage, data on statin medication in clinical studies is scarce.
Objective: To assess the risk of symptomatic CCM-related hemorrhage at presentation and during follow-up in patients on statin and antiplatelet medication.
Methods: A single-center database containing patients harboring CCMs was retrospectively analyzed over 41 years and interrogated for symptomatic hemorrhage at diagnosis, during follow-up, and statin and antiplatelet medication.
Results: 212 of 933 CCMs (22.7%), harbored by 688 patients, presented with hemorrhage at diagnosis. Statin medication was not associated with a decreased risk of hemorrhage at diagnosis (OR 0.63, CI 0.23–1.69, $p = 0.355$), antiplatelet medication (OR 0.26, CI 0.08–0.86, $p = 0.028$) and combined statin and antiplatelet medication (OR 0.19, CI 0.05–0.66; $p = 0.009$) showed a decreased risk. In the antiplatelet only group, 2 (4.7%) of 43 CCMs developed follow-up hemorrhage (137.1 lesion-years) compared to 67 (9.5%) of 703 CCMs (3228.1 lesion-years) in the non-medication group. No follow-up hemorrhages occurred in the statin and the combined statin and antiplatelet medication group. Antiplatelet medication was not associated with follow-up hemorrhage (HR 0.7, CI 0.16-3.05; $p = 0.634$).
Conclusions: Antiplatelet medication alone and its combination with statins were associated with a lower risk of hemorrhage at CCM diagnosis. The risk reduction of combined statin and antiplatelet medication was greater than in patients receiving antiplatelet medication alone, indicating a possible synergistic effect. Antiplatelet medication alone was not associated with follow-up hemorrhage.

O06

Detection of Glioma and Glioblastoma Liquid Biomarkers through Proteomic Plasma Profiling

M Ritz [1], M Etter [2], W Duchemin [3], T Shekarian [1], C Durano[1], J Vogel [2] and G Hutter [2]

[1] University of Basel;
[2] Basel University Hospital;
[3] sciCORE Center for Scientific Computing, University of Basel, Switzerland

Background: Advancement in the diagnosis and surveillance of gliomas has been limited posing both diagnostic and therapeutic challenges. Definitive diagnosis, distinction of progression versus pseudoprogression and prognosis assessment still depend on invasive neurosurgical biopsy procedure. Minimally-invasive plasma sampling could minimize the risks associated with invasive tissue sampling.
Aim: Therefore, we aimed to identify specific plasma protein patterns of low- and high-grade glioma patients, compared to healthy individuals and investigated whether different plasma-derived protein signatures were associated with survival in glioma patients.
Material and Methods: Plasma samples were from patients with glioma grades I to IV collected during tumor removal and from healthy controls donating blood were processed for Liquid Chromatography Mass Spectrometry (LC/MS) proteomics after depletion of the 14 most abundant plasma proteins, in order to specifically detect low-abundant tumor-derived proteins.
Results: Overall, 646 proteins were measured across 104 plasma samples from glioma patients and 57 plasmas from the healthy cohort. PCA showed 2 clusters of samples, one containing low- and high-grade glioma samples and the other containing healthy and some grade IV (GBM) plasma samples. Interestingly, a spatial analysis of tumor location by MRI associated the GBM samples separated from healthy samples with subventricular vicinity. 26 differentially expressed proteins (DEPs) were identified discriminating between glioma and healthy samples and 30 DEPs discriminating GBM and healthy samples. The top most overexpressed proteins in gliomas vs. controls were SERPINA3, F13A1, and TKT. Multivariate analysis identified SERPINA3, PPBP and MYH9 as strong discriminators of healthy vs. GBM but also of low-grade vs. GBM, indicating that these proteins may represent specific plasma biomarkers for GBM. SERPINA3, MYL1 and CLU were associated with poor survival in GBM.
Conclusions: In this study, we describe sets of plasma-derived proteins, in particular SERPINA3, as predictive biomarkers that could be used to assess glioma progression allowing patient-centered treatment options.

O07

Surgical Management of Pineal Region Tumor: A Case Series in Pediatric and Young Adult Patients

L Greuter [1], V Narayanan [2], F Ebel [3], N Frank [3], T Hallenberger [4], R Guzman [5] and J Soleman [5]

[1] Universitätsspital Basel;
[2] University of Basel;
[3] University Hospital of Basel;
[4] University Hospital Basel/University of Basel;
[5] University Hospital of Basel/University Children's Hospital of Basel/University of Basel, Switzerland

Access to the pineal region, which is the origin of a multitude of different pathologies, is challenging due to its complex anatomy. The aim of this abstract is to describe our experience with the different surgical management strategies for tumors in pineal region.

Methods: Retrospective case series from 1.7.2013–30.7.2022, including consecutive pediatric and young adults ("<30" years) undergoing pineal region tumor surgery at the University Hospital of Basel or Children's' Hospital (UKBB) Basel.
Results: We included 10 patients with a mean age of 14.8 (±8.28) years and (7, 70%) were male. The mean preoperative GCS was 14.9 (±0.32). Seven patients (70%) showed clinical signs of raised intracranial pressure while six (60%) suffered from diplopia. Mean tumor size was 9.98 (±11.55) cm^3.
In all patients the aim for the first surgery was to alleviate the hydrocephalus and reach a histological diagnosis with an endoscopic biopsy and third ventriculostomy (ETV). One patient underwent subtotal resection instead of a biopsy during his first procedure. Six patients underwent a subsequent 2nd surgery, five patients (50%) had an open craniotomy and tumor resection, while one patient underwent a re-biopsy. Apart from one patient that received an interhemispheric craniotomy, all patients underwent infratentorial supracerebellar craniotomy. In these patients, we achieved one (10%) gross total resection (GTR), four (40%) subtotal resections (STR) and one (10%) biopsy, which was the desired extent of resection in all patients. Glioma was the most common pathology (n = 3, 30%), followed by germinomas (n = 2, 20%) and pineal cysts (n = 2, 20%). Three patients (30%) suffered from a postoperative hydrocephalus requiring further surgical intervention. Seven patients (70%) improved after surgery and no patients got worse or suffered a surgical complication. Two patients died after a mean of 606.00 (±12.73) days without any surgery-related morbidity.
Conclusions: A combination of endoscopic and microsurgical approaches is required to successfully treat pineal region tumors in children and young adults. Endoscopic third ventriculostomy and simultaneous biopsy is the mainstay of the initial treatment. Despite the complex anatomy of the pineal region, surgical morbidity and mortality rates are low, if the approach and the extent of resection are tailored to the pathology itself and its surrounding anatomy.

O08

Utility of the LACE Index in Predicting Outcomes in Patients with Spinal Infections

R Schär, M Branca [1], A Raabe [2] and CM Jesse [2]

[1] CTU Bern, University of Bern, Bern, Switzerland;
[2] Department of Neurosurgery, Inselspital, Bern University Hospital, University of Bern, 3010, Bern, Switzerland

Aims: The aim of this study was to assess the utility of the LACE (Length of stay, Acuity of admission, Comorbidities, Emergency department visits) index to predict death and readmissions in patients with spinal infections (SI).
Methods: This was a retrospective cohort study from a single academic teaching hospital. LACE indices were calculated for all patients treated for spinal infections between 2012 and 2021. Data analysis included parametric and non-parametric tests, Student's t-test and Wilcoxon-Mann-Whitney U-test for continuous, and Fisher's exact test for categorical variables. ROC analysis was performed to estimate the AUC of the score to discriminate between patients with and without the outcome and the estimated cut-off was extracted for the available sample based on the Youden Index that maximizes the sum of the sensitivity and specificity.
Results: A total of 167 patients were analyzed. Mean age was 64.8 (±15.1) years, 73 (44%) were female. Ten (6.0%) of the 167 patients died <30 days, and 16 (9.6%) <90 days after discharge. Mean LACE indices were 13.4 (±3.6) and 13.8 (±3.0) for the deceased patients, compared to 11.0 (±2.8) and 10.8 (±2.7) for surviving patients (p = 0.01, p < 0.001), respectively. Forty-eight patients (28.7%) were readmitted <90 days following discharge. Readmitted patients had a significantly higher mean LACE index compared to non-readmitted patients (12.8 ± 2.3 vs. 10.5 ± 2.8, p < 0.001). For death <30 days and readmission <90 days,

ROC analysis estimated cut-off LACE indices of 15.0 and 12.0, respectively, with sensitivity of 50% and 71%, and specificity of 86% and 70%, respectively.
Conclusions: Patients with SI had high LACE indices that correlated with high mortality and readmission rates. The LACE index can be applied to this patient population to recognize high-risk patients, and to predict unplanned readmission and mortality.
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O09

The Evidence Challenge of Intraoperative Neurophysiological Monitoring in Surgeries of Spinal Meningioma

P Alvarez Abut, CM Jesse, J Wermelinger, A Raabe, R Schär and K Seidel

Inselspital—Universitätsspital Bern, Switzerland

Aims: The evidence of improving neurological or surgical outcome by applying intraoperative neurophysiological monitoring (IOM) of motor evoked potentials (MEP) and somatosensory evoked potentials (SEP) during surgery of spinal meningioma (SM) is unclear. The aim of this study was to assess the usefulness of IOM in a consecutive cohort of patients.
Methods: Eighty-six patients with spinal cervical (n = 15, 17.4%), cervico-thoracic junction (n = 4, 7.4%) and thoracic (n = 67, 77.9%) meningioma were included. Accordingly to availability of IOM and discretion of the surgeon, 51 (59.3%) patients were assigned to IOM (IOM group) and 35 (40.7%) were operated without IOM (non-IOM group). Pre- and postoperative modified McCormick Scale (mMCS) was evaluated by an independent surgeon.
Results: The IOM and non-IOM groups were homogeneous in age, tumour/canal ratio, sex, location, level, preoperative mMCS and neurological deficits, and postoperative Simpson grade and mMCS. Three patients in the non-IOM group (8.57%) and one in the IOM group (1.96%) had worsened neurological status after surgery. Two of the former (5.71%) and none of the later (0%) had persistent deficit at follow up (FU). The worsening of neurological status between both groups yielded no statistically significant difference after surgery (p = 0.300, OR 0.213, 95% CI 0.021–2.141), nor at FU (p = 0.163). At FU, the odds ratio could not be determined because there was no worsening in the IOM group. In the documented reports, there were found 13 cases of IOM alterations reported to the surgeon and three of direct influence on the surgical strategy.
Conclusions: There was a tendency towards a better neurological outcome in the IOM group for SM surgeries, although it was not statistically supported. The small sample size of patients with worsening of neurological status in the IOM group, constrains the statistical analysis. Further studies with larger cohorts are required to evaluate the preventive benefit of IOM in SM surgery.

O10

Current State of Preoperative Embolization for Spinal Metastasis—A Survey by the EANS Spine Section

S Motov [1], FC Stengel [1], F Ringel [2] and MN Stienen [1]

[1] Kantonsspital St. Gallen, Department of Neurosurgery, Switzerland;
[2] Johannes Gutenberg-Universität Mainz, Germany

Introduction: Preoperative embolization (PE) for spinal metastasis is a minimally-invasive procedure to reduce blood supply in tumor masses and alleviate pain in certain patients. It is effective in reducing bleeding during surgery for hypervascular lesions and has low complications. However, the decision whether and when to perform PE varies largely among spine surgeons and centers. The aim was to understand PE's current usage and decision-making process in European spine centers.

Methods: The European Association of Neurosurgical Societies (EANS) spine section designed a 13-item online survey. It was distributed to neurosurgical residents and board-certified neurosurgeons between 7th of February and 5th of May 2023.
Results: We analyzed 120 survey responses. Most participants were board-certified neurosurgeons (71%) or residents (26%) in university hospitals (76%). The majority performed <20 surgeries per year (n = 97), with 23 conducting more than 20 surgeries per year. Routinely performed PE was stated not a common practice in 62%. Of those using PE, 25% indicated to perform PE only in selected cases requiring vertebral body resection and replacement. Reasons for not performing PE included lack of time (44%), unclear benefits (25%), no significant bleeding without PE (19%), and significant bleeding despite PE (8%). Key factors for the indication of PE included suspected tumor histopathology (48%) and preoperative MRI/CT features (36%). Regarding the timing of PE for subsequent surgery, most participants opted for PE < 24 h before surgery in separate anesthesia (54%). Based on the respondents' level of experience, expressed by the performed procedures per year, we found in the regression analysis that the most experienced participants (>20 PE/year, n = 23) were significantly more likely to observe reduced estimated intraoperative blood loss (EBL) after PE (p = 0.014; 95% CI (0.063–0.55)). Complications associated with PE were observed in 43% (neurological deterioration due to spinal cord infarction (15%) and swelling-related tumor necrosis (13%)). However, 72% reported no PE-associated complications.
Conclusions: PE is not routine in European centers. Specialists prefer PE for hypervascularized tumors without urgent neurological deterioration, scheduling it in separate anesthesia <24 h before subsequent surgery. Most participants noted reduced intraoperative blood loss, though procedure-related complications cannot be neglected.

O11

Comparison of Interlaminar Full-Endoscopic Versus Microscopic Approach for Lumbar Disc Herniation with Motor Deficit: A Retrospective Monocentric Study

G Stauffacher [1], J Fournier [2] and A Simonin [2]

[1] Université de Lausanne (UNIL), Switzerland;
[2] Hôpital de Sion, Switzerland

Introduction: Non-inferiority of interlaminar full-endoscopic disectomy (ILFED) surgery for lumbar disc hernia (LDH) regarding pain improvement and safety is well established1-2. However, the current literature has not evaluated specifically the outcome of LDH presenting with a motor weakness. We present the first case-series comparing motor recovery with both techniques (microscopy versus interlaminar full-endoscopy) in a single institution.
Methods: In this retrospective study, we plan to compare two operative technical methods routinely practiced in Sion hospital in order to define the impact of the recovery of a motor deficit. We reused the data routinely captured in patients files at Sion Hospital, for 138 patients who underwent surgery for lumbar disc herniation with motor deficit between 1 January 2020 and 31 March 2023. All patients consented for the reuse of their data in the field of this project, as explained in the protocol approved by the local Ethics Committee.
Results: For this preliminary analysis, we retrospectively analyzed 109 patients (40 females, 69 males, mean age 54.42 $\pm$ SD 15.77) that benefitted from a surgery for a LDH presenting with a motor deficit rated with Medical Research Council (MRC) M4 or less, operated at Sion Hospital between January 2020 and December 2022. Patients were separated into two groups according to the operative technical method: those operated with standard microsurgical technique versus those operated by interlaminar full-endoscopy. Pre- and post-operative strength, rated with MRC at discharge, 1 month and 3 months was considered as primary outcome. For microscopy, the pre-operative MRC was improved by 1.09, 1.30 and 1.44 point at discharge, 1 month and 3 months postoperatively ($p < 0.0001$). For endoscopy, there was an improvement of 0.93, 1.29 and 1.31 point respectively ($p < 0.0001$). Thus, both techniques significantly improved motor deficits. When comparing the 2 tech-

niques there was no significant difference between endoscopy and microscopy at discharge ($p = 0.83$), at 1 month ($p > 0.9999$) or at 3 months ($p = 0.9525$).
Conclusions: Interlaminar full-endoscopic discectomy (ILFED) seems to be an effective procedure for improving motor weakness in lumbar disc hernia (LDH). In our retrospective comparative study, we did not find a statistically significant difference in improvement when compared to standard microsurgical technique.

O12

Full-Endoscopic Posterior Cervical Foraminotomy: A First Case-Series of 6 Patients in Switzerland

S Nazeeruddin [1], P Vonlanthen [2], J Fournier [3] and A Simonin [1]

[1] Hôpital de Sion;
[2] Université de Lausanne (UNIL);
[3] Hôpital de Sion, Switzerland

Introduction: Full-endoscopic posterior cervical foraminotomy (FEPCF) is the most minimally invasive procedure that allows to decompress a nerve root in the cervical spine from a posterior approach1-4. Because it is a novel surgical technique, its efficacy and safety has to be evaluated carefully. We retrospectively analyzed to the best of our knowledge the first case-series of FEPCF in Switzerland and and present our results.
Methods: We retrospectively analyzed data from a consecutive series of 6 patients (1 female, 5 males, mean age: 52.7 $\pm$ 12.5 SD) who underwent a FEPCF in our institution, from October 2022 to May 2023. Primary outcome was pain reduction evaluated with the Visual Analog Scale (VAS) for neck and arm, as well as Neck Disability Index (NDI) preoperatively and one month postoperatively. Surgical time, length of stay, opioid consumption, complications were also analyzed as secondary outcomes.
Results: Pre-operative arm and neck pain was 7.7 $\pm$ 1.0 SEM and 7.2 $\pm$ 1.5 SEM respectively on the VAS. One month post-operative arm and neck pain was 3.2 $\pm$ 1.4 SEM and 4.2 $\pm$ 1.1 SEM. Pain reduction was significant for arm pain ($p = 0.02$) but not for neck pain ($p = 0.14$). NDI was 48.4% $\pm$ 7.9 SEM pre-operatively, and 16.4% $\pm$ 8.7 SEM postoperatively, which was highly significant ($p = 0.0006$). Mean length of stay was 2.3 days. Mean surgical time was 126 minutes. Mean total oxycodone consumption during hospital stay was 9.8 mg. There was no particular complication.
Conclusions: Full-endoscopic posterior cervical foraminotomy (FEPCF) seems to be a safe and effective procedure for cervical foraminal stenosis. Prospective comparative studies should be performed to assess any potential advantage compared to the open or tubular minimally-invasive technique.

O13

Skull Fractures Resulting From E-Scooter Accidents: A Single Center Retrospective Cohort Study from Switzerland

L Marques [1], G Fischer [2], A El-Garci [3], O Bozinov [3] and MN Stienen [4]

[1] Universitätsspital Basel;
[2] Kantonspital St Gallen;
[3] Kantonsspital St Gallen;
[4] Kantonsspital St. Gallen, Switzerland

Background: The introduction of standing electric (e-) scooters in early 2019 revolutionized mobility. With increasing usage, numbers of e-scooter related accidents have increased, as well. While international data demonstrates occurrence of head injuries in most accidents, wearing helmets is not mandatory.
Objective: To assess the traumatic brain injury (TBI) related to e-scooter related accidents, with focus on the pattern of skull fractures.

Methods: We conducted a single center retrospective analysis of e-scooter accidents with trauma of the neurocranium. Common data elements for TBI were used to describe cases.
Results: Between January 2018 and April 2022, our electronic search identified 17 patients, of which 8 patients were excluded. Nine patients with e-scooter accidents were reviewed, and 5 patients with skull fractures were included. They were mostly male (80%), not wearing a helmet (80%) and intoxicated (100%). All accidents were self-inflicted. In all cases, fractures of the lateral neurocranium were involved. Three patients showed neurological deficits and were sent to in-patient rehabilitation after hospitalization. The only one patient wearing a helmet showed a similar fracture pattern as the non-helmet wearing patients. However, the helmet wearing patient showed no intracranial hemorrhage and lower injury severity score.
Conclusions: We observed a high rate of TBI and typical pattern of cranial fractures in e-scooter related accidents, likely due to a specific fall pattern in low height but high velocity vehicles, combined with intoxication with patients often not wearing a helmet. The typical fracture pattern suggests an impact predominantly on the lateral aspect of the skull.

O14

Towards Individual Treatment in Cervical Artery Dissection—An In-Depth Analysis of the TREAT-CAD Randomised Trial

JE Kaufmann [1], H Gensicke[1], S Schaedelin [2], AR Luft [3], B Goeggel-Simonetti [4], U Fischer [5], P Michel [6], D Strambo [6], G Kägi [7], J Vehoff [8], K Nedeltchev [9], T Kahles [10], L Kellert [11], S Rosenbaum [12], R von Rennenberg [13], C Riegler [13], D Seiffge [14], H Sarikaya [14], A Zietz [1], J Wischmann [15], A Polymeris [16], M Hänsel [17], C Globas [17], LH Bonati [18], A Brehm [19], GM De Marchis [20], N Peters [1], CH Nolte [21], H Christensen [12], S Wegener [17], M Psychogios [19], M Arnold [14], P Lyrer [16], C Traenka [1] and S Engelter [1]

[1] Department of Neurology and Stroke Center, University Hospital Basel and University of Basel, Switzerland and Neurology and Neurorehabilitation, University Department of Geriatric Medicine FELIX PLATTER, University of Basel, Basel Switzerland;
[2] Department of Clinical Research, Clinical Trial Unit, University Hospital Basel and University of Basel, Switzerland;
[3] Division of Vascular Neurology and Neurorehabilitation, Department of Neurology, University Hospital of Zurich, and University of Zurich, Switzerland and Cereneo, Center for Neurology and Rehabilitation, Vitznau, Switzerland;
[4] Department of Neurology, University Hospital Bern, University of Bern, Switzerland and Department of Neuropediatrics, Institute of Pediatrics of Southern Switzerland, San Giovanni Hospital, 6500 Bellinzona;
[5] Department of Neurology and Stroke Center, University Hospital Basel and University of Basel, Switzerland and Department of Neurology, University Hospital Bern, University of Bern, Switzerland;
[6] Stroke Center and Neurology Service, Department of Clinical Neurosciences, Centre Hospitalier Universitaire Vaudois and University of Lausanne, Switzerland;
[7] Department of Neurology, University Hospital Bern, University of Bern, Switzerland and Department of Neurology and Stroke Center, Cantonal Hospital St.Gallen, St.Gallen, Switzerland;
[8] Department of Neurology and Stroke Center, Cantonal Hospital St.Gallen, St.Gallen, Switzerland;
[9] Department of Neurology and Stroke Center, Cantonal Hospital Aarau, Aarau, Switzerland;
[10] Department of Neurology and Stroke Center, Cantonal Hospital Aarau, Aarau, Switzerland and University Basel, Basel, Switzerland;
[11] Department of Neurology, Ludwig Maximilian University (LMU), Munich, Germany and Institute for Stroke and Dementia Research (ISD), University Hospital, LMU Munich, Munich, Germany;
[12] Department of Neurology, Bispebjerg Hospital & University of Copenhagen, Copenhagen, Denmark;

[13] Department of Neurology with Experimental Neurology, Center for Stroke Research Berlin (CSB), Charite-Universitätsmedizin Berlin, Berlin, Germany;
[14] Department of Neurology, University Hospital Bern, University of Bern, Switzerland;
[15] Department of Neurology, Ludwig Maximilian University (LMU), Munich, Germany;
[16] Department of Neurology and Stroke Center, University Hospital Basel and University of Basel, Switzerland;
[17] Division of Vascular Neurology and Neurorehabilitation, Department of Neurology, University Hospital of Zurich, and University of Zurich, Switzerland;
[18] Department of Neurology and Stroke Center, University Hospital Basel and University of Basel, Switzerland and Research Department, Reha Rheinfelden, Rheinfelden, Switzerland;
[19] Department of Neuroradiology, Clinic of Radiology and Nuclear Medicine, University Hospital Basel, Basel, Switzerland;
[20] Department of Neurology and Stroke Center, University Hospital Basel and University of Basel, Switzerland and Department of Neurology and Stroke Center, Cantonal Hospital St.Gallen, St.Gallen, Switzerland;
[21] Department of Neurology with Experimental Neurology, Center for Stroke Research Berlin (CSB), Charite-Universitätsmedizin Berlin, Berlin, Germany and Berlin Institute of Healths at Charite, (BIH), Charite-Universitätsmedizin Berlin, Germany

Aims: Uncertainty remains about antithrombotic treatment in cervical artery dissection. This analysis aimed to explore if certain patient profiles influence the effects of different types of antithrombotic treatment.
Methods: This was a post-hoc exploratory analysis based on the per-protocol dataset from TREAT-CAD (NCT02046460), a randomised controlled trial comparing aspirin to anticoagulation in patients with cervical artery dissection. We explored the potential effects of distinct patient profiles on outcomes in participants treated with either aspirin or anticoagulation. Profiles included (i) presenting with ischemia (no/yes), (ii) occlusion of the dissected artery (no/yes), (iii) early versus delayed treatment start (</> median), and (iv) intracranial extension of the dissection (no/yes). Outcome included clinical (stroke, major haemorrhage, death) and MRI-outcomes (new ischemic or haemorrhagic brain lesions) and were assessed for each subgroup in separate logistic models, including a test for interaction.
Results: All 173 participants (100%) of the TREAT-CAD per-protocol dataset were eligible for analyses. Participants without occlusion (OR 0.28 [95% CI 0.07–0.86]), had fewer outcome events if treated with anticoagulation than with aspirin. This effect was particularly present in participants presenting with ischemia (n = 118) (OR 0.16 [95% CI 0.04–0.55]). Moreover, in participants presenting with ischemia, those with early treatment (OR 0.26 [95% CI 0.07–0.85]), and those without intracranial extension of the dissection (OR 0.34 [95% CI 0.11–0.97]) had less outcome events if treated with anticoagulation.
Conclusions: Whether anticoagulation is preferable in patients with cervical artery dissection presenting with ischemia and no occlusion or no intracranial extension of the dissection requires further research.

O15

Susceptibility Vessel Sign, a Predictor of Long-Term Outcome in Stroke Patients Treated with Mechanical Thrombectomy

M Beyeler [1], E Rea [1], L Weber [1], N Belachew [2], E Aleman [2], M Kielkopf [1], C Kurmann [3], L Grunder [3], E Piechowiak [3], T Meinel [1], M Heldner [1], D Seiffge [1], S Pilgram-Pastor [3], T Dobrocky [3], T Pabst [4], M Berger [4], S Jung [1], M Arnold [1], J Gralla [3], U Fischer [5], J Kaesmacher [3] and A Mujanovic [3]

[1] Department of Neurology, Inselspital, Bern University Hospital, and University of Bern, Switzerland;
[2] Department of Neuroradiology, Medical Center—University of Freiburg, Faculty of Medicine, University of Freiburg, Germany;

[3] Institute for Diagnostic and Interventional Neuroradiology, Inselspital, Bern University Hospital, and University of Bern, Switzerland;
[4] Department of Medical Oncology, Inselspital, Bern University Hospital, and University of Bern, Switzerland;
[5] Neurology Department, University Hospital of Basel, University of Basel, Basel, Switzerland

Background: The absence of the susceptibility vessel sign (SVS) in patients treated with mechanical thrombectomy (MT) is associated with poor radiological and clinical outcomes after 3 months. Underlying conditions, such as cancer, are assumed to influence SVS status and could potentially impact the long-term outcome. We aimed to assess SVS status as an independent predictor of long-term outcomes in MT-treated patients.
Methods: SVS status was retrospectively determined in consecutive MT-treated patients at a comprehensive stroke center between 2010 and 2018. Predictors of long-term mortality and poor functional outcome (modified Rankin Scale [mRS] $\geq$ 3) up to 8 years were identified using multivariable Cox and logistic regression, respectively.
Results: Of the 558 patients included, SVS was absent in 13% (n = 71) and present in 87% (n = 487) on baseline imaging. Patients without SVS were more likely to have active cancer (p = 0.003) and diabetes mellitus (p < 0.001) at the time of stroke. The median long-term follow-up time was 1058 days (interquartile range 533–1671 days). After adjustment for active cancer and diabetes mellitus, among others, the absence of SVS was associated with long-term mortality (adjusted hazard ratio [aHR] 2.11, 95% CI 1.35–3.29) and poor functional outcome in the long term (adjusted odds ratio [aOR] 2.90, 95% CI 1.29–6.55).
Conclusions: MT-treated patients without SVS have higher long-term mortality rates and poorer long-term functional outcome. It appears that this association cannot be explained by comorbidities alone, and further studies are warranted.

O16

Bilateral Staged MR-Guided Focused Ultrasound Thalamotomy for Essential Tremor Patients

S Mahendran, F Büchele, M Uhl, C Freudinger, MF Oertel, CR Baumann and LH Stieglitz

UniversitätsSpital Zürich, Switzerland

Objective: To evaluate the safety and efficacy outcomes of bilateral staged magnetic resonance guided focused ultrasound (MRgFUS) thalamotomy for medication-refractory essential tremor (ET) and ET plus one year after the second MRgFUS thalamotomy.
Background: Unilateral MRgFUS thalamotomy showed long-lasting therapeutic efficacy in medication-refractory ET with a reasonable safety profile. However, this unilateral treatment only improves contralateral tremor, and ipsilateral tremor in bilaterally affected ET patients continues to affect quality of life. To improve the quality of life of patients with severe bilateral tremor, bilateral thalamotomy is being considered. So far, only short-term results up to six months after the second thalamotomy with significant tremor improvement and without relevant permanent side effects have been described.
Methods: Data from patients with medication-refractory ET or ET plus who underwent bilateral MRgFUS thalamotomy at the University Hospital Zurich, Switzerland, were retrospectively collected. We describe the efficacy and safety outcomes one year after the second thalamotomy. Relative tremor improvement was defined as change in Whiget Tremor Rating Scale score from baseline to one year after the second thalamotomy. Safety outcomes were described as mild (no impact on quality of life), moderate (moderately disturbing) and severe (clear impact on quality of life), depending on the impact on quality of life.
Results: Fifteen patients underwent bilateral MRgFUS thalamotomy between January 2019 and February 2022. In most patients, the right side was treated first. The interval between the first and second thalamotomy was at least six months. The mean age of the patients was 66.8 $\pm$ 13.58 years at the time of the second thalamotomy. The mean skull density Ratio (SDR) was 0.49 $\pm$ 0.13. The mean Whiget score decreased by 53.25% ($\pm$25.82) from baseline to one year after the second thalamotomy. Three patients reported no adverse

events one year after the second thalamotomy, 7 patients reported mild adverse events, 4 patients moderate adverse events, and 1 patient severe adverse events.
Conclusions: Our results show that bilateral staged MRgFUS thalamotomy is feasible and that one year after the second thalamotomy, the tremor response persists and the safety profile is adequate. However, larger prospective studies are needed.

O17

VEGFR2-Specific CAR T Cells with Anti-Glioma and Anti-Angiogenic Activity against Glioblastoma

M Mastall [1], D Villars [1], M Silginer [1], C Rössig [2], T Weiss [1], M Weller [1] and P Roth [1]

[1] Department of Neurology, Clinical Neuroscience Center and Brain Tumor Center, University and University Hospital Zurich, Switzerland;
[2] University Hospital Münster, Germany

Aims: Chimeric antigen receptor (CAR) T cell therapy has emerged as a potent immunotherapy against hematological malignancies. In glioblastoma, however, limited infiltration of the tumor by CAR T cells, tumor heterogeneity, antigen escape and an immunosuppressive tumor microenvironment remain significant obstacles. Vessel-targeting CAR T cells have been shown to infiltrate solid tumors more efficiently and have the additional benefit of co-targeting the tumor vasculature. Therefore, vascular endothelial growth factor receptor 2 (VEGFR2)-CAR T cells may represent a promising strategy by targeting the tumor vasculature as well as VEGFR2-expressing tumor cells. Here, we explored the efficacy of VEGFR2-specific CAR T cells against experimental gliomas as well as the contribution of anti-tumor and anti-vasculature-dependent effects of this strategy.
Methods: Tissue microarrays of glioblastoma patients (n = 113) were stained for VEGFR2 expression. Human CAR T cells were generated by lentiviral transduction to express a second generation CAR construct against either mouse or human VEGFR2 (mVEGFR2 or hVEGFR2). Their activity was assessed in co-culture assays in vitro against murine endothelial and human glioma cells, respectively. Several orthotopic xenograft mouse glioma models were used to test the in vivo activity of the newly generated CAR T cells.
Results: We confirmed high VEGFR2 expression on endothelial cells in glioblastoma tissue of stained tissue microarrays as well as in 20.3% of tissue samples also on tumor cells. In co-culture assays, hVEGFR2-CAR T cells were exclusively active against human glioma cells and mVEGFR2-CAR T cells against mouse endothelial cells, respectively. In all three in vivo glioma models, intratumoral treatment of hVEGFR2-CAR T cells significantly prolonged the survival of glioma-bearing mice and cured a substantial fraction of these animals in one model. Additionally, we found that survival was prolonged after mVEGFR2-CAR T cell treatment in one glioma model, which correlated with high vascularization of these tumors.
Conclusions: Our dataset demonstrates that VEGFR2-CAR T cells prolong the survival of glioma-bearing mice through anti-glioma and anti-glioma vasculature activity. The results suggest that the magnitude of the vasculature-targeting activity depends on vessel-density within the tumor. VEGFR2 might be a relevant target that could be exploited for a novel CAR T cell-based immunotherapeutic approach against glioblastoma.

O18

Protein Fibril Aggregation on Red Blood Cells Studied Using Atomic Force Microscopy: A Potential Biomarker to Distinguish Neurodegenerative Diseases from Healthy Aging

T Schneider [1], L Stöckli [1], A Felbecker [1] and P Nirmalraj [2]

[1] Kantonsspital St. Gallen, Switzerland;
[2] Swiss Federal Laboratories for Materials Science and Technology, Department Materials meet Life, St Gallen, Switzerland

Neurodegenerative diseases like Alzheimer's disease (AD) are characterized by misfolded protein aggregation and fibril accumulation in the brain. Atomic force microscopy (AFM) is a nanoscale imaging technique that can be used to resolve and quantify protein aggregates from oligomers to fibrils. Recently, we showed that by using AFM it is possible to characterize protein fibrillar aggregates adsorbed on the surface of red blood cells (RBCs) from patients with neurocognitive disorders, which may serve as a potential AD biomarker. However, the age association of fibril deposits on red blood cells (RBCs) has not yet been studied in detail in healthy adults. Here, we used AFM to visualize and quantify fibril coverage on RBCs in 50 healthy adults and 37 memory clinic patients. Fibril deposits sporadically appeared in healthy individuals but were prevalent in patients with neurodegenerative disease, especially those with Alzheimer's as confirmed by positive cerebrospinal fluid Aβ 1–42/1–40 ratios. However, age showed no significant correlation with fibril prevalence in both healthy and Alzheimer's patients. The observed overlap in the fibril prevalence on RBCs between Alzheimer's and amyloid-negative neurodegenerative disease patients suggests fibril deposition on RBCs could occur in various neurodegenerative diseases. Quantification of protein fibril morphology and prevalance on RBCs could be a potential sensitive biomarker for neurodegeneration, differentiating patients with neurodegenerative diseases from healthy individuals. By combining AFM with infrared and Raman spectroscopy in future larger scale studies, we may further chemically characterize these fibrils, aiding in proteinopathy identification and establishing a comprehensive, non-invasive neurodegenerative disease biomarker platform.

O19

Novel Biosensor Cell Lines for the Specific Quantification of Tau Seeding Competency from Human Samples in Alzheimer's Disease

A Lathuilière [1], Y Jo [2], R Perbet [2], N Quittot [2], Z Fan [2] and BT Hyman [2]

[1] Geneva University Hospitals (HUG), Switzerland; Massachusetts General Hospital and Harvard Medical School, Boston, USA;
[2] Massachusetts General Hospital and Harvard Medical School, Boston, USA

Aims: The prion-like propagation of tau implies that some misfolded pathological tau can recruit the normal protein and template its aggregation. Several groups have demonstrated that the amount of seeding-competent tau species correlates with rate of disease progression in Alzheimer's disease (1, 2). Here, we aimed at developing ultrasensitive biosensor cell lines for the detection of tau seeding activity in human biofluids.
Methods: We performed the rational design of novel tau probes based on the current structural knowledge of pathological tau aggregates in AD. We generated Förster resonance energy transfer (FRET)-based biosensor stable cell lines and characterized their sensitivity, specificity, and overall ability to detect bioactive tau in human samples. We characterized the solubility and structure of the generated intracellular tau probe aggregates.
Results: As compared to the reference biosensor line, the optimized probe design resulted in an increased efficiency in the detection of tau seeding. The newly formed aggregates accumulated in the insoluble fraction and recapitulated some features of AD aggregates. The increased sensitivity allowed for the detection of tau seeding competency in human brain samples, while preserving specificity for tau.
Conclusions: This next generation of FRET-based biosensor cells can be used to quantify minute amount of tau seeds in human samples and opens to way to the detection of seeding capacity in biofluids such as lumbar cerebrospinal fluid. Since tau seeding activity correlates with rate of disease progression, the novel cell-based assay will be tested in the near future as a potential prognostic biomarker.

O20

Analysis of Visual Evoked Potentials in Cases of Unstable Electroretinograms

E Cochard [1], N Bérard [2], K Schaller [3] and C Boëx [3]

[1] Faculty of Medicine, "Université de Genève"; Department of Neurosurgery, "Hôpitaux Universitaires de Genève";
[2] Department of Neurosurgery, "Centre Hospitalier Universitaire Vaudois";
[3] Department of Neurosurgery, "Hôpitaux Universitaires de Genève"; Faculty of Medicine, "Université de Genève", Switzerland

Aims: The objectives of this study were to evaluate the validity of visual evoked potentials (VEPs) as a tool for detecting early alterations in visual pathways when the electroretinogram (ERG) is unstable; to compare the ERG obtained with white light emitting diodes (LEDs) versus red LEDs; and to assess the impact of stimulation on the stability of ERGs and the variability of VEPs.
Methods: This study was approved by the Geneva Ethics Committee for Human Research (CE 2022-00337). Thirty patients were included (Inomed neuromonitoring system, both preoperatively and postoperatively visual fields). VEPs were performed with flashes delivered at 1.1 Hz (60 repetitions; duration 10 ms). They were recorded from occipital electrodes (O1, O2, Cz as reference, both mastoids as ground).
The mean deviation of Goldmann perimetry was used to assess possible changes in the visual field (comparison of preoperative and postoperative visual fields in decibels).
The validity of VEPs was determined by calculating their sensitivity and specificity for alarm criteria ranging from 0% to 100% (receiver operating characteristic, ROC curve).
Results: VEPs and ERGs could be analyzed for 32 eyes in 20 patients (11 females, 9 males; 47.5 [33.5; 57.5] years), in cases of gliomas (8/20), meningiomas (6/20), metastasis (3/20), dysplasia (1/20), optic nerve schwannoma (1/20), clivus chordoma (1/20). With the surgery 1/20 patients had a severe deterioration of the visual field (−12 dB), and 7/20 a mild deterioration of the visual field [−5; −11 dB]. The normalization of VEPs amplitude by their baseline and the correction of VEPS by possible changes in ERG amplitude were found necessary for their interpretation. The ROC curve indicated an alarm threshold of 25% decrease in normalized and corrected VEPs amplitudes. Furthermore, it was observed that the spreading of the electric field could cause a decrease in contralateral VEPs regardless of the lesion site. There was no significant difference in the standard deviations of VEPs obtained with white or red LEDs. However, increased luminance had a significant impact on the stability of ERGs and of VEPs.
Conclusions: Normalization and correction of VEPs were found necessary when ERGs were instable. The alarm threshold was determined as a 25% decrease in normalized and corrected VEPs. This normalization and correction technic could be applied to others intraoperative modalities as the somatosensory evoked potentials for improving their specificity.

O21

Adaptor FITC CAR T-Cells and OCTO-FLUO Elicit Promising Antitumor Activity in Meningioma via SSTR2

J Chen [1], C Pellegrino [2], M Mastall [1], L Padevit [3], N Favalli [4], G Bassi [4], M Neidert [5], F Vasella [1], P Roth [1], P Roth [1], D Neri [4], M Manz [2], M Weller [1] and H Wirsching [1]

[1] Department of Neurology, University Hospital and University of Zurich, Zurich, Switzerland;
[2] Department of Medical Oncology and Hematology, University HospitalZurich and University of Zurich, Zürich, Switzerland;
[3] Department of Neurosurgery, Clinical Neuroscience Center, University Hospital andUniversity of Zurich, Zürich, Switzerland;
[4] Philochem AG, Otlfingen, Switzerland;
[5] Department of Neurosurgery, Cantonal Hospital St. Gallen, St.Gallen, Switzerland

Background: Effective treatment options for meningioma patients beyond surgical resection and radiotherapy are lacking. Somatostatin receptor (SSTR) 2 is expressed by most meningiomas. Here, we report pre-clinical and translational evidence for the activity of an SSTR2-targeted adaptor CAR T cell system in meningiomas.

Material and Methods: Tissue microarrays of meningioma ($n = 384$) patient samples stained for SSTR2. Fluorescein-linked, octameric cyclic peptide SSTR2 antagonist OCTO-FLUO (kindly provided by Philogen, Otelfingen, Switzerland). Adaptor FITC CAR T-cells generated by lentiviral transduction of healthy donor T-cells. Flow cytometry-based killing assays in vitro in SSTR2-expressing meningioma (Ben-Men-1 IOMM-Lee) cells, and ex vivo utilizing freshly dissociated surgical meningioma specimens, by co-incubation with OCTO-FLUO and adaptor FITC CAR T-cells. Orthotopic growth and mouse survival following subdural implantation of IOMM-Lee cells, genetically engineered to express luciferase, i.v. treated with OCTO-FLUO and intratumoral injection of CAR T-cells.
Results: SSTR2 expression was overall heterogeneous and was high or intermediate in most World Health Organization (WHO) grade 2 (87.8%) or grade 3 (87.5%) meningiomas. In vitro, 10 nM was determined as the optimal concentration of OCTO-FLUO, yielding tumor cell killing within 72 h at effector-target cell (ET) ratios as low as 1:100 in Ben-Men-1 (CAR vs. untransduced T-cells [UTT] 47.9% vs. 4.7%, $p < 0.001$) and IOMM-Lee (CAR vs. UTT 40.2% vs. 4.9%, $p < 0.001$) cells. Tumor growth inhibition by the adaptor FITC CAR T-cell system in vivo was confined to SSTR2expressing cells and was paralleled by prolonged survival compared to UTT in IOMM-Lee (hazard ratio [95% confidence interval], 0.3 [0.1–0.9], $p = 0.030$). Preliminary ex vivo killing assays employing freshly dissociated patient samples yielded specific lysis-rates in the range of 15–20% (ET1:1) at 12 h. Updated ex vivo results employing optimized protocols will be presented at the conference.
Conclusions: Targeting SSTR2 positive meningioma cells with an adaptor FITC CAR T-cell system is feasible. Syngeneic murine models and the use of adaptor molecules directed against murine SSTR2 will be required to explore secondary immune reactions and off-tumor effects prior to proceeding to early phase clinical trials.

O22

Neurophysiological Identification/Differentiation between the Dorsal and Anterior Roots in Pediatric Spinal Cord Lipoma Surgery

T Müller and K Lutz

Inselspital—Universitätsspital Bern, Switzerland

Introduction: Due to the complex anatomical conditions, surgical resection of spinal cord lipomas can be challenging. According to the literature, radical surgery is associated with a lower recurrence rate. Neurophysiological monitoring and mapping techniques may assist intraoperative decision making. Here we present a cohort of pediatric patients in whom mapping with the double-train paradigm was used to distinguish between anterior (motor neurons) and posterior (sensory neurons) roots.
Methods: Children (age 0–18 years) with spinal cord lipoma resection between January 2016 and January 2022 were included. For intra-operative distinction between anterior and posterior roots we used a newly developed double-train mapping paradigm with an inter-train interval of 60 ms. Given the longer recovery time due to the H-reflex a single muscle response was judged to be elicited from a sensory root, and a double muscle response from the motor root. The primary endpoint was postoperative outcome (neurological outcome and bladder function). Secondary endpoints were extent of resection, neurological outcome and bladder function one year postoperatively.
Results: We included 7 children with a median age of two years (7 months- 13 years) who underwent 8 lipoma resections. A double response for motor roots could be elicited in all surgeries and a single response for sensory roots in 80% of cases. All except one patient experienced bladder dysfunction prior to the surgical resection. Two patients presented with neuro-orthopedic issues, specifically clubfoot, and motor deficits. Three cases underwent gross total resection (GTR), two cases underwent near-total resection (NTR), and three cases underwent subtotal resection (STR). We did not observe any deterioration in sensory and motor function after the surgery, even after a 6-month follow-up period. However, one patient experienced worsening bladder dysfunction after re-tethering.

Conclusions: Intraoperative mapping with the double train paradigm may differentiate between anterior and posterior roots in pediatric lipoma surgery. Thus, technique may guide surgical resection during critical steps.

P01

Early-Onset Focal Epilepsy in Children—Resection in Accordance with Ecog or Lesion Guidance?

N Frank [1], L Greuter [1], R Guzman [2] and J Soleman [2]

[1] Universitätsspital Basel und Universität Basel;
[2] Universitätsspital Basel und Universitäts-Kinderspital beider Basel UKBB, Switzerland

Background: Epilepsy is the most common neurological disease in children and early-onset focal epilepsy is commonly associated with developmental brain lesions, such as long-term epilepsy-associated tumors (LEAT) and focal cortical dysplasia (FCD). If seizures remain intractable, surgery is warranted. Electrocorticography (ECoG) helps determine to extent of resection but remains controversial. We aim to analyze the value of ECoG during epilepsy surgery for structural lesions in pediatric patients.
Methods: We conducted a retrospective chart review of consecutive children treated at our institutions between 1 January 2015–30 June 2023. All patients received surgery with intraoperative ECoG recording. The primary outcome is seizure frequency. Secondary outcomes were reduction of postoperative antiepileptic drugs (AED), morbidity, and mortality.
Results: We included thirteen children with a mean age at surgery of 5.7 years (±4.2, range 0–14 years), 46% male. Histopathology presented 5 LEAT (WHO I) (38%), one embryonal tumor (not classified) (10%), five focal cortical dysplasia (38%) and two Sturge-Weber syndrome (15%).
The mean duration of seizures prior to surgery was 2.8 years (±2.7). Two patients (16%) suffered from generalized seizures, and 10 children from focal seizures (84%). The mean number of AED preoperatively was 2.3 (±1.1). At 24 months, two children (22%) were off antiepileptic medication, one child (11%) reduced the compounds by 1 AED, and all other children remained on AED but with reduced doses. 12 months follow-up was available for 5 children (38%), all improved to ILAE class 1. In 4 cases resection was terminated according to ECoG recording, with residual cortical foci on postoperative MRI. Both patients remained seizure-free. Two patients with FCD received an extended resection due to pathological intraoperative ECoG and were seizure-free afterward. No surgical morbidity or mortality occurred.
Conclusions: Based on our experience of pediatric patients undergoing resection of lesions causing AED refractory epilepsy, ECoG changed the course of surgery in 46% of the patients. Following surgery, AED treatment was reduced in all cases with a follow-up longer than 12 months. Similarly, in all cases, either seizure freedom or a significant reduction in seizure frequency was achieved. Although our cohort showed very satisfactory results using ECoG, comparative studies with larger cohorts are still needed to underly our results.

P02

COveRs to impRove EsthetiC ouTcome after Surgery for Chronic Subdural Hematoma by buRr Hole Trepanation (CORRECT-SCAR)—Results of a Swiss Single-Blinded, Randomized Controlled Trial

M Stienen [1], K Akeret [2], F Vasella [2], J Velz [2], E Jehli [3], S Voglis [2], O Bichsel [2], NR Smoll [4], O Bozinov [5], L Regli [2] and M Germans [2]

[1] Kantonsspital St. Gallen, Switzerland;
[2] Department of Neurosurgery, University Hospital Zurich, Clinical Neuroscience Center, University of Zurich, Zurich, Switzerland;

[3] Translational Research Center, University Hospital of Psychiatry and Psychotherapy, University of Bern, Bern, Switzerland;
[4] School of Population and Global Health, University of Melbourne, Melbourne, Australia;
[5] Department of Neurosurgery, Kantonsspital St.Gallen, St.Gallen, Switzerland

Aims: Burr hole trepanation to evacuate chronic subdural hematoma (cSDH) results in bony skull defects that can lead to esthetically unsatisfactory skin depressions. The effect of titanium burr hole covers to prevent skin depressions and its influence on the esthetic result of the scar is not well studied.
Methods: We conducted a single-center, randomized trial in Zurich, Switzerland that enrolled adult patients with symptomatic cSDH. The patients were randomly assigned in a 1:1 ratio to receive burr hole trepanation with (intervention) vs. without titanium burr hole covers (control). Patients requiring evacuation of bilateral cSDHs served as their internal control, as burr hole covers were placed on one side only. The primary outcome was the satisfaction with the esthetic result of the scar, measured from 0 (dissatisfied)–10 (very satisfied) on the Aesthetic Numeric Analogue (ANA) scale at 90 days postoperative. Secondary outcomes included ANA scale, rates of skin depression, complications, as well as neurological, disability and health-related quality of life (hrQoL) outcomes until 12 months postoperative.
Results: From March 2019 through May 2021 a total of 78 patients (55 with unilateral and 23 with bilateral cSDH) were included—resulting in 50 trepanations for the intervention and 51 trepanations for the control group. There were no group differences at baseline. The median age was 78 years and 83% were male. In an intention-to-treat analysis, the ANA scale score was 9.0 in the intervention and 8.5 in the control arm at 90 days ($p = 0.498$). At 12 months, the ANA scale scores were 9.0 and 8.0 for the intervention and control group, respectively ($p = 0.183$). Skin depressions over the frontal burr hole were noted by 35% (intervention) and 63% (control) of patients at 90 days ($p = 0.009$), and by 35% and 79% ($p < 0.001$) at 12 months, respectively. There were no differences in complications, neurological, disability and hrQoL outcomes.
Conclusions: Satisfaction with the esthetic result of the scar among patients with cSDH undergoing burr hole trepanation is inherently high. This study does not show evidence for improvement on the ANA scale by applying a burr hole cover. The application of burr hole covers resulted in less skin depressions over the burr holes and did not negatively impact complication rates or outcomes.
Trial registration: ClinicalTrials.gov identifier: NCT03755349.

P03

Resection of Low-Grade Gliomas in the Face Area of the Primary Motor Cortex and Neurological Outcome

K Lutz, L Häni, C Kissling, A Raabe, P Schucht and K Seidel

Inselspital-Universitätsspital Bern, Universitätsklinik für Neurochirurgie, Switzerland

Objective: During surgery on low-grade gliomas (LGG), reliable data relevant to the primary motor cortex (M1) for the face area are lacking. We analyzed the impact of tumor removal within the M1 face area on neurological deficits.
Methods: We included LGG patients with resection within the M1 face area between May 2012 and November 2019. The primary endpoint was postoperative facial motor function. Secondary endpoints were postoperative aphasia, dysarthria, and dysphagia. Surgery was performed either with the awake protocol or under anesthesia with continuous dynamic mapping. The alarm criteria were speech arrest or a mapping threshold of 3 mA or less. Resection was completed in five patients. The resection was stopped due to the alarm criteria in three patients and for other reasons (vascular supply, patient performance) in four patients. A total of 66.7% ($n = 8$) presented with new-onset facial paresis (62.5% left LGG) and 41.7% ($n = 5$) with aphasia (all left LGG) postoperatively. After one year, all

eight patients had recovered from the facial paresis. Tumor removal within the M1 face area was not associated with permanent facial motor deficits.

P04

Mastoid Size Does Not Affect Clinical Outcomes after Translabyrinthine Resection of Large Vestibular Schwannomas

D Croci, A Tai, J Kim, R Mhaskar, C Danner, K Boyev, H Van Loveren and S Agazzi

University of Southern Florida, Tampa, FL, USA

Introduction: The translabyrinthine (TL) approach is frequently used for vestibular schwannomas (VS) especially in patients without serviceable hearing. There is a concern that this approach is limited with contracted mastoids, high jugular bulbs and when resecting large VSs.
Objective: To determine if the size of the mastoid corridor influences facial nerve outcomes (FNO) or degree of resection (DOR) for TL VS surgery.
Methods: 99 patients with VSs > 15 mm who underwent TL approach for their VS from 2015 to 2022 were included in this retrospective study. Preoperative MR imaging was used to measure the size of the mastoid corridor, the anterior-posterior distance between the intercochlear line and sigmoid sinus, and the height of the jugular bulb (JB), distance between the internal auditory canal and the JB. Patient medical records were queried for complications, FNO and to determine the DOR.
Results: The mean size of the mastoid corridor in our study was 20.6 mm (SD 2.9 mm) and the mean JB height was 6.2 mm (SD 2.7 mm). There was no significant correlation between FNO or DOR with the mastoid corridor size or JB height. Even for tumors larger than 30 mm, the size of the mastoid corridor or height of the jugular bulb did not correlate with worse outcomes. There was no significant association between complications and mastoid corridor size or JB height.
Conclusions: We did not find that the size of the mastoid corridor or JB height were associated with FNO, DOR or complications in TL resection of large VSs. This study also defines what is considered a "small" mastoid corridor and a "high" JB for a TL approach in a surgical series.

P05

Early Minimally Invasive Image-Guided eNdoscopic Evacuation of iNTracerebral Haemorrhage: A Pilot Trial (EMINENT-ICH Pilot Trial)

TJ Hallenberger[1], L Bonati[2], U Fischer[1], R Guzman[1] and J Soleman[1]

[1] Universitätsspital Basel, Switzerland;
[2] Rehabilitationsklinik Rheinfelden, Switzerland

Background: Spontaneous supratentorial intracerebral haemorrhage (SSICH) is the most devastating form of stroke with mortality rates over 50%. Currently, no sufficiently effective treatment is available. Endoscopic surgery (ES) seems to improve survival and functional outcome rates. We present results of our pilot trial assessing feasibility and safety of ES for SSICH. Further, functional outcome and mortality rates will be presented.
Methods: Patients at the University Hospital Basel with a hematoma volume between 20 mL and 100 mL between July 2021 and January 2023 were enrolled. Endoscopic evacuation was performed within 24 hours after bleeding onset. Co-primary outcomes were (1) good functional outcome, defined as mRS $\leq$ 3 at 6 months and (2) adequate hematoma removal to below 15 mL. Secondary outcomes were mortality and morbidity rates. Patients were followed up over 6 months including clinical assessment, imaging and laboratory studies.
Results: Ten Patients (median age 72.5 years [IQR 68.25–79.75], 70% male) were enrolled. Favourable outcome after 6 months was achieved in 83% (5/6) of the patients with completed follow-up while favourable outcome at the last registered visit was achieved in 70% (7/10). Satisfactory hematoma evacuation was achieved in 70% (7/10) with a median evac-

uation percentage of 69.5% [IQR 60–93%]. Two patients (20%) died from pneumonia and re-bleeding respectively while one patient died due to a glioblastoma. Four patients experienced a total of five complications, one re-bleeding, three pneumonias and one seizure. The median duration of surgery was 92 minutes [IQR 78–108].
Conclusions: ES seems feasible, safe and leads to improved favourable outcome. Adequate hematoma removal is achievable and a steep learning curve is observed. Based on this pilot trial a national multicentre RCT comparing ES to best medical treatment is planned (NCT05681988).

P06

Recurrent Stroke in Symptomatic Steno-Occlusive Disease: Identifying Patients at High-Risk Using Impaired BOLD Cerebrovascular Reactivity

M Sebök[1], B van Niftrik[2], M Germans[2], A Luft[2], Z Kulcsar[2] and L Regli[2]

[1] UniversitätsSpital & Universität Zürich;
[2] Universitäts Spital Zürich, Switzerland

Background: Patients with symptomatic cerebrovascular steno-occlusive disease (SOD) harbor a high risk for recurrent ischemic stroke. For a patient specific risk assessment, blood oxygenation-level dependent cerebrovascular reactivity (BOLD-CVR) may provide additional information about severity and spatial location of cerebrovascular reserve impairment at brain tissue level. We assessed the association between impaired BOLD-CVR and risk for recurrent ischemic events. Furthermore, we hypothesized that brain areas exhibiting paradoxical—i.e., steal phenomenon—BOLD-CVR are spatially associated with recurrent acute ischemic events.
Methods: Patients with symptomatic SOD who had undergone a standardized BOLD-CVR as part of initial stroke work-up and at least one clinical follow-up MRI with diffusion-weighted images (DWI) sequence were included. Regions with BOLD-CVR below minus 2 standard deviations of a healthy cohort were introduced as severely impaired. The voxel-wise spatial agreement of steal phenomenon with recurrent DWI lesions was calculated. Using a multivariate Cox proportional hazards model, the association between impaired BOLD-CVR and ischemic stroke recurrence was assessed. Kaplan-Meier survival analysis and Cox proportional hazard model were used to assess the association between steal volume and ischemic stroke recurrence.
Results: 130 patients were included. Of these, 28 had recurrent stroke. After adjustment for sex, age, history of atrial fibrillation and hypertension, reduced CVR showed a hazard ratio of 11.71 (4.38–29.76, $p < 0.001$) for recurrent ischemic stroke. Using a voxel-wise spatial agreement, 80.31% of recurrent ischemic lesions lied within voxels exhibiting steal phenomenon (i.e., paradoxical BOLD-CVR response). Patients with steal volume >73 mL had 6.40 higher hazard ratio to suffer a recurrent acute ischemic stroke.
Conclusions: In patients with symptomatic SOD, those with impaired BOLD-CVR in the affected hemisphere had an 11.71-fold increased risk for recurrent ischemic stroke events compared to those with non-impaired BOLD-CVR. Furthermore, brain areas exhibiting steal phenomenon are spatially associated with recurrent acute ischemic events.

P07

Perioperative Continuation or Ultra-Early Resumption of Antithrombotics in Elective Neurosurgical Cranial Procedures

J Rychen, V Weiger, F Halbeisen, F Ebel, M Ullmann, L Mariani, R Guzman and J Soleman

Universitätsspital Basel, Switzerland

Objective: Discontinuation of antithrombotics (AT) prior to elective cranial procedures is common practice, despite the higher risk of thromboembolic complications in these patients. The aim of this study is to investigate the risks and benefits of a newly established

perioperative management protocol of continuation or ultra-early resumption of AT in elective cranial procedures.
Methods: This study is an analysis of a prospectively collected database of patients undergoing elective cranial surgery with and without AT (AT-Group versus Control-Group). For extra-axial or shunt surgeries, Aspirin (ASA) was continued during the perioperative period. For intra-axial pathologies, ASA was discontinued 2 days before surgery and resumed on postoperative day (POD) 3. All other AT were discontinued according to their own pharmacokinetics, and resumed on POD3 after unremarkable postoperative imaging. Additionally, we performed a retrospective analysis of patients with AT who underwent surgery before implementation of this newly established perioperative AT management protocol (Historical AT-Group). Primary and secondary outcomes were the incidence of hemorrhagic and thromboembolic complications within 3 months after surgery.
Results: Outcomes of 312 patients were analyzed (26.6% in the AT-Group, 34% in the Control-Group and 39.4% in the Historical AT-Group). For all 3 patient groups, the most common type of surgery was craniotomy for intra-axial tumors (16.9% in the AT-Group, 26.4% in the Control-Group and 48.8% in the Historical AT-Group). The most common used AT were ASA (45.8% in the AT- and 63.4% in the Historical AT-Group), followed by NOACs (38.6% in the AT- and 14.6% in the Historical AT-Group). The total perioperative discontinuation time in the AT-Group was significantly shorter than in the Historical AT-Group (median of 4 vs.16 days; $p < 0.001$). The rate of hemorrhagic complications was 3.6% (95% CI 0.8–10.2) in the AT-Group, 5.7% (95% CI 2.1–12) in the Control-Group and 7.3% (95% CI 3.4–13.4) in the Historical AT-Group ($p = 0.5$). The rate of thromboembolic complications was 4.9% (95% CI 1.3–12) in the AT-Group, 7.7% (95% CI 3.4–14.6) in the Control-Group and 6.7% (95% CI 2.9–12.7) in the Historical AT-Group ($p = 0.7$).
Conclusions: The presented perioperative management protocol of continuation or ultra-early resumption of AT in elective cranial procedures appears to be safe. Moreover, it seems to protect patients from thromboembolic complications.

P08

Rickham Reservoir Placement after Transcranial Endoscopic Sur

N Poletti, F Ebel and J Soleman

USB Basel and University of Basel, Switzerland

Transcranial endoscopy is nowadays a common and safe procedure in neurosurgery. Once the main part of the surgery is done there is the option to put a Rickham or Ommaya Reservoir. The main benefit of doing so is the easy access to CSF in case of a postoperative complication. Intracranial pressure can be measured indirectly, if necessary, CSF can be drained. If eventually a ventriculoperitoneal shunt is needed, it can be connected directly to the Reservoir. It can also be used to keep a cyst or stomy connected to the ventricles. As it is a foreign body there is the concern of increased infection rates. To date there are no guidelines when to leave a CSF access device after an endoscopy procedure and literature is scarce. The aim of this study is to better understand when Rickham placement is indicated.
Methods: We retrospectively reviewed all transcranial endoscopic surgeries of University Hospital Basel and Childrens University Hospital Basel from January 2010 until June 2020. We then went through medical records of the cases where a Rickham has been placed and checked how many times it has been accessed, for what reason and what additional surgeries have been performed. Results were then compared to the cases where no Rickham has been placed.
Results: 132 patients did undergo transcranial endoscopic surgeries, 85 adult patients and 47 pediatric patients. A Rickham Reservoir has been placed in 20 adult patients (24%) and 10 pediatric patients (21%). The indication for surgery in these cases was very heterogenous. In most cases reviewed there is no distinct reason mentioned why a Rickham Reservoir has been placed. The Reservoir has been accessed in 10 patients (33%). In two cases it led to the decision not to do another intervention because pressure was normal.

In one case the Reservoir was used for intrathecal chemotherapy. In three cases a shunt was connected to the previously inserted Rickham. There were three confirmed infections. 8 patients eventually did get a ventriculoperitoneal shunt surgery. Compared to the patients where no Reservoir has been placed there were no significant differences neither concerning the indication nor the postoperative infection rate or shunting rate.
Conclusions: Based on our study it seems safe to place a Rickham and in some cases it might be indicated. Further investigation is needed to create guidelines on when to place a CSF access device after endoscopy.

P09

Management of External Ventricular Drain: To Wean or Not to Wean?

TJ Hallenberger, T Tharmagulasingam, M Licci, L Mariani, R Guzman and J Soleman

Universitätsspital Basel, Switzerland

Objective. External ventricular drain (EVD) is one of the most frequent procedures in neurosurgery. However, EVD is only a temporizing measurement that should be removed as soon as possible to avoid complications. In around 15 to 30% of the cases, the patients require a permanent cerebrospinal fluid (CSF) diversion, usually in form of a ventriculoperitoneal shunt (VPS). Despite this, the optimal EVD weaning strategy is still unclear. Whether gradual EVD weaning, as opposed to rapid EVD closure, reduces the rate of permanent CSF diversion remains controversial. The aim of this trial is to compare the rates of permanent CSF diversion (i.e., VPS) after gradual weaning and rapid closure of an EVD.
Methods. A single-center, retrospective analysis of patients treated with EVD at the University Hospital of Basel between 2010 and 2020. Based on the management regimen, the patients were divided into two groups: weaning group (WG) and non-weaning group (NWG). Baseline characteristics were retrospectively collected from the electronic patient file and compared between the groups. The primary endpoint was the need for permanent CSF diversion in form of a VPS. Secondary endpoints included hospitalization time, discharge location, EVD-related morbidity, and clinical outcome at discharge.
Results. Out of 412 patients, 123 (29.9%) patients were excluded due to early death or palliative treatment. We registered 178 (61.6%) patients in the WG and 111 (38.4%) in the NWG. Baseline characteristics were well-matched between the two groups. The VPS rate was comparable in both groups (NWG 37.8% and WG 39.9%, $p = 0.728$). EVD related infection rate (13.5% vs. 1.8%, $p < 0.001$), as well as non-EVD related infection rate (2.8% vs. 0%, $p < 0.001$), were significantly higher in the WG. Hospitalization time was significantly shorter in the NWG compared to the WG (WG 24.93 $\pm$ 9.50 days and NWG 23.66 $\pm$ 14.51 days, $p = 0.039$).
Conclusion. Gradual EVD weaning does not seem to reduce the need for permanent CSF diversion, while infection rates were significantly higher and hospitalization time significantly longer. Therefore, direct closure should be considered in the clinical setting.

P10

Systematic Review and Meta-Analysis of The Diagnostic Accuracy of Spontaneous Nystagmus Patterns in Acute Vestibular Syndrome

M Wüthrich [1], Z Wang [2], C Martinez [3], S Carmona [4], G Mantokoudis [5] and AA Tarnutzer [6]

[1] University of Zurich, Zurich, Switzerland;
[2] Johns Hopkins University School of Medicine, Baltimore, USA;
[3] Hospital Jose Maria Cullen, Santa Fe, Argentinia;
[4] Fundación San Lucas para la Neurociencia, Santa Fe, Argentinia;
[5] Bern University Hospital, Switzerland;
[6] Kantonsspital Baden AG, Switzerland

Aims: For the assessment of patients presenting with acute prolonged vertigo meeting diagnostic criteria for acute vestibular syndrome (AVS), bedside oculomotor examinations are essential to distinguish peripheral from central causes. Here we assessed patterns of spontaneous nystagmus (SN) observed in AVS and its diagnostic accuracy at the bedside.
Methods: MEDLINE and Embase were searched for studies (1980–2022) reporting on the bedside diagnostic accuracy of SN-patterns in AVS patients. Two independent reviewers determined inclusion. We identified 4186 unique citations, examined 219 full manuscripts, and analyzed 39 studies. Studies were rated on risk of bias (QUADAS2). Diagnostic data were extracted and SN beating-direction patterns were correlated with lesion locations and lateralization.
Results: Included studies reported on 1603 patients, with ischemic strokes (n = 748) and acute unilateral vestibulopathy (n = 712) being most frequent. While a horizontal or horizontal-torsional SN was significantly more often found in peripheral AVS (pAVS) than in central AVS (cAVS) patients (777/816 [95.2%] vs. 339/779 [43.5%], $p < 0.001$), torsional and/or vertical SN-patterns were more prevalent in cAVS than in pAVS (14.8% vs. 2.5%, $p < 0.001$). For an (isolated) vertical/vertical-torsional SN or an isolated torsional SN specificity (97.8% [95% CI = 95.6–100.0%]) for a central origin etiology was high, whereas sensitivity (18.7% [10.7–26.6%]) was low. Absence of any horizontal SN was more frequently observed in cAVS than in pAVS (55.2% vs. 5.9%, $p < 0.001$). Ipsilesional and contralesional beating directions of horizontal SN in cAVS were found at similar frequency (15.8% vs. 13.1%, $p = 0.12$), whereas for pAVS a contralesional SN was significantly more frequent (92.5% vs. 2.5%, $p < 0.001$). For PICA strokes presenting with horizontal SN, beating direction was ipsilesional more often than contralesional (25.4% vs. 10.2%, $p = 0.02$), while the opposite was observed for AICA strokes (2.0% vs. 62.7%, $p < 0.001$).
Conclusions: (Isolated) vertical and/or torsional SN is found in a minority (14.8%) of cAVS patients only. When present, it is highly predictive for a central cause. A combined torsional-downbeating SN-pattern may be observed in pAVS also in cases with isolated lesions of the inferior branch of the vestibular nerve. Furthermore, in cAVS patients the SN beating direction itself does not allow a prediction on the lesion side.

P11

Spatial Synchronization of Subthalamic Nucleus Beta Activity in Parkinson's Disease

L Alva [1], A Averna [1], A Nowacki [2], K Peterman [1], E Bernasconi [1], I Debove [1], M Sousa [1], ML Lachenmayer [1], TK Nguyen [3], P Krack [1], C Pollo [2] and G Tinkhauser [1]

[1] Department of Neurology, Bern University Hospital and University of Bern, Bern, Switzerland;
[2] Department of Neurosurgery, Bern University Hospital and University of Bern, Bern, Switzerland;
[3] ARTORG Center for Biomedical Engineering Research, University of Bern, Bern, Switzerland

Aims: Subthalamic nucleus (STN) beta activity (13–30 Hz) is pathologically elevated in patients with Parkinson's disease (PD). The beta amplitude distribution across stimulation contacts can be used to inform about the symptom state and optimal site of chronic deep brain stimulation (DBS). Amplitude measures may however suffer technical limitations and do not inform about the oscillatory temporal dynamics within the anatomical structure. The aim of this work is to characterize the temporo-spatial synchronisation of STN beta activity as amplitude-independent metric and proxy of the STN oscillopathy.
Methods: Local field potentials (LFPs) were recorded from 70 PD patients (130 hemispheres) awake and at rest using multicontact DBS electrodes. The degree of beta activity synchronization was estimated using wavelet coherence analyses between all possible contact combinations within hemispheres. The mean level and variance of coherence across all contact combinations in each hemisphere, as well as their Euclidean distance were computed.

Result: The mean coherence analyses between all possible contact pairs, including ring and segmented contacts, show a bimodal distribution of coherence within the STN. The variance of beta synchronisation is patient-specific, ranging from very spread patterns involving large regions of the STN to rather spatially refined synchronisation states within the STN.
Conclusions: Our work demonstrates a non-uniform degree and spatial extent of synchronisation within the STN in PD patients. These neurophysiological metrics can further elucidate upon the degree of disease pathology and may help inform next generation, neurophysiology guided-DBS technologies for more individualized therapy regimes.

P12

Protein Fibril Length in Cerebrospinal Fluid Is Increased in Alzheimer's Disease

P Nirmalraj [1], T Schneider [2] and A Felbecker [3]

[1] Empa, Dübendorf;
[2] Kantonsspital St. Gallen, Department of Neurology;
[3] Kantonsspital St. Gallen, Switzerland

Alzheimer's disease (AD) associated proteins exist in cerebrospinal fluid (CSF). This paper evidences that protein aggregate morphology distinctly differs in CSF of patients with AD dementia (ADD), mild cognitive impairment due to AD (MCI AD), with subjective cognitive decline without amyloid pathology (SCD) and with non-AD MCI using liquid-based atomic force microscopy (AFM). Spherical-shaped particles and nodular-shaped protofibrils were present in the CSF of SCD patients, whereas CSF of ADD patients abundantly contained elongated mature fibrils. Quantitative analysis of AFM topographs confirms fibril length is higher in CSF of ADD than in MCI AD and lowest in SCD and non-AD dementia patients. CSF fibril length is inversely correlated with CSF amyloid beta (Aβ) 42/40 ratio and CSF p-tau protein levels (obtained from biochemical assays) to predict amyloid and tau pathology with an accuracy of 94% and 82%, respectively, thus identifying ultralong protein fibrils in CSF as a possible signature of AD pathology.

P13

Increased Central Obesity and Decreased Physical Activity in Persons with Multiple Sclerosis—Should We Prioritize a Healthier Lifestyle in Multiple Sclerosis?

G Thévoz [1], NE Phillips [2], J Rebeaud [1], A Revaz [1], A Gauthier-Jaques [1], P Lim-Dubois-Ferrière [1], M Théaudin [1], R Du Pasquier [1], S Panda [3], T Collet [4] and C Pot [1]

[1] Division of Neurology, Department of Clinical Neurosciences, Lausanne University Hospital (CHUV) and University of Lausanne, Rue du Bugnon 46, 1011 Lausanne, Switzerland;
[2] 1. Division of Neurology, Department of Clinical Neurosciences, Lausanne University Hospital (CHUV) and University of Lausanne, Rue du Bugnon 46, 1011 Lausanne, Switzerland. 2. Service of Endocrinology, Diabetology, Nutrition and Therapeutic Education, HU;
[3] Salk Institute for Biological Studies, La Jolla, CA 92037, USA.;
[4] 1. Service of Endocrinology, Diabetology, Nutrition and Therapeutic Education, Geneva University Hospitals (HUG), Rue Gabrielle-Perret-Gentil 4, 1211 Geneva 14, Switzerland, 2. Diabetes Centre, Faculty of Medicine, University of Geneva, Rue Michel-Servet, Switzerland

Aims: Environmental and lifestyle factors are associated with an increased risk of multiple sclerosis (MS). The metabolic syndrome (MetS) and its components have been proposed to influence MS disease course. We thus compared metabolic and lifestyle parameters between persons with MS (PwMS) and controls.
Methods: PwMS were prospectively recruited within the Lausanne MS Cohort and controls into SwissChronoFood cohort with the same inclusion and exclusion criteria. We matched PwMS and controls with a 1:2 ratio by sex, age, and body mass index (BMI).

We compared anthropometrics, laboratory, and lifestyle parameters. Eating events were recorded with a smartphone application over 4 weeks.
Results: We included 53 PwMS and 106 controls with a median age of 35 years (IQR 29–43). PwMS had low Expanded Disability Status Scale (EDSS, median 1.5). Waist-to-hip ratio (WHR) was increased in PwMS vs. controls (median 0.91, IQR 0.87–0.94 vs. 0.83, IQR 0.79–0.89, resp., $p < 0.001$). Eating duration was shorter in PwMS vs. controls (median 14h12, IQR 12h44–14h47 vs. 14h37, IQR 13h50–15h33, resp., $p = 0.01$) and physical activity was reduced (1058 METs/min/week, IQR 537–1992 vs. 1399.5, IQR 861–2804, resp., $p = 0.03$). We used lifestyle factors, age, and sex to predict central obesity and compared two models to predict their values. The positive lifestyle factors associated with the control of central obesity included: the percentage of unprocessed or minimally processed foods, vigorous activity, moderate activity, and walking. The negative contributors to central obesity included: the percentage of ultra-processed foods and a sleep duration different from 7.5 h.
Conclusions: Although both groups were matched by age, sex, and BMI, we found increased central obesity in PwMS vs. controls. PwMS, even minimally impaired with low EDSS, practiced less physical activity and had a shorter eating duration. Having identified differences in central obesity between the pwMS and control groups, we then used smartphone data and multivariate modelling to show that physical activity and a diet rich in unprocessed foods were associated with a better control of central obesity. This suggests that a healthy lifestyle and metabolic parameters should be targeted in MS clinical care and highlights the need of lifestyle measures for the promotion of better brain health.

P14

Effects of Music Therapy with a "Monochord" on Anxiety, Pain and Body Perception in Patients with Multiple Sclerosis

J Kuhlmann [1], KA Ebner [1], N Rommers [2], N Cerdá Fuertes [1], B Fischer-Barnicol [1], L Dinsenbacher [3], A Zimmer [4], K Parmar [5], J Kuhle [1], L Kappos [4] and A Papadopoulou [1]

[1] Multiple Sclerosis Centre, Neurology, Departments of Head, Spine and Neuromedicine, Biomedicine and Clinical Research, University Hospital Basel and University of Basel;
[2] Department of Clinical Research, Basel University;
[3] Neurostatus AG, University Hospital Basel;
[4] Research Center for Clinical Neuroimmunology and Neuroscience (RC2NB) Basel, University Hospital Basel and University of Basel, Switzerland;
[5] Rehabilitationsklinik Rheinfelden, Neurorehabilitation, Switzerland

Introduction: Prior studies with Music therapy (MT) in Multiple Sclerosis (MS) were typically performed at an in-patient setting and were uncontrolled or too small to detect a significant therapeutic effect.
Aim: To investigate the effect of ambulatory MT on anxiety (primary end-point), as well as depression, fatigue, health-related quality of life, body perception and pain thresholds (secondary outcomes) in a randomized-controlled study design.
Methods: We included 57 patients from our MS center (age: 50.1 $\pm$ 12.4 years, sex: 47 women, disease course: 46 relapsing-remitting, median Expanded Disability Status Scale (EDSS) 3.0 (1.0–6.5), disease modifying treatment: 53). Patients were randomized 1:1 to two groups: 30 to the MT group (MTG) and 27 to the control group (CG). Patients in the MTG had six weekly sessions of MT, relaxing on top of the "monochord" instrument and perceiving its music played by the therapist, while patients in the CG had the same number of sessions (lying on the "monochord"), without music. A blinded rater assessed the endpoints with standardised questionnaires (Hospital Anxiety and Depression Scale, HADS; Modified Fatigue impact scale, MFIS; Short Form 36, SF36) and quantitative sensory testing (QST), examining pain thresholds (thermal-, mechanical- and pressure pain). Assessments took place at study baseline and after the last session. Additionally, effects on body

perception were obtained by a non-validated questionnaire before and after each session (Questionnaires: Q A&B). Data was analysed using linear mixed models.
Results: The primary outcome, anxiety ($p = 0.109$) and depressive symptoms ($p = 0.667$) did not differ between the two groups after six weeks. However in the MTG, the psychosocial aspect of fatigue (MFIS) was significantly reduced ($p = 0.029$). The threshold for heat pain was significantly higher in the MTG at end-of-study ($p = 0.024$). Immediate effects of each session on body perception (Q A&B) were in favour of the MTG group (feeling relaxed: $p < 0.001$, balanced: $p < 0.001$, in touch with their body: $p < 0.001$ as well as less pain: $p < 0.001$).
Conclusions: In this controlled, rater-blinded trial we observed high adherence and positive effects on fatigue, pain and body perception, compared to relaxation alone. No significant group differences were shown in anxiety and depressive symptoms. Overall, MT with a "monochord" expands the non-pharmacological therapeutic options for people with MS in an outpatient settting.

P15

COVID-19 Infections and Vaccinations in the Swiss MS Cohort Study

V Epple [1], L Demuth [1], L Develioglu [1], A Orleth [1], S Subramaniam [1], S Schädelin [1], P Benkert [1], A Frentzel [1], M Kaech [1], N Sanderson [1], K Ivanek [1], L Kappos [1], J Oechtering [1], L Achtnichts [2], J Saxer [2], C Pot [3], P Lim Dubois-Ferrière [3], PH Lalive [4], G Breville [4], C Bridel [4], C Gobbi [5], C Zecca [5], G Disanto [5], S Müller [6], A Salmen [7], T Derfuss [1], CT Berger [1], R Pedotti [8], C Raposo [8], K Leuzinger [1], HH Hirsch [1], C Granziera [1], J Kuhle [1] and M Mehling [1]

[1] Universitätsspital Basel;
[2] Kantonsspital Aarau;
[3] Centre Hospitalier Universitaire Vaudois;
[4] Hôpitaux Universitaires de Genève;
[5] Ospedale regionale di Lugano;
[6] Kantonsspital St. Gallen;
[7] Inselspital Bern;
[8] F. Hoffman-La Roche Ltd., Basel, Switzerland

Aims: Patients with multiple sclerosis (pwMS) are at higher risk for severe courses of COVID-19 attributable to various factors, including higher Expanded Disability Status Scale (EDSS) score, comorbidities and B-cell-depleting therapies (1). The impact of the SARS-CoV-2 pandemic with high rates of infections and vaccinations on MS disease course is less studied. This study characterizes a well-defined and prospectively followed cohort of pwMS during the SARS-CoV-2 pandemic in Switzerland.
Methods: Within the Swiss MS Cohort, a nationwide multicenter study, data on SARS-CoV-2 infections and vaccinations were collected with questionnaires between February 2021 and January 2023. PwMS who were enrolled in the Swiss MS Cohort before the start of the pandemic in Switzerland on 25 February 2020 with at least one completed questionnaire thereafter were included in this study. The cumulative incidence of SARS-CoV-2 infections and vaccinations was calculated using Kaplan-Meier estimates. The severity of COVID-19 was graded according to the WHO scale (2). The cumulative probability of confirmed disability worsening (CDW, 3) and the relapse rate were monitored until May 2022.
Results: 924 pwMS (median age 47 years, 608 females, median EDSS 2.5) were included. 114 (12%) pwMS had a progressive disease course. 813 (88%) were treated with a disease modifying therapy. Treatment remained stable in the majority of pwMS. Median time intervals between infusions in pwMS treated with B-cell-depleting therapies were significantly longer in 2020–2022 than in 2017–2019. As of 31 December 2021, 89% (716/805) of observed pwMS were vaccinated at least once. As of 31 May 2022, 45% (266/597) of pwMS reported at least one SARS-CoV-2 infection during observational time. PwMS with more

severe COVID-19 were older, more disabled and had more comorbidities at baseline. Relapse rate and CDW did not increase during the nationwide vaccination campaign and the period with the highest infection rate in Switzerland.
Conclusions: The pwMS observed in this study showed expected SARS-CoV-2 infection dynamics over time and an active participation in vaccination program. From an overall perspective, no increase in clinical disease activity was monitored during SARS-CoV-2 pandemic period in Switzerland.

P16

MOG-IgA Characterizes a Subgroup of Patients with Central Nervous System Semyelination

AB Ayroza Galvao Ribeiro Gomes [1], L Kulsvehagen [1], P Lipps [1], A Cagol [1], N Cerdá-Fuertes [1], T Neziraj [1], J Flammer [1], J Lerner [1], A Lecourt [1], N Oliveira S. Siebenborn [1], R Cortese [2], S Schaedelin [1], V Andreoli Schoeps [3], A de Moura Brasil Matos [3], N Trombini Mendes [3], C dos Reis Pereira [3], M Luiz Ribeiro Monteiro [3], SL dos Apostolos Pereira [3], P Schindler [4], C Chien [4], C Schwake [5], R Schneider [5], T Pakeerathan [5], O Aktas [6], U Fischer [1], M Mehling [1], T Derfuss [1], L Kappos [1], I Ayzenberg [5], M Ringelstein [6], F Paul [4], D Callegaro [3], J Kuhle [1], A Papadopoulou [1], C Granziera [1] and A Pröbstel [1]

[1] Universitätspital Basel, Switzerland;
[2] University of Siena, Siena, Italy;
[3] University of Sao Paulo, Brasilia;
[4] Charité—Universitätsmedizin Berlin, Germany;
[5] Ruhr-Universität Bochum, Germany;
[6] Heinrich Heine University Düsseldorf, Germany

Background: The differential diagnosis of patients with seronegative demyelinating central nervous system (CNS) disease is challenging. While co-existing MOG-IgA has been described in a small subset of patients with MOG-IgG associated disease (MOGAD)1, little is known about the clinical relevance of IgA antibodies against myelin oligodendrocyte glycoprotein (MOG) in MOG- and AQP4-IgG double seronegative CNS demyelination.
Aims: To investigate the frequency and associated clinical features of MOG-IgA in a cohort of patients with demyelinating CNS disease and healthy participants.
Design/Methods: We conducted an observational, retrospective, longitudinal, multicenter study which investigated MOG-IgA, -G, and -M in sera and cerebrospinal fluid (CSF) of patients assessed from September 2012 to April 2022 (median follow-up time [months]: 39, range 0–227). We included 1339 patients with suspected or confirmed MOGAD1, multiple sclerosis (MS)2, or NMOSD3, and 110 healthy controls (HC) from five centers in a discovery and confirmation set-up.
Results: Of included isolated MOG-IgA patients, 61% (n = 11/18) were females and median age was 31.5 years (range: 3–76). Among patients double-seronegative for AQP4-IgG and MOG-IgG (n = 1126/1339; 84%), isolated MOG-IgA was identified in 6% (n = 3/50) of patients with NMOSD, in 2% (n = 5/228) of patients with other CNS demyelinating disease, and in 1% (n = 10/848) of patients with multiple sclerosis (MS), but in none of the HC (n = 0/110). The most common disease manifestation in isolated MOG-IgA seropositive patients was myelitis (65%), followed by more frequent brainstem syndrome (44% vs. 19%, p = 0.048), and infrequent manifestation of ON (27% vs. 63%, p = 0.02) compared to MOG-IgG patients. Among patients fulfilling 2017 McDonald criteria for MS, MOG-IgA was associated with less frequent CSF-specific oligoclonal bands (OCBs) (44% vs. 93%, $p < 0.0001$) compared to MOG-IgG/IgA seronegative MS patients. Further, most patients with isolated MOG-IgA presented events of demyelination after recent infection/vaccination (64%, n = 7/11).
Conclusions: We identified MOG-specific IgA in a subgroup of AQP4-/MOG-IgG double-seronegative patients, suggesting MOG-IgA as a potential diagnostic biomarker for patients with CNS demyelination.

P17

Cervical Spinal Cord Gray Matter Area and the Reversed Split Hand Index as Surrogate Markers in Spinal Muscular Atrophy (SMA)

EM Kesenheimer [1], MJ Wendebourg [2], C Weidensteiner [3], L Sander [2], M Weigel [3], T Hass [3], D Fischer [4], C Neuwirth [5], N Braun [5], M Weber [5], C Granziera [6], O Bieri [3], M Sinnreich [6] and R Schläger [2]

[1] Departments of Neurology, Clinical Research and Biomedical Engineering, University Hospital Basel, University of Basel and RehaB Basel;
[2] Departments of Neurology, Clinical Research and Biomedical Engineering, University Hospital Basel, University of Basel;
[3] Division of Radiological Physics, Department of Radiology and Biomedical Engineering, University Hospital Basel and University of Basel;
[4] Division of Neuropediatrics and Developmental Medicine, University Childrens' Hospital of Basel (UKBB), University of Basel;
[5] Neuromuscular Diseases Unit/ALS Clinic, Kantonsspital St.Gallen;
[6] Departments of Neurology and Biomedicine, University Hospital Basel, University of Basel, Switzerland

Aims: There is an unmet need for valid biomarkers for disease course and therapeutic response monitoring in SMA. rAMIRA (radially sampled Averaged Magnetization Inversion Recovery Acquisitions) MR-imaging enables spinal cord (SC) gray matter area (GMA) quantification in clinically feasible acquisition times [1],2. Motor Unit Number Index (MUNIX) is a quantitative neurophysiological estimate of lower motor neurons that supply a muscle 3. The MUNIX reversed split hand index (RSHI) describes the relative preservation of abductor pollicis brevis compared to first dorsal interosseous and abductor digiti minimi muscles in SMA4.
Study aims were to evaluate associations of SC GMA with MUNIX in corresponding muscles and the diagnostic utility of these methods in patients with SMA.
Methods: We prospectively investigated 21 patients with 5q-SMA (mean age/SD 41.3/11.6y and 21 age- and sex-matched healthy controls (HC) (mean age/SD 41.7/11.4y) by axial 2D rAMIRA imaging at 3T at the intervertebral disc level C5/C6. SC GMA was determined using a semi-automated approach. MUNIX of the biceps brachii (BB) and hand muscles were measured following the ENCALS protocol, the RSHI4 was determined. Receiver Operating Characteristic (ROC) curves for predicting SMA vs. HC status by binary logistic models were calculated. Multivariable regression analysis was used to assess associations between SC GMA at C5/C6 with MUNIX of the corresponding muscle, covarying for age and sex.
Results: SC GMA at C5/C6 was reduced in patients compared to HC by 17% (mean GMA in mm2 (SD): SMA 17.5 (2.4); HC 21.1 (1.5); $p < 0.0001$). MUNIX was reduced in BB and hand muscles ($p < 0.0001$). In multivariable regression analyses SC GMA at C5/C6 explained 53% of MUNIX (BB) variance in SMA patients. In a binary logistic model, the RSHI and SC GMA at C5/C6 as combined predictors showed a sensitivity of 89% and specificity of 95% for predicting SMA vs. HC status.
Conclusions: Adult patients with 5q-SMA show significant cervical SC GM atrophy using rAMIRA imaging. SC GMA is associated with MUNIX in corresponding muscles indicating the functional relevance of the atrophy observed. We can confirm the concept of a reversed split hand pattern in SMA using MUNIX, which in combination with SC GM area at C5/C6 discriminates patients from HC with high accuracy.
Further longitudinal investigations are necessary next steps to evaluate this novel imaging marker for disease course and therapeutic response monitoring in SMA.

P18

Lasso Prediction of Futile Recanalization in Patients with Large Vessel Occlusion Stroke Randomised to Mechanical Thrombectomy

H Handelsmann [1], L Herzog [2], A Hoving [3], C Majoie [3], W Van Zwam [4], A van der Lugt [5] and S Wegener [6]

[1] University of Zurich, University Hospital Zurich, Switzerland;
[2] University of Zurich, Zurich University of applied Sciences, University Hospital Zurich, Switzerland;
[3] University of Amsterdam, Netherlands;
[4] Maastricht University Medical Center, Netherlands;
[5] Erasmus MC, University Medical Center, Rotterdam, Netherlands;
[6] University Hospital Zurich, Switzerland

Aims: Mechanical thrombectomy (MT) is an effective treatment of large vessel occlusion (LVO) stroke. However, about 50% of patients remain functionally dependent despite successful recanalization, which is considered futile recanalization (FR). We aimed at identifying factors associated with (1) full vessel recanalization (technical success) and (2) FR (no clinical success) in LVO stroke patients randomised to MT.
Methods: We retrospectively analysed the MR CLEAN trial [1] data (n = 500) including 115 patients with anterior LVO strokes randomised to MT with successful recanalization according to the modified thrombolysis in cerebral infarction (mTICI) score of 2b or 3.
FR was defined as a modified Rankin scale (mRS) score of $\geq$4 three months after stroke in patients with mTICI 2b or 3. Logistic regression with interaction terms was conducted to assess patient factors for association with treatment response and to investigate factors associated with technical (mTICI) and clinical (mRS) success of MT. We predicted FR in a five-fold cross validation using least absolute shrinkage and selection operator (LASSO) regression based on age, sex, systolic blood pressure, blood glucose, blood thrombocyte count, pre-stroke mRS, admission NIHSS, ASPECTS, collateral status on computed tomography angiography and time from symptom onset to MT.
Results: Only onset-to-groin time was associated with a successful recanalization (=mTICI 2b or 3) (odds ratio 0.658, 95% confidence interval 0.476–0.909, p = 0.011).
Forty% of patients experienced FR, correctly predicted in 70% of cases (sensitivity = 52.2%, specificity = 81.2%). The area under the curve was 0.7032 (0.6054–0.8011). Most important predictors for FR were female sex and poor collateral status.
Conclusions: Different patient factors seem to be relevant for achieving a successful revascularisation by MT according to TICI (onset-to-groin time) versus predicting functional outcome after successful MT (sex, collateral status). With LASSO regression, we predicted FR with an AUC of 0.7032. We expect to further improve outcome prediction by implementing machine-learning algorithms in the interpretation of imaging data.

P19

Multiuser 3D-Virtual Reality (SpectoVR) and 3D-Printed Model: Two Effective Teaching Tools in Pediatric Neurosurgery

L Greuter [1], D Croci [1], M Licci [1], F Thieringer [1], P Cattin [2], J Soleman [3] and R Guzman [4]

[1] University Hospital of Basel;
[2] University of Basel;
[3] University of Basel/University Hospital Basel;
[4] University of Basel/University Hospital of Basel, Switzerland

Abstract

Background: Surgical training has been based on learning through observation. However, nowadays with working hour limitations and increasing patients' safety concerns, surgical training is urged to explore new learning methods. Our aim is to evaluate the user experience and possible negative effects of a Virtual-Reality (VR) platform and 3D-printed models for interactive multiuser case discussions in pediatric neurosurgery.
Methods: During the pediatric neurosurgery symposium in Basel, Switzerland, users attending an interactive case discussion in a full immersion VR platform called SpectoVR

and developed at the Department of Bioengineering at the University of Basel, Switzerland, were asked to fill in a questionnaire regarding their experience with VR focusing on simulator sickness symptoms. Another workshop at the same conference used a 3D-printed model to train endoscopy and was evaluated with a separate questionnaire.
Results: Out of 60 questionnaires returned, 29 (48.3%) participants completed the 3D-printed model vs. VR survey, and 31 (51.7%) filled in the VR-related simulator sickness syndrome survey. Most (87.1%) participants had previously heard of VR, however, only a third had used it before. Both, SpectoVR and the 3D-printed model were rated accurate in representing the relevant anatomy, useful for teaching and training. Twenty-five (80.6%) participants believe that VR models would enhance their clinical practice. VR models were ranked significantly better regarding their users' engagement and likeability than 3D-printed models (96.2 ± 7 compared to 87.7 ± 8.3, $p = 0.015$).
Using SpectoVR as a fully immersive platform, only a few experienced severe simulator sickness symptoms (16%), and none of the participants had to interrupt their VR experience due to symptoms.
Conclusions: VR platforms and 3D-printed models allow accurate representation of the surgical anatomy. SpectoVR allows patient-specific 3D model rendering for interactive case discussion with up to seven participants, while 3D-printed models are more suitable for practicing a surgical skill. Simulator sickness symptoms in our cohort were rare and nobody had to interrupt their VR experience due to such symptoms. Fully immersive VR tools and 3D-printed models have opened a new realm of medical teaching and surgical training.

P20

Validation of the TDN Grade in an Independent Cohort of Aneurysmal Subarachnoid Haemorrhage Patients

V Kaelin, A Terrapon, A Zeitlberger, S Maschke, S Bonasia, A El-Garci, O Bozinov, M Neidert, M Neidert and IC Hostettler

Canton Hospital St. Gallen, St. Gallen, Switzerland

Aims: Adverse events (AE) associated with a specific illness or its treatment are common and can to new neurological deficits and reduced functional outcome. Aneurysmal subarachnoid haemorrhage (aSAH) is a devastating disease with a high mortality and morbidity, partly due to the high rate of disabling AE. Common classifications of AE are not designed to predict these outcome variables and are therefore less applicable for neurosurgical patients. A previously proposed classification, the Therapy-Disability-Neurology (TDN) grade, addresses this by grading AE severity depending on the associated treatment, the resulting disability and/or neurological deficits. Our aim was to validate the usefullness of the TDN grade in predicting length of hospital stay (LOS) and functional outcome in a our cohort of aSAH patients.
Methods: We conducted a retrospective analysis of a prosepecitvely collected single-center database on aSAH patients. Patients were continously recruited between 2009–2022. We retrospectively applied the TDN grade to this cohort. Our primary outcome variables were LOS and functional outcome using Karnofsky Performance Status (KPS) and Glasgow Outcome Scale (GOS) at discharge and follow-up.
Results: We inlcuded 384 patients, 31 were treated conservatively. In the 353 patients undergoing aneurysm treatment, the TDN grade was associated and correlated with increasing LOS (rho = 0.43, Rs2 = 18.5%, $p < 0.001$) and decreasing KPS/GOS at discharge and one-year follow-up (KPS discharge: tau = -0.27, $p < 0.001$; KPS follow-up: tau = -0.20, $p = 0.001$; GOS discharge: tau = -0.25, $p < 0.001$; GOS follow-up: tau = -0.24, $p < 0.001$). When applying the TDN grade to conservatively treated patients, it was again a strong predictor of LOS (rho = 0.88, Rs2 = 77.8%, $p = 0.04$).
Conclusions: In our cohort of aSAH patients, the TDN grade correlated well with both LOS and functional outcome measured by KPS and GOS. This indicates its adequate re-

flection of AE severity in this patient cohort. By combining it with other scores, the TDN grade could significantly improve prediction-making.

P21

Endovascular Treatment of Rabbit Bifurcation Aneurysm with Biodegradable Embolization Materials—Preliminary Results

J Rey [1], S Ulmer [1], G Canzanella [1], R Schmied [2], T Franssen [2], K Catalano [1], S Wanderer [1], HR Widmer [2], P Gruber [1], L Remonda [1], L Andereggen [1], S Marbacher [1] and BE Gruter [1]

[1] Kantonsspital Aarau;
[2] Universität Bern, Switzerland

Introduction: Current endoluminal devices for treatment of intracerebral aneurysm (IA) comprise stents and flowdiverters, which remain permanently in-situ, far beyond time of complete IA healing. These endovascular devices have several disadvantages such as requirement of lifelong antiplatelet therapy, risk of in-stent stenosis and restriction of vasomotion. A possibility to overcome these drawbacks is the use of bioresorbable materials. After successful treatment of saccular sidewall aneurysm in a rat model with bioresorbable magnesium (Mg)-alloy-stents and resorbable thread we aimed to transfer this therapy option to a bifurcation aneurysm in a rabbit model. The elastase digested bifurcation rabbit model has hemodynamic, morphologic and histologic characteristics similar to human IAs.
Methods: Saccular bifurcation aneurysms were microsurgically created by suturing an elastase digested arterial graft in an artificially created bypass between left and right common carotid artery in New Zealand white rabbits. The aneurysm was then treated either with an intraluminal bioembolization material (Vicryl 0-0) alone, Mg-alloy-stent alone or intraluminal embolization material plus bioresorbable Mg-alloy-stent. Four weeks after creation, MR-angiography was performed to assess aneurysm perfusion status, and neointima formation was histologically analyzed.
Results: Of n = 9 rabbits n = 4 were treated with endoluminal bioembolization material alone, n = 3 with a bioresorbable Mg-alloy-stent alone and n=2 with bioembolization plus bioresorbable Mg-alloy-stent. MR-angiographic follow-up showed residual perfusion in all stent alone treated aneurysm. After intraluminal bioembolization two aneurysm were completely occluded, two had small remnants at the aneurysm base. All aneurysm with bioembolization plus Mg-alloy-stent treatment showed complete aneurysm healing and strong neointima formation. No animal developed ischemic complications after 4 weeks.
Conclusions: In a complex rabbit bifurcation aneurysm model, aneurysm treatment with endoluminal application of short-lasting resorbable thread in combination with bioresorbable Mg-alloy-stents is feasible and safe. Further studies are needed to evaluate long-term patency rates of the vessels and to evaluate long-term aneurysm recurrence.

P22

Thrombocyte Transfusion Reduces the Rebleed Rate in Patients Using Antiplatelet Agents before Aneurysmal Subarachnoid Hemorrhage

M Sebök, N Zaugg, E Keller, J Willms, L Regli and M Germans

UniversitätsSpital & Universität Zürich, Switzerland

Background: The reason for rebleed after initial hemorrhage in aneurysmal subarachnoid hemorrhage (aSAH) patients is considered to be multifactorial. One of factors which has been related to early rebleed and worse outcome after aSAH, is antiplatelet use. Thrombocyte transfusion overcomes the inhibitory effects of antiplatelet agents by increasing the number of functional thrombocytes, however, the impact on rebleed rate and clinical outcome remains unknown. Our aim is to assess the effect of thrombocyte transfusion on rebleeding and clinical outcome in aSAH patients with prehemorrhage antiplatelet use, considering confounding factors.

Methods: Data were prospectively collected at a single tertiary reference center for aSAH in Zurich, Switzerland. Patient with aSAH and prehemorrhage antiplatelet use were divided into "thrombocyte transfusion" and "non-transfusion" group according to the transfusion status during hospital admission. Using multivariate logistic regression analysis the impact of thrombocyte transfusion on rebleed rate and clinical outcome, defined as Glasgow Outcome Scale (GOS) 1–3, was calculated.
Results: One hundred and thirty-four patients were included, 76 (56.7%) of them received thrombocyte transfusion. After adjusting for confounders, thrombocyte transfusion showed strong evidence for a large reduction in a rebleed rate (adjusted OR 0.22, 95% CI 0.07 to 0.71). However, thrombocyte transfusion was not associated with poor clinical outcome at six months' follow-up (adjusted OR 1.09, 95% CI 0.40 to 2.95).
Conclusions: Thrombocyte transfusion in aSAH patients with prehemorrhage antiplatelet use is independently associated with reduction in rebleeds but shows no impact on clinical outcome at six months´ follow-up. Larger, or maybe randomized, studies are needed to better investigate the impact of thrombocyte transfusion on rebleed and outcome.

P23

STA-MCA Bypass for Acute and Subacute Ischemic Stroke Due to ICA Occlusion: The Role of Advanced Neuroimaging

M Sebök, LM Höbner, J Fierstra, T Schubert, S Wegener, Z Kulcsar, A Luft, L Regli and G Esposito

UniversitätsSpital & Universität Zürich, Switzerland

Objective: A major clinical challenge is the adequate identification of patients with acute (within one week) and subacute (1–6 weeks) ischemic stroke due to internal carotid artery (ICA) occlusion who could benefit from a surgical revascularization after a failure of endovascular and/or medical treatment. Recently, two novel quantitative imaging modalities have been introduced: (1) Quantitative magnetic resonance angiography (qMRA) with non-invasive optimal vessel analysis (NOVA) for quantification of blood flow in major cerebral arteries (in mL/min), and (2) blood oxygenation level–dependent (BOLD) functional magnetic resonance imaging (fMRI) to assess cerebrovascular reactivity (CVR). The aim of this study is to present our cohort of patients who underwent surgical revascularization in the acute and subacute phase of ischemic stroke as well as to demonstrate the importance of hemodynamic and flow assessment for the decision-making regarding surgical revascularization in patients with acute and subacute stroke and ICA-occlusion.
Methods: Symptomatic patients with acute and subacute ischemic stroke because of persistent ICA-occlusion despite optimal medical/endovascular recanalization therapy underwent both qMRA-NOVA and BOLD-CVR to study the hemodynamic and collateral vessel status. Patients selected for surgical revascularization according to our previously published flowchart were included in this study. Repeated NOVA and BOLD-CVR investigations were done after bypass surgery as follow up as well as clinical follow up.
Results: Between May 2019 and September 2022, STA-MCA bypass surgery was performed in 12 patients with acute and subacute stroke because of ICA-occlusion despite of optimal endovascular and/or medical treatment prior to the surgery. Impaired BOLD-CVR in the occluded vascular territory as well as reduced hemispheric flow with qMRA-NOVA were measured indicating insufficient collateralization. Post-operative NOVA qMRA showed improved hemispheric flow (via bypass) and the 3-month-follow-up with BOLD-CVR showed improved cerebral hemodynamics in all patients studied.
Conclusions: Quantitative assessment of cerebral hemodynamics with BOLD-CVR and collateral vessel status with qMRA-NOVA is useful for selecting patients with acute/subacute stroke due to ICA occlusion who may benefit from surgical revascularization after failure of endovascular/medical treatment.

P24

Profiling the Cellular Immune Response after Aneurysmal Subarachnoid Hemorrhage

N Schwendinger [1], A Kevin [1], R Buzzi [1], B Thomson [2], E Dürst [2], E Colombo [1], A Grob [1], L Egli [2], M Grüttner Durmaz [1], L Baselgia [1], L Regli [1], D Schaer [1] and M Hugelshofer [1]

[1] USZ UniversitätsSpital Zürich;
[2] University of Zurich UZH, Switzerland

Aims: Subarachnoid hemorrhage accounts for 5–10 percent of all strokes. Apart from the impact of the initial bleeding, especially secondary brain injury (SAH-SBI) results in long-term morbidity and mortality [1]. Its delayed onset potentially allows for disease modulation and outcome improvement in patients.
Within this study, we collected serial CSF leukocyte samples from our cohort of aSAH and subjected them to RNA single-cell sequencing. We characterized the time-dependent accumulation of leukocytes and mapped cellular phenotypes to clinical endpoints.
Methods: The ethics committee in Zurich, BASEC number 2022-00132, approved the protocol. Patients 18 years or older at the time of hospital admission who had a confirmed aneurysmal subarachnoid hemorrhage and a CSF diversion were included in the study. Clinical data were collected regarding age, sex, H&H grade, WFNS grade, DCI/DIND, vasospasm, secondary brain injury, mRS at discharge and three months follow-up, and shunt dependency at three months. CSF samples of patients were collected at three different time points. The cells were processed according to the 10× Genomics Chromium Single Cell 3′ v3.1 Reagent Kit instruction guide (10× Genomics). The Cell Ranger Count (version 7.1.0) generated expression matrices. The resulting gene expression matrices were further analyzed with R (R version 4.2.1) using the Seurat package (version 4.3.0).[2]
Preliminary Results: We could include 21 aSAH patients in the study. Samples were acquired at three predefined times After quality control, 201798 high-quality leukocyte profiles were included in the analysis. We classified double-negative-T-cells (dn-T-cells), three types of CD4+ T-cells, CD8+ T cells, T regulatory cells (Tregs), natural killer (NK) cells, plasmacytoid dendritic cells, B cells, myeloid dendritic cells, classical monocytes, non-classical monocytes, intermediate monocytes and two types of neutrophils within the CSF of our aSAH cohort. We identified significantly differentially expressed genes between patients that sustained SAH-SBI and patients with a more favorable course of the disease.
Conclusions: Characterizing the cellular immune response after aneurysmal subarachnoid hemorrhage is critical to understanding the pathophysiological course of the disease. Cell composition and cellular phenotypes within the CSF will allow us to conclude about potentially modifiable adaptive processes.

P25

The Impact of Subarachnoid and Ventricular Hemorrhage Extension on Ventriculostomy-Related Infections in Patients with Aneurysmal Subarachnoid Hemorrhage

F Ebel [1], S Stohler [2], J Rychen [1], A Saemann [1], R Guzman [1], L Mariani [1] and M Roethlisberger [1]

[1] Department of Neurosurgery, University Hospital of Basel, Basel, Switzerland;
[2] Faculty of Medicine, University of Basel, Basel, Switzerland

Background. Ventriculostomy is a common neurosurgical intervention to treat acute hydrocephalus in aneurysmal subarachnoid hemorrhage (aSAH), associated with ventriculostomy-related infection (VRI) as a relevant complication. How the quantity and distribution of subarachnoid and ventricular hemorrhage impact VRI-rates has not been studied sufficiently to date.
Methods. Retro- and prospective single-center cohort study of aSAH patients who received an external ventricular drain (EVD) between January 2009 and December 2018. Uni- and multivariable logistic regression analysis was used to assess potential predictors of VRI, including the intraventricular hemorrhage (IVH) and the Barrow Neurological Insitute (BNI) SAH grading score.

Results. A total of 138 aSAH patients received 164 EVDs with a total EVD in situ time of 1374 days (median 9 days). VRI occurred in 20/138 patients (12% rate per EVD and 15% per patient). A higher IVH-score (OR 1.3, $p = 0.037$ per point), a left lateral ventricle with 33–66% blood filling (OR 5.04, $p = 0.004$), a BNI grade 4 defined as a subarachnoid clot of 10–15 mm diameter (OR 4.42, $p = 0.004$) and the number of EVDs (OR 2.46, $p = 0.027$) were associated with VRI in the univariate analysis. In the multivariable logistic regression analysis, a left lateral ventricle with 33–66% blood filling (OR 5.14, [95% CI 1.38–19.07]; $p = 0.02$) and a BNI grade 4 (OR 5.42, [95% CI 1.77–16.57]; $p = 0.003$) remained significant risk-factors for VRI.
Conclusion. The VRI rate per EVD in patients with aSAH was 12%. The quantity of subarachnoid and left ventricular blood positively correlates as an independent risk-factor of VRI in aSAH patients. These findings are helpful in identifying aSAH patients at risk and guiding future research on VRI in aSAH patients.

P26

Impact of local Human Basic Fibroblast Growth Factor Application on Neointima Formation in a Rat Sidewall Aneurysm Model—Preliminary Analysis

J Rey, G Canzanella, S Wanderer, L Andereggen, L Remonda, S Marbacher and BE Gruter

Kantonsspital Aarau, Switzerland

Background: Long-term aneurysm occlusion after endovascular treatment relies on cell-mediated processes including thrombus organisation and neointima formation. Thereby, basic fibroblast growth factor (bFGF) is a potent stimulator for this remodelling process by enhancing fibroblast migration. Therefore, local intra-aneurysmal application of human bFGF is hypothesized to promote aneurysm healing in an experimental rat sidewall aneurysm model.
Methods: Vital and decellularized saccular sidewall aneurysms were microsurgically created in 24 Lewis rats and treated with bioembolization material (bioabsorbable thread) soaked with 5 ug ($n = 6$), 10 ug ($n = 6$) and 20 ug ($n = 6$) of bFGF. A control group ($n = 6$) received the biomaterial alone without bFGF. Histological specimens were harvested at 21 days follow-up. Healing status, local inflammation and degree of neointima formation was microscopically evaluated.
Results: All specimen of the control group showed a neointima formation with a complete occlusion of the aneurysm's orifice. All groups with bFGF application showed a poorer aneurysm occlusion rate, with a an enhanced neointima formation upon the biomaterial instead at the orifice of the aneurysm. This was observe with a dose-response effect: In the 5 ug bFGF-group, the neointima upon the biomaterial tended to be thin and incomplete, and an incomplete neointima still appeared at the orifice of the aneurysm. In the 10ug bFGF-group, intraluminal perfusion in a dog-ear pattern was observed. In the 20 ug bFGF-group, the neointima mostly covered the bioimplant isolating it from the aneurysm wall and allowing a persisting perfusion in between. The effect observed was more pronounced in decellularized aneurysms compared with vital ones.
Conclusions: Local application of bFGF by means of a bioimplant seems to enhance cellular migration and neointima formation on the surface of the embolization material with a dose-effect response. However, it results in a poor occlusion of the aneurysm orifice. A larger series is needed to confirm these results and to provide quantitative analyses.

P27

Correlating Cerebral Aneurysm Size Measurements Based on Virtual Reality Versus Standard 2D DSA Measurements; A Randomized Comparative Study

D de Wilde [1], A Saemann [1], J Rychen [1], M Röthlisberger [1], M Żelechowski [2], B Faludi [2], P Cattin [2], J Soleman [1] and R Guzman [1]

[1] University Hospital of Basel, Basel, Switzerland;
[2] University of Basel, Basel, Switzerland

Aims: Critical factors in determining rupture risk for unruptured intracranial aneurysms (UIA) are UIA size diameters and their derived ratios. However, conventional imaging modalities, such as 2D digital subtraction angiography (DSA), may need to improve their ability to adequately measure UIAs due to their decreased 3D visibility and limited resolution. Virtual-reality (VR) models provide 3D and intraluminal visualization, potentially enhancing the accuracy of measurements. This study aims to correlate measurements in 3D VR with those derived from corresponding source 2D images to assess the accuracy and feasibility of 3D VR as a measurement tool.
Methods: Ten UIA cases from the University Hospital of Basel were included. The latest DSA image before intervention was converted into a 3D VR model using "SpectoVR." A patient-specific transfer function was applied to segment the bone and injected vessels precisely. A mesh model of the injected vessels was generated, allowing intraluminal visualization. Five neurosurgeons with varying experience levels were randomly assigned to the cases. Each neurosurgeon performed measurements in a completely immersed 3D VR and a 2D on-screen format, resulting in three independent 3D VR and 2D measurements for each case. 3D VR measurements utilized two custom-definable points in the 3D space, allowing for precise evaluation. Interrater variability, measurement duration, and VR user experience were assessed.
Results: Measurements of anteroposterior (3D VR 5.65 $\pm$ 5 vs. 2D 5.64 $\pm$ 5, p = 0.652), mediolateral (5.44 $\pm$ 3.7 vs. 5.70 $\pm$ 5.1, p = 0.703), craniocaudal (5.81 $\pm$ 5 vs. 6.19 $\pm$ 4.6, p = 0.219), and dome diameters (5.29 $\pm$ 5.8 vs. 5.78 $\pm$ 4.6, p = 0.127) showed significant correlations between 3D VR and 2D measurements. However, parent artery (2.14 $\pm$ 2.9 vs. 2.32 $\pm$ 3.8, p = 0.0280) and neck diameters (3.37 $\pm$ 3.6 vs. 4.36 $\pm$ 3.8, p = 0.0263) differed significantly. No significant differences in interrater variability were observed. Measurement duration did not vary significantly (8.31 $\pm$ 15 min vs. 7.1 $\pm$ 11 min, p = 0.118). All investigators found 3D VR models more intuitive and desired increased utilization.
Conclusions: 3D VR technology provides significantly correlated basic measurements to 2D images. It improves accuracy for non-axial sizes such as parent artery and neck diameters due to its enhanced precision in 3D space without significantly increasing measurement duration.

P28

Real-Time Rotational Angiographic Footage of an Intracranial Aneurysm Rupture Resulting in a Subdural Hemorrhage

C Kissling [1], A Raabe [1], J Gralla [2] and D Bervini [1]

[1] Inselspital, Universitätsklinik für Neurochirurgie, Bern, Switzerland;
[2] Inselspital, Universitätsinstitut für Diagnostische und Interventionelle Neuroradiologie, Bern, Switzerland

A 48-year-old woman presented with acute severe headaches and seizure. CT images showed an acute subdural hematoma along the tentorium extending to the convexity, a temporal lobe intra-parenchymal hemorrhage on the left hand-side and a subarachnoid hemorrhage limited to the basal cisterns. Digital subtraction angiography (DSA) confirmed a 3 x 6 mm left internal carotid artery aneurysm at the departure of the posterior communicating artery (PcomA). The PcomA aneurysm re-ruptured at the time of its endovascular treatment, leading to extravasation of the contrast agent directly in the subdural space (see Video and Figures). Subdural hematoma due to aneurysm ruptures was first described in 1950 and ever since remained seldomly reported. 1, 2 No comparable recordings showing a real-time capture of PcomA aneurysm rupture and bleeding in the subdural space have been published so far according to a recent literature search.

P29

Re-Assessing Risk-Benefit Calculations for Preventive Interventions in Asymptomatic Patients

I Zubak [1], U Fischer [2], P Rothwell [3], R Luengo-Fernandez [3], D Bervini [1], J Goldberg [1], J Beck [4] and A Raabe [1]

[1] Department of Neurosurgery, Bern University Hospital, Inselspital Bern, Switzerland;
[2] Universitätsspital Basel, Switzerland;
[3] The Nuffield Department of Clinical Neurosciences, Oxford, United Kingdom;
[4] Universitätsklinikum Freiburg im Breisgau, Germany

Background: The decision to treat an incidental finding in an asymptomatic patient results from a careful risk-benefit consideration and is often challenging. The natural history of the disease, the treatment risk, the individual life expectancy, and quality of life are the main factors to be considered for an objective decision, however, they are often not well defined.
Methods: We sought to identify a common error when comparing the natural risk of a disease with the risk of intervention. We illustrate how the classical break-even point analysis using Kaplan-Meier curves can be misleading and advocate for a restricted mean survival time-based (RMST) calculation.
Results: The risk of treatment-related morbidity and mortality and the risk of natural history is not broken even at the crossing point of the classical Kaplan-Meier survival curves as commonly applied in clinical routine, but rather at a time point twice as long. The restricted mean survival time is an alternative measure to capture the true risk/benefit profile by reflecting the absolute event-free survival time of a patient.
Conclusions: We advocate the use of RMST-based decision-making to avoid the overtreatment of patients with asymptomatic disease. The fundamental difference of this approach may largely influence our decision-making and deserves to be discussed more frequently in the context of management recommendations.

P30

Occurence, Severity and Clinical Outcome of SSI in Intracranial Vascular Neurosurgical Patients

A Grob [1], E Colombo [2], M Germans [1], L Regli [2] and J Sarnthein [1]

[1] Universitätsspital Zürich;
[2] UniversitätsSpital & Universität Zürich, Switzerland

Aim: Surgical site infections (SSI) represent a relevant cause of morbidity and mortality in neurosurgical departments. Nevertheless, there are currently very few reports on the incidence and risk factors of SSI in intracranial vascular neurosurgery, notably featured by high technical complexity. Authors aim to determine the rate and severity of SSIs after intracranial neurovascular interventions and asses the risk factors in a tertiary neurosurgical centre.
Methods: Following the analysis performed by our group and published in 2019, a case control study was performed by data of patients operated in our institution between January 2013 and January 2022. We analyzed diagnosis and type of index surgery, time to clinical occurrence of SSI, functional outcome with modified Rankin scale (mRS) and NIHSS pre- and postoperatively, risk factors and treatment. SSI were characterized according to our internal SSI SOP and graded by means of the Clavien-Dindo grade (CDG).
Results: We counted 1500 intracranial vascular surgeries whereof 36 needed a revision surgery due to SSI. Median age was 54 (45–60) whereof 44.5% were women. Elective treatment of unruptured aneurysms was the most common diagnosis (n = 16, 44.4%) for index surgery and aneurysm clipping the most common surgery (n = 18, 50%). Median interval to diagnosis of SSI was 29 days (19–44). Clinical outcome after wound revision showed no significant decrease in mRS or NIHSS (p = 0.08 and 0.22). Regarding risk factors, 2 patients were under use of dexamethasone preoperatively and 2 were immunosuppressed. Antibiotic treatment after perioperative sampling was administered in 34 patients (94.4%).
Conclusions: The present study provides a first report of SSI in a prospective single-centre cohort of patients who underwent surgery for intracranial vascular pathologies. Emer-

gency surgical revision and antibiotic administration count for main treatment options resulting in no clinical worsening.

P31

Severe Neuro-COVID Is Associated with Peripheral Immune Signatures, Autoimmunity and Neurodegeneration: A Prospective Cross-Sectional Study

MM Etter [1], TA Martins [2], L Kulsvehagen [3], E Pössnecker [3], W Duchemin [4], S Hogan [2], G Sanabria-Diaz [5], J Müller [6], A Chiappini [7], J Rychen [7], N Eberhard [7], R Guzman [7], L Mariani [7], l Melie-Garcia [5], E Keller [8], I Jelcic [9], H Pargger [10], M Siegemund [10], J Kuhle [11], J Oechtering [11], C Eich [2], A Tzankov [12], MS Matter [12], S Uzun [12], Ö Yaldizli [6], JM Lieb [13], M Psychogios [13], K Leuzinger [14], HH Hirsch [15], C Granziera [6], A Pröbstel [3] and G Hutter [1]

[1] Department of Neurosurgery, University Hospital Basel, and Brain Tumor Immuno-Therapy and Biology Laboratory, Department of Biomedicine, University Hospital of Basel, University of Basel, Basel, Switzerland;
[2] Brain Tumor Immuno-Therapy and Biology Laboratory, Department of Biomedicine, University Hospital of Basel, University of Basel, Basel, Switzerland;
[3] Departments of Neurology, Biomedicine and Clinical Research, & Research Center for Neuroimmunology and Neuroscience Basel, University Hospital Basel, University of Basel, Switzerland;
[4] sciCORE Center for Scientific Computing, University of Basel;
[5] Translational Imaging in Neurology (ThINk) Basel, Department of Biomedical Engineering, University Hospital Basel and University of Basel;
[6] Translational Imaging in Neurology (ThINk) Basel and Neurology Clinic and Policlinic, Departments of Head, Spine and Neuromedicine, MS Center and Research Center for Clinical Neuroimmunology and Neuroscience (NC2NB), Department of Biomedical Engineering;
[7] Department of Neurosurgery, University Hospital of Basel, Switzerland;
[8] Neurosurgical Intensive Care Unit, Department of Neurosurgery and Institute of Intensive Care Medicine, University Hospital Zurich, Zurich, Switzerland;
[9] Neuroimmunology and Multiple Sclerosis Research Section, Department of Neurology, University Hospital Zurich, Zurich, Switzerland;
[10] Department of Intensive Care Medicine, University Hospital Basel, Basel, Switzerland;
[11] Department of Neurology, University Hospital of Basel, Switzerland;
[12] Department of Pathology, University Hospital Basel, University of Basel, Switzerland;
[13] Department of Neuroradiology, University Hospital Basel, Switzerland;
[14] Division of Medical Immunology and Clinical Virology, University Hospital of Basel, Switzerland;
[15] Transplantation and Clinical Virology, Infectious Diseases & Hospital Epidemiology, Department of Biomedicine, University of Basel and University Hospital of Basel, Switzerland

Aim: There is increasing evidence that the central nervous system (CNS) is among the affected targets of SARS- CoV-2 causing COVID-19 related neurological sequelae. These short- and long-term neurological manifestations are abundant and disabling. However, the underlying pathophysiological mechanisms resulting in CNS derogation remain unclear. Here, we performed a prospective and in depth-characterization of cerebrospinal fluid (CSF) and plasma targeted proteomics in different Neuro-COVID severity classes and patients suffering form long-COVID with corresponding clinical, imaging and histopathological data.
Methods: We conducted a prospective, two-center, cross-sectional study (EKNZ 2020-01503, NCT04472013), including COVID-19 patients during the ongoing pandemic (August 2020 to April 2021). Forty COVID-19 patients were subdivided into Neuro-COVID classes I, II or III based on their severity of neurological symptoms. Study interventions included cranial imaging, lumbar puncture and blood withdrawal. Age- and sex-matched Non-multiple sclerosis (MS) inflammatory neurological disorder patients ($n = 25$) and heal-

thy individuals (n = 25) served as control groups. Targeted CSF and plasma proteomics was performed as well as antibody assays to detect potential autoantibodies. Further, we assessed the association with regional brain volumes and inflammatory CSF parameters. To establish predictive post-acute COVID-19 biomarkers, a13 months patient reported outcome follow-up was performed.
Results: The most prominent signs of severe Neuro-COVID are blood-brain barrier (BBB) impairment, elevated microglia activation markers and a polyclonal B cell response targeting self- and non-self- antigens. COVID-19 patients had decreased regional brain volumes associating with specific CSF parameters, However, COVID-19 patients characterized by a plasma cytokine storm are presenting with a non-inflammatory CSF profile. Post-acute COVID-19 syndrome strongly associated with a distinctive set of CSF and plasma mediators.
Conclusions: A vigorous microglia reactivity, a dysfunctional blood-brain barrier and CNS ingressing B cells mainly characterized severe Neuro-COVID. We observed a plasma cytokine storm combined with a non- inflammatory CSF profile, even in severe Neuro-COVID. Particular CSF and plasma inflammatory parameters are associated with decreased regional brain volumes in COVID-19 patients and post-acute COVID-19 syndrome.

P32

Cerebral Aspergilloma with Trigeminal Neuralgia, Ophthalmoplegia and Amaurosis in an Immunocompetent Patient: A Case Report

S Golshani [1], L Issler [2] and A Alfieri [1]

[1] Department of Neurosurgery, Cantonal Hospital of Winterthur;
[2] Clinic of Orthopaedics and Traumatology, Cantonal Hospital of Winterthur, Switzerland

Introduction: Cerebral Aspergillosis is an infrequent fungal infection caused by Aspergillus fumigatus, a mold commonly found in the environment.A It primarily affects individuals with compromised immune systems, and cases in immunocompetent individuals are rare due to the mold's low pathogenicity. Cerebral involvement typically originates from the paranasal sinuses and can lead to abscess formation, cerebral infarction, and mycotic aneurysms. The prognosis of cerebral aspergillosis remains unfavorable, with a mortality rate of approximately 60% despite the current standard treatment involving surgery and extended antifungal therapy.
Case Presentation: A 79-year-old male patient presented with persistent right-sided trigeminal pain and unintended weight loss. His condition rapidly deteriorated, resulting in ptosis, ophthalmoplegia, and visual impairment in his right eye. He also experienced slurred speech and decreased alertness, leading to referral to our center. MRI revealed a mass-like lesion resembling an abscess in the right temporomesial region involving the trigeminal nerve. Emergent craniotomy confirmed the abscess, which was later identified as an infection with Aspergillus fumigatus. Intravenous antifungal therapy with voriconazole was initiated, providing initial symptom relief. However, a follow-up MRI showed lesion progression, leading to re-craniotomy, abscess re-evacuation, and resection of affected tissue. Subsequent symptom improvement was achieved, with mild persisting trigeminal pain and slight ptosis but unchanged amaurosis affecting the right eye. The patient was discharged with oral voriconazole therapy and showed complete remission of the infection during follow-up. Follow-up consultation at eight weeks after initial surgery showed further improvement of symptoms with MR-imaging demonstrating complete remission of the infection.
Discussion: Cerebral aspergillosis is a rare condition, and limited data are available regarding outcomes. Prompt surgical intervention and prolonged adjusted antifungal treatment are crucial in preventing further spread of the infection and improving survival prognosis. The introduction of new antifungal therapies, such as voriconazole, has shown promise in reducing mortality rates. Thorough assessment of the patient's medical history is essential for prognosis estimation, while recurrent imaging is important for treatment monitoring.

P33

Feasibility a Accuracy af CARLO© Guided Extradural Anterior Clinoidectomy

TT Ha [1], M Schicker [1], Y Luder [1], M Morawska [2] and M Röthlisberger [1]

[1] University and University Hospital of Basel;
[2] AOT Swiss (Advanced Osteotomy Tools), Basel, Switzerland

Introduction: Anterior clinoidectomy is a surgical procedure used to access the central skull base, providing access to sellar and parasellar pathologies and vascular lesions in and around the cavernous sinus. However, the procedure is challenging and risky due to limited working space, restricted surgical view, and proximity to critical anatomical structures such as the carotid artery, oculomotor nerve, and optic nerve.
Advancements in medical robotics technology offer potential improvements in various areas of neurosurgery.
Aims: This study aimed to assess the feasibility and accuracy of using CARLO© (Cold Ablation Roboter-guided Laser Osteotome) to create burr holes and hollow out the anterior clinoid bone. Success was defined as the successful excavation of the anterior clinoid, confirmed through post-experimental CT scans and photographic documentation.
Material and Methods: The experiment utilized five fresh frozen skulls, fixed in a Mayfield clamp to ensure a stable setup. Preoperative planning was performed using NeuroPlan©, which segmented critical anatomical structures and planned trajectories with a safety distance of 2 mm from danger zones. A navigation system and additional referencing screws were employed for precise bone ablation. The target structure was reached by performing a pterional craniotomy and extradural preparation of the anterior clinoid.
Results: Data evaluation is still ongoing, but initial results indicate a successful excavation of the anterior clinoid while preserving critical anatomical structures. These findings hold potential to stimulate further research in robotic and laser technology within neurosurgery. The study highlights the feasibility and high accuracy of robotic technology, which can be leveraged to develop additional procedures aimed at improving patient outcomes and reducing perioperative risks in neurosurgical interventions.

P34

Velocity and Growth Pattern of Intracranial Meningiomas: A Serial Volumetric Analysis of 240 Tumors

L Häni, P Thomann, T Maragkou, S Vulcu, A Schütz, CM Jesse, N Söll, A Hakim, A Raabe and P Schucht

Inselspital—Universitätsspital Bern, Switzerland

Aims: We aimed to assess the velocity and pattern of growth of meningiomas and to correlate the kinetics of tumor growth with our previously reported two-item radiological risk stratification and their pathological grade.
Methods: We performed a serial volumetric analysis of meningiomas diagnosed radiologically at our institution between 2003 and 2015. The primary endpoint was velocity of diametric expansion (VDE), which represents the slope of a linear regression of the mean tumor diameter against time. For a secondary analysis, we categorized growth patterns as linear or exponential by fitting time-volume curves to a linear and exponential function. Three radiological risk categories based on T2 iso-/hyperintensity and absence of calcifications were compared based on our previous results.1 Low risk tumors were T2 hypointense meningiomas, intermediate risk tumors were T2 iso-/hyperintense meningiomas with calcifications, and high risk tumors were T2 iso-/hyperintense meningiomas without calcifications.
Results: In the entire cohort of 240 meningiomas, median VDE was 0.33 mm/year (IQR 0.09–0.84). Distribution of VDE differed significantly among radiological risk categories (0.53 vs. 0.35 vs. 0.06 mm/year; $p < 0.001$). High risk and intermediate risk tumors tended to grow more frequently exponentially compared to low risk tumors (45.1% vs. 38.5% vs.

8.3%; $p = 0.053$). There was a tendency for a higher VDE (1.30 vs. 4.01 mm/year; $p = 0.185$) and more frequent exponential growth pattern (exponential in 21.1% vs. 40%; $p = 0.586$) in CNS-WHO grade 2 tumors compared to CNS-WHO grade 1. Of note, out of seven meningiomas demonstrating rapid tumor growth with a VDE $\geq$ 3 mm/year, only three were WHO grade 2. We found no TERT promotor mutation or CDKN2A/B deletion among these rapid growing tumors.
Conclusions: A radiological risk assessment using two parameters, T2 signal iso-/hyperintensity and absence of calcifications, allows the estimation of growth velocity and characteristics of untreated intracranial meningiomas. Only high risk tumors harbor the potential for rapid growth. However, rapid tumor growth does not indicate a higher CNS-WHO grade per se.

P35

Training of Denoising Diffusion Models for Prediction of Real-Time Growth of Primary and Recurrent Gliomas

S Leu [1], J Wolleb [2], S Schaub [2], R Guzman [1], L Mariani [1], D Cordier [1] and P Cattin [2]

[1] University Hospital of Basel, Basel, Switzerland;
[2] Department of Biomedical Engineering, University of Basel, Switzerland

Aims: Glioma significantly limit the life expectancy of patients. Therapeutic options are so far limited and not satisfactory. Anticipation of real-time glioma growth and prediction of areas where the tumor is most likely to spread or recur would help to guide and tailor glioma therapy.
Methods: We apply deep learning algorithms to model the growth pattern of gliomas. For this, we apply denoising diffusion models to take longitudinal MR-imaging data into account, and model images from a first time point to images showing the same patient at future time points. Previous work has already used this method for weakly supervised brain tumor detection on the cross-sectional BRATS2020 dataset. We further develop this method to train the model to predict future scenarios for a given input image.
For this, we use retrospective MR images of glioma patients from at least two time points during their course of disease. We consider two different cohorts. The first one is a cohort of 100 glioma patients with primary tumors that underwent follow-up MR imaging without undergoing resection in between. A second cohort contains 100 patients with recurrent gliomas that underwent follow-up MR imaging without undergoing re-resection in between. We train a denoising diffusion model on both cohorts to predict the pattern of possible glioma growth for both cohorts separately.
Results: After completion of training, the two models are prospectively evaluated using MR images from glioma patients with primary and recurrent gliomas that were not used for training of the two models before to assess the differences between prediction and reality.
Conclusions: Models with the ability to predict real-time growth of primary and recurrent gliomas will potentially help to guide and tailor focal glioma therapies such as (re-)resection or (re-)irradiation.

P36

Towards Real-Time Integration of Polarimetric Image-Processing for Neurosurgery with Artificial Intelligence

S Moriconi [1], R Gros [2], O Rodriguez-Nunez [3], LA Felger [3], E Hewer [4], T Maragkou [2], T Novikova [5], A Pierangelo [5], P Schucht [3] and R McKinley [1]

[1] Inselspital—Universitätsspital Bern—Universitätsinstitut für Diagnostische und Interventionelle Neuroradiologie, Switzerland;
[2] Institute of Tissue Medicine and Pathology, University of Bern, Bern, Switzerland;
[3] Inselspital—Universitätsspital Bern, Switzerland;
[4] Institut de pathologie, CHUV;

[5] Laboratoire de Physique des Interfaces et des Couches Minces, CNRS, École Polytechnique, Palaiseau, France

Aim: Mueller polarimetric imaging (MPI) is a form of non-invasive imaging which can reveal properties of brain tissue and enable white matter fibre tracking. Physical parameters of wide-field MPI can reveal disrupted arrangement of white matter fibre bundles, suggesting lesions at different degrees of infiltration. This provides intra-operative guidance and enhanced visual feedback in neurosurgery. However, high-quality and accurate MPI requires long acquisitions and computationally intensive processing, impeding translation to an intra-operative setup. We aim to bridge this gap by introducing a polarimetric image-processing pipeline compatible with neurosurgical in-vivo applications.
Methods: Technical advances improve the accuracy and computational performance of MPI. Computation time is reduced by an optimised pipeline, integrating parallel computing for image processing into a framework compatible with artificial intelligence (AI) designs. Imaging time is reduced with a novel denoising architecture for polarimetric images. Diffusion networks (DDNs) boost the accuracy of low quality, short-time, single-shot scans, with a multi-fold reduction in imaging time.
Results: The MPI image-processing pipeline is validated against state-of-the-art and achieves real-time (40 ms) performance for a localised field of view and nearly real-time performance for a full wide-field scan. The accuracy of the AI-based denoising is tested on real experimental data, including healthy and diseased human brain tissues from both fresh and formalin-fixed samples, accounting for a range of physio-pathological conditions, for different noise levels and patterns, simulating realistic neurosurgical scenarios. High-quality polarimetric images were recovered from the DDNs, with significant improvements ($p < 0.05$, paired Wilcoxon rank sum test) on quantitative scores of image quality, compared to reference high-quality data. Polarimetric parameters of clinical relevance, including depolarisation, retardance and azimuth of optical axis, underlying the orientation of white-matter axonal pathways, reported minimal deviations compared to high-quality imaging data.
Conclusions: The optimised designs allow for integrating MPI into neurosurgery, with high accuracy, quality, and computational performance. Future work on downstream analyses will enable in-vivo tissue delineation, classification, and prediction for next-generation augmented visualisations in translational neuro-oncology.

P37

ChatGPT in Glioma Adjuvant Therapy Decision Making: Ready to Assume the Role of a Doctor in the Tumour Board?

L Sveikata [1], J Haemmerli [2], A Nouri [2], A May [2], K Egervari [3], C Freyschlag [4], JA Lobrinus [3], D Migliorini [5], S Momjian [6], N Sanda [7], K Schaller [6], S Tran [8], J Yeung [9] and P Bijlenga [6]

[1] Department of Clinical Neurosciences, Division of Neurology, Geneva University Hospitals;
[2] Department of Clinical Neurosciences, Division of Neurosurgery, Geneva University Hospitals, Geneva Switzerland;
[3] Department of Pathology and Immunology, Geneva University Hospitals, Geneva, Switzerland;
[4] Department of Neurosurgery, Medical University of Innsbruck, Innsbruck, Austria;
[5] Department of Oncology, Geneva University Hospitals, Geneva, Switzerland;
[6] Department of Clinical Neurosciences, Division of Neurosurgery, Geneva University Hospitals, Geneva, Switzerland;
[7] Department of Clinical Neurosciences, Division of Neurology, Geneva University Hospitals, Geneva, Switzerland;
[8] Department of Radiation Oncology, Geneva University Hospitals, Geneva, Switzerland;
[9] Department of Neurosurgery, Yale University School of Medicine, New Haven, Connecticut, USA

Objective: To evaluate ChatGPT's performance in brain glioma adjuvant therapy decision-making.

Methods: We randomly selected 10 patients with brain gliomas discussed at our institution's central nervous system tumour board (CNS TB). Patients' clinical status, surgical outcome, textual imaging information and immuno-pathology results were provided to ChatGPT V.3.5 and seven CNS tumour experts. The chatbot was asked to give the adjuvant treatment choice, and the regimen while considering the patient's functional status. The experts rated the artificial intelligence-based recommendations from 0 (complete disagreement) to 10 (complete agreement). An intraclass correlation coefficient agreement (ICC) was used to measure the inter-rater agreement.
Results: Eight patients (80%) met the criteria for glioblastoma and two (20%) were low-grade gliomas. The experts rated the quality of ChatGPT recommendations as poor for diagnosis (median 3, IQR 1–7.8, ICC 0.9, 95% CI 0.7 to 1.0), good for treatment recommendation (7, IQR 6–8, ICC 0.8, 95% CI 0.4 to 0.9), good for therapy regimen (7, IQR 4–8, ICC 0.8, 95% CI 0.5 to 0.9), moderate for functional status consideration (6, IQR 1–7, ICC 0.7, 95% CI 0.3 to 0.9) and moderate for overall agreement with the recommendations (5, IQR 3-7, ICC 0.7, 95% CI 0.3 to 0.9). No differences were observed between the glioblastomas and low-grade glioma ratings.
Conclusions: ChatGPT performed poorly in classifying glioma types but was good for adjuvant treatment recommendations as evaluated by CNS TB experts. Even though the ChatGPT lacks the precision to replace expert opinion, it may serve as a promising supplemental tool within a human-in-the-loop approach.

P38

Lateral Orbital Approaches to Resect Tumors within the Cavernous Sinus, Middle Fossa and Temporal Lobe: A Systematic Review

D Croci, M Monsour, A Tai and S Agazzi

University of Southern Florida, Tampa, FL, USA

Abstract

Introduction: Skull base tumors may invade the orbital apex, cavernous sinus (CS), middle fossa or temporal lobe. Recently, different types of orbital approaches have been described as minimally invasive techniques for the treatment of this subset of skull base tumors. Due to these tumors' proximity to the internal carotid artery and cranial nerves (CNs) II-VI, these vital structures may be at risk. With this systematic review we aimed at analyzing the typology of intracranial tumors treated through through the lateral orbital wall, and analyzing the complication rates, and outcomes.
Methods: A Pubmed/Medline search was performed using the criteria: "orbitotomy" and "lateral orbitotomy" in combination with the words "cavernous sinus", "middle fossa" and "temporal lobe". From these reports, we collected diagnoses, lesion sizes, lesion locations, approaches used, outcomes (total, near-total, subtotal resection), aesthetic outcomes, post-operative ptosis, postoperative CN palsies, length of CN deficits post-operatively, overall complications, and follow-up length.
Results: A total of 11 papers matched our inclusion criteria totaling 35 patients. 19 (54.3%) of these patients were treated for meningiomas, 6 (17.1%) for cavernous hemangiomas, and 10 (28.6%) for other pathological indications. The approaches included LO approach (n = 16; 47.1%), deep transorbital (n = 4; 11.8%), mini-LO (n = 2; 5.9%), and modified LO (n = 12; 35.3%). While not all cases reported excision success, the LO approaches achieved total (n = 15; 42.9%), near-total (n = 10; 28.6%) or subtotal (n = 9, 22.9%) resection margins. There were two mentions of CSF leak, which occurred from a typical LO and modified LO approach (5.7%). Only some reported post-operative ocular complications (including CN palsies, proptosis, or ocular disturbances) totaling 9 new CN palsies (25.7%), 3 occurrences of vision loss (8.6%), and 7 other complications (20%).
Conclusions: Orbital approaches to resect tumors located in the cavernous sinus and temporal lobe are less frequently reported compared to compared to the more standard routes. However, those approaches, especially in the era of radiosurgery where subtotal resection

with maintenance of neurological function is favorable, may become a more frequent treatment modality for these tumors, which normally require more extensive and invasive approaches. Further research is warranted to optimize these novel neurosurgical approaches.

P39

Subacute 4th Ventricle Hematoma from A Bulbar Choroid Plexus Papilloma: A Case Report

D Valsecchi and P Otten

Hôpital fribourgeois/freiburger spital HFR, Freiburg, Switzerland

Tumors and masses of the 4th ventricle are rare manifestations in adults, representing 1–5% of all intracranial lesion. Among those, the most frequent ones are the sub ependymomas, hemangioblastomas and metastasis. Other lesions, like the papilloma of the choroid plexus (CPP), count for less than 1%. We present a case of a 69-year-old female patient with progressive story of morning headache and one recent episode of vomiting, admitted and investigated at our Emergency Department. The CT-scan showed a hyper-dense mass in the posterior fossa, inside the 4th ventricle, without ventricular bleeding nor acute hydrocephalus. At the MRI the lesion was located along the floor of the 4th ventricle, it didn't enhance the contrast and had a SWI-hypersignal, with a homogeneous round shape. Our first hypothesis was about a hemorrhagic subependymoma or an exophytic brainstem cavernoma. The patient underwent a suboccipital osteoplastic craniotomy and we reached the lesion by telo-velar approach. Surprisingly the intraventricular lesion consisted of an organized and capsulated 10×10 mm hematoma at different stages of bleeding. Once performed the gross total resection, at the microscopical exploration of the floor of the 4th ventricle we identified a 2×1 mm exophytic vascular lesion, which we meticulously dissected and biopsied. The patient recovered without further symptoms and the discharge was possible 7 days after the surgery. Pathological, biological and genetic investigations of the lesion gave as result a choroid plexus papilloma without signs of malignancy. The CPP is a rare manifestation in adults and in our case it presented itself not as an intraventricular mass but as a bulbar exophytic lesion that chronically bled intro the 4th ventricle and produced the hematoma responsible of the symptoms. According to the pathological result, no further therapies were proposed. At the 6-month follow-up we did not find any sign of new bleeding nor bulbar lesion in the MRI.

P40

Management of a Large En Plaque Meningioma Featuring 3D Holographic Anatomical Reconstruction and Custom Made Cranioplasty: Technical Note

A Stauffer, E Colomo and A Küffer

USZ UniversitätsSpital Zürich, Switzerland

Aims: En plaque meningiomas, accounting for 2–9% of all meningiomas, lack management guidelines due to limited data. Surgical resection is challenging due to neurovascular structure invasion, especially venous sinuses. These tumors require specific diagnostic and therapeutic strategies. We present a 51 y/o patient with a cosmetically disturbing bony skull lesion. MRI showed a large parieto-occipital left en plaque meningioma compressing the brain parenchyma, with invasion and occlusion of the left transverse and sigmoid sinuses, and involvement of the tentorium. We propose a technical strategy for en plaque meningioma resection using a patient-specific PEEK template and implant, as well as 3D holographic rendering. We evaluated the potential of mixed reality as a future tool for performing complex craniectomies.
Methods: Automatic segmentation of the relevant intracranial anatomical structures was achieved based on MRI data using a validated expanding meshes algorithm, supplemented with manual segmentation on 3D Slicer. The resulting hologram was visualized using mixed reality glasses, enabling neurosurgeons to interact with the hologram and plan patient positioning, skin incision, craniotomy, and intraoperative trajectory. As for the oper-

ative strategy, a patient-specific PEEK implant with a craniectomy template was preoperatively manufactured. We exposed the bony tumor and excised it using multiple burr holes, followed by craniotomies along the inner and outer edges of the burr holes, guided by the previously manufactured template.
Results: The patient-specific 3D hologram assisted in patient positioning, incision planning, and craniotomy simulation. Postsurgical analysis confirmed the accuracy of the holographic model, demonstrating precise localization of the tumor borders and the corresponding craniectomy. Previous laboratory evaluations have shown the accuracy and efficacy of augmented reality headsets for planning and performing craniotomies, and their implementation on cadavers and real patients is anticipated.
Conclusions: Premanufactured templates and patient-specific implants provide excellent possibilities for craniectomy and cranioplasty in large en plaque meningiomas. Patient-specific 3D holographic technology complements craniectomy planning and may replace 3D templates. Further studies comparing augmented reality-guided craniectomies with patient-specific templates are warranted.

P41

Cranioplasty with 3d-Printed Titanium Flap in Rare Case of Isolated Cranial Meloreostosis: A Case-Report

D Valsecchi, L Sprenger, G Maestretti and P Otten

Hôpital fribourgeois/freiburger spital HFR, Freiburg, Switzerland

Background: Melorheostosis, also referred to in the literature as Leri's disease, is an unusual mesenchymal dysplasia with the clinical appearance of benign sclerosing bone dysplasia; it frequently occurs in late adolescence and typically affects the appendicular skeleton in a limited segmental fashion. Since its first description in 1922, about 400 cases of melorheostosis have been reported, either as single reports or in small case series. The craniofacial localization is anectodical and isolated skull melorheostosis has not been found in the literature.
Materials: In late 2022 we evaluated a 20-yr old female patient with a bulging lesion of the left frontal bone. The patient was asymptomatic and the main aim was an aesthetic correction. In the anamnesis we found a syndrome on Noonan. In the suspicion of an osteoma, we decided to propose an osteoclastic craniotomy with cranioplasty by custom made titanium flap 3D-printed with Electron Beam Melting (EBM) technique, according to the recent evidence in the literature about the ability to trigger osteogenic differentiation.
Result: The patient underwent the operation on 27 January 2023, with excision of the pathologic frontal bone and satisfactory cranioplasty. Discharged at day-5 postop, she didn't complain about any further symptoms. The pathological results showed a very rare diagnosis of melorheostosis of the skull, with no malignancies.
Discussion: The melorheostosis is known to be linked to RASsyndromes, among those we found also the syndrome of Noonan, as our patient had. The isolated localization on the skull is unknown and further follow up will be necessary. Three months postop the patient underwent both head MRI and CT-scan, with signs of radical excision of the known lesion and good integration of the titanium flap.

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Deep Brain Stimulation for Central Poststroke Pain Syndrome: International Multicenter Study

D Zhang [1], A Nowacki [1], KN Thuy Anh [1], A Segura Amil [1], W Eisner [2], S Bajaj [2], JK Krauss [3], A Saryyeva [3], T Aziz [4], A Green [4], GJ Elias [5], C Sarica [5], AM Lozano [5], A Franzini [6], AF Franzini [6] and C Pollo [1]

[1] Department of Neurosurgery, Inselspital, Bern University Hospital, University Bern, Bern, Switzerland;
[2] Department of Neurosurgery, Innsbruck Medical University Innsbruck Austria;

[3] Department of Neurosurgery, Hannover Medical School, Hannover, Germany;
[4] Nuffield Department of Clinical Neurosciences and Nuffield Department of Surgical Sciences, University of Oxford, United Kingdom;
[5] Division of Neurosurgery, Department of Surgery, University Health Network and University of Toronto, Toronto, Canada;
[6] Department of Neurosurgery, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy

Objective: Deep Brain Stimulation (DBS) is an established treatment option for Central Poststroke Pain Syndrome (CPSP). However, despite numerous target sites being described in the literature, the overall effectiveness and stimulation site remains elusive. The objective of the present study was to determine longterm outcomes of DBS for CPSP and possible predictors of outcome in an individual patient data meta-analysis. Further objectives were to construct a stimulation map of effective DBS and to obtain differences of connectivity profiles by comparing lesion network between responders and non-responders.
Methods: We invited investigators of published cohorts of patients undergoing DBS for CPSP, identified by a systematic review of MEDLINE from inception to January 2019, as well as previously unpublished cohorts to provide individual patient data on baseline parameters, pre-and postoperative pain scores at 12-month and individual image data. DBS leads were reconstructed and projected onto a three-dimensional stereotactic atlas. A stimulation map was constructed based on individual stimulation parameters. Furthermore, we projected stroke lesions into a normalized human connectome and obtained individual lesions' connectivity profiles.
Results: Among 39 eligible patients from six different cohorts, we found 16 (41%) responders with pain relief according to the Visual Analogue Scale (VAS) of at least 30% at 12-month follow-up, from which 14 (36%) had a pain improvement of at least 50%. Stimulation mapping identified the Posterior Limb of Internal Capsule (PLIC) to be associated with good outcomes. Due to the small sample size, no statistical testing could be applied. Baseline characteristics and connectivity profiles were not different between responders and non-responders.
Conclusions: This multicenter study confirms the effectiveness of DBS for CPSP in a relevant number of patients. Although the PLIC was identified as a possible stimulation sweet spot, no statistically significant predictors of outcome could be identified. Further well-designed prospective trials incorporating new stimulation paradigms are highly warranted.

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Evaluation of Virtual Reality in Neurosurgery for Patients' Understanding and Satisfaction

K Binda [1], GN Castro Fernandes [2], J Fournier [2] and A Simonin [2]

[1] Université de Lausanne (UNIL), Switzerland;
[2] Hôpital de Sion, Switzerland

Background: Virtual reality is increasingly used during neurosurgical training but rarely used to inform and educate patients. To date, studies evaluating the use of virtual reality to improve patient understanding are limited, and to the best of our knowledge, no such study has yet been performed in the field of neurosurgery. Therefore, the aim of this study was to evaluate in the context of spinal fractures whether virtual reality increased patients' understanding and satisfaction.
Methods: Patients with a spinal fracture who were to undergo neurosurgical surgery were prospectively registered in this study (n = 19). These patients performed the routine imaging protocol and were subsequently randomized to undergo preoperative standard consultation through the use of 2D CT or MRI images or by the use of VR. Two questionnaires, one for understanding and the other for satisfaction, were specifically created and presented to the participants following their preoperative consultation. The results of the two groups were compared using the two-sample t-test and the Mann-Whitney U test.

Results: All 19 patients responded to the two questionnaires. 10 patients performed the consultations with VR and the other 9 underwent standard consultations. There were 2 females and 17 males. Mean age was 48.0 ± 17.6. Patients who benefited from VR had slightly better understanding and satisfaction outcomes overall, but statistical analysis showed that the latter were not considerably important to be significant (understanding: average 23.7/25 vs. 19.4/25, $p = 0.226$; satisfaction: average 30.2/32 vs. 28.6/32, $p = 0.472$).
Conclusions: The use of VR did not show a significant improvement of patient's understanding nor satisfaction in our study. However, average comprehension and satisfaction were high in both groups and the number of participants may be too small to show a significant positive effect.

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Spinal Intradural Extramedullary Cystic Schwannoma: A Case-Based Systematic Review

APR Terrapon, M Stienen, O Bozinov and N Hejrati

Kantonsspital St. Gallen, Switzerland

Aims: Schwannomas are the second most common intradural extramedullary tumors, but they rarely present as predominantly cystic intradural lesions. Thus, such lesions may be misdiagnosed which may delay optimal treatment. Because of their rarity, cystic schwannomas are only reported in a few case reports and series. As a result, a standardized approach in the management of these tumors remains challenging to establish. The aim of this study is to compile all reported cases of the published literature in order to report on potential management strategies and the perioperative course of patients with such lesions.
Methods: We conducted a systematic review, searching the MEDLINE and CENTRAL databases on 2 June 2023 for spinal intradural extramedullary cystic schwannomas. All title/abstracts were screened, and a full-text review of the remaining articles was conducted. The results were compiled in a table and summarized using means accompanied by standard deviation, median by interquartile range, and percentages by 95% confidence intervals. We then added an additional case treated at our institution.
Results: We identified 263 articles, of which 35 articles reporting 54 cases of predominantly cystic intradural, extramedullary schwannomas were included. Patients had a mean age of 48 years (SD ± 13.14 years) at presentation, 57% were males, and most lesions were lumbar (43%). The most common symptoms were pain (81%) and muscle weakness (67%) with 83% of patients showing some sort of neurological abnormality. 69% of patients showed a complete relief of symptoms after surgery and 96% an improvement. Only four complications were reported. Additionally, we present a case of a 44-year-old female with back pain, mild paraparesis, sub T12 hypoesthesia, gait ataxia, and sphincter dysfunction with a cystic schwannoma extending from T7 to T11. The patient underwent microsurgical complete resection and showed significant improvements following surgery.
Conclusions: Schwannomas should be considered in the differential diagnosis of intradural extramedullary cystic lesions. Patients typically present with subacute to chronic pain and/or neurologic changes. Surgical resection is the primary therapeutic modality and usually has an excellent outcome.

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An Explainable Multicentric Analysis for Understanding the Aetiology of Intracranial Aneurysm Disease

M Delucchi [1], G Spinner [2], P Bijlenga [3], S Morel [4], IC Hostettler [5], D Werring [6], M Wostrack [7], B Meyer [7], R Bourcier [8], A Lindgren [9], MK Bakker [10], YM Ruigrok [10], R Furrer [11] and S Hirsch [2]

[1] Centre of Computational Health, Institute for Computational Life Sciences, Zurich University of Applied Sciences (ZHAW); Department of Mathematics, University of Zurich, Zürich, Switzerland;

[2] Centre of Computational Health, Institute for Computational Life Sciences, Zurich University of Applied Sciences (ZHAW), Switzerland;
[3] Neurosurgery, Department of Clinical Neurosciences, Geneva University Hospitals and Faculty of Medicine, University of Geneva, Switzerland;
[4] Neurosurgery, Department of Clinical Neurosciences, Geneva University Hospitals and Faculty of Medicine, University of Geneva; Department of Pathology and Immunology, Faculty of Medicine, University of Geneva, Switzerland;
[5] Stroke Research Centre, Department of Brain Repair and Rehabilitation, University College London, Institute of Neurology; Department of Neurosurgery, Canton Hospital St. Gallen;Department of Neurosurgery, Technical University of Munich, School of Medicine;
[6] Stroke Research Centre, Department of Brain Repair and Rehabilitation, University College London Institute of Neurology, United Kingdom;
[7] Department of Neurosurgery, Technical University of Munich, School of Medicine, Germany;
[8] Institut National de la Santé et de la Recherche Médicale, Centre National de la Recherche Scientifique, University Hospital Centre Nantes, University of Nantes, L'institut Du Thorax, France;
[9] Neurosurgery NeuroCenter Kuopio, University Hospital Kuopio; Institute of Clinical Medicine, Faculty of Health Sciences, University of Eastern Finland; Department of Clinical Radiology, Kuopio University Hospital;
[10] Department of Neurology and Neurosurgery, University Medical Center Utrecht Brain Center, Utrecht University;
[11] Department of Mathematics, University of Zurich, Zürich, Switzerland; Institute of Computational Science, University of Zurich, Zürich, Switzerland

Aims: Intracranial aneurysms (IAs) are present in approximately 3% of the population [Vlak et al., 2011]. Rupture of IA leads to an aneurysmal subarachnoid haemorrhage with often poor functional outcomes [Lawton and Vates, 2017]. Unruptured IA (UIA) detection rates increase with advances in imaging technologies [Bijlenga et al., 2017]. The complexity of UIA treatment decision making is compounded by the difficulty of accurately predicting the risk of rupture and the lack of understanding of how modifiable factors affect IA rupture [Lognon et al., 2022]. Here, we show an explainable model for IA rupture based on easily accessible phenotypic risk factors.
Methods: This model development study was validated on IA patient-level registry data in a multicenter ($n = 7$) retrospective case-control design with 9 phenotypic risk factors. Data were analysed using discrete and additive Bayesian network (BN) models. Expert knowledge a priori restricted the model search space, leading to a sparse network representing clinical expertise [Delucchi et al., 2022].
Results: We included 8604 patients with IA (median age 54y, IQR 45−63, 67% female), of whom 4254 (49%) patients had IA at the time of diagnosis. The point prevalence of recommended follow-up patients with UIA [Bijlenga et al., 2013] was estimated to be approximately 43%. The joint probability distribution estimates patient-specific disease management recommendations. Preliminary results indicate, for example, that older women with an IA in a low-risk location are unlikely to experience a rupture (OR_{rupture} = 0.05), and patients who are active smokers at the time of IA diagnosis generally have a higher likelihood to be diagnosed with a ruptured IA (OR_{rupture} = 1.46).
Conclusions: This study shows that mixed-effect additive BNs can help clinicians understand the aetiology of IA rupture and may have potential for providing personalised guidance for UIA management. Our findings anticipate the starting point for IA disease models that encompass the entire evolution of the disease and could be refined in a more extensive prospective cohort study to develop a user-friendly bedside decision support application.

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Supervised Machine Learning Methods to Identify Muscles from MEP Traces—A Proof of Concept Design

Q Parduzi

Luzerner Kantonspital, Switzerland

Aims: Even for an experienced neurophysiologist, it is challenging to look at a single graph of an unlabeled motor evoked potential (MEP) and identify the corresponding muscle. We demonstrate that supervised machine learning (ML) can successfully perform this task and surpass trained neurophysiologists.
Methods: Intraoperative MEP data from surgery on 36 patients was included for the classification task with 4 muscles: Extensor digitorum (EXT), abductor pollicis brevis (APB), tibialis anterior (TA) and abductor hallucis (AH). Three different supervised ML classifiers (random forest (RF), k-nearest neighbors (kNN) and logistic regression (LogReg)) were trained and tested on either raw or compressed data (PCA or feature extracted). Patient data was classified considering either all 4 muscles simultaneously, 2 muscles within the same extremity (EXT versus APB), or 2 muscles from different extremities (EXT versus TA). For comparison, we asked 30 experienced neurophysiologists to carry out a similar 4-muscle classifying task with MEP data from one patient.
Results: In all cases, RF classifiers performed best and kNN second best. The highest performances were achieved on raw data. In the 4-muscle comparison, the RF classifier achieved an accuracy of 83%. Across limbs (EXT versus TA) it reached 97% accuracy, while in the within limb comparison (EXT versus APB) the dropped to 89%. On the other hand, human performance reached 64% accuracy on the 4-muscle comparison.
Conclusions: Standard ML methods show surprisingly high performance on a classification task with minimally processed intraoperative MEP signals. This study illustrates the power and challenges of standard ML algorithms when handling intraoperative signals. Ultimately, ML might help improve warning criteria in IOM and safety in the operating room.

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Does the Entry Site Affect the Rate of Proximal Catheter Misplacement in Ventriculoperitoneal Shunt Insertion?

F Ebel [1], S Amstutz [2], S Wanderer [3], M Unterhose [3], N Toulany [3], L Mariani [1], R Guzman [1], S Marbacher [3] and J Soleman [1]

[1] Department of Neurosurgery, University Hospital of Basel, Basel, Switzerland;
[2] Faculty of Medicine, Basel;
[3] Department of Neurosurgery, Kantonsspital Aarau, Aarau, Switzerland

Background. The insertion of a ventriculoperitoneal shunt (VPS) is a frequent neurosurgical procedure, but the optimal entry site of the ventricular catheter is still under debate. Our study compares the parietal (Keen's) and frontal (Kocher's) entry sites regarding the rate of proximal catheter misplacement.
Methods: We retrospectively analyzed data of consecutive adult patients ($\geq$18 years) from two Swiss Neurosurgical centers who received a primary VPS between 2010 and 2020. In center A, the ventricular catheter's entry site was frontal (group A), and in center B, parietal (group B). The primary outcome was the rate of ventricular catheter (VC) misplacement, defined as a misplacement requiring revision surgery. Secondary outcomes were the functional outcome, measured through the modified Rankin Scale (mRS), the rate of revision surgery due to any type of VPS dysfunction and infection as well as the 30-day mortality rate. Logistic regression analysis was used to identify predictive factors for revision surgery due to VC misplacement.
Results: We included 539 patients in the analysis, while 301 patients (55.8%) were allocated to group A and 238 patients (44.2%) to group B. The postoperative rate of revision surgery due to misplacement was comparable between both groups (group A: 17 patients (5.6%); group B: 11 patients (4.6%); $p = 0.594$). The rate of good functional outcome (mRS $\leq$ 2) did not differ between group A (n = 164, 75.6%) and B (n = 174, 76%; p = 0.058). The rate of revision surgery due to any type of VPS dysfunction (group A: 10 patients (3.3%); group B: 10 patients (4.2%); $p = 0.592$) and infection (group A: 22 patients (7.3%); group B: 10 patients (4.2%); p = 0.13) was comparable as well. The 30-day mortality rate showed no difference

between the groups (group A: 5 patients (1.7%); group B: 6 patients (2.5%); $p = 0.483$). In the multivariable logistic regression analysis, postinfectious hydrocephalus was found to be predictive for revision surgery due to VC misplacement (OR 7.6, 95%CI (1.34–43.02), $p = 0.022$).

Conclusion: The entry site of the ventricular catheter in VPS surgery does not seem to affect proximal revision rates due to catheter misplacement. Similarly, overall VPS revision rates, functional outcome, and 30-day mortality are comparable, independent of the entry site.

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Pediatric Neurosurgery Training during Residency in Switzerland and the Need for Dedicated Subspecialization Training

L Greuter [1], M Licci [2], R Guzman [3] and J Soleman [3]

[1] Universitaetsspital Basel;
[2] University Hospital of Basel;
[3] University of Basel/University Hospital Basel, Switzerland

Introduction: Pediatric Neurosurgery as its own subspeciality started to emerge during the late 1950-is in the Western world, with only a few dedicated pediatric neurosurgeons. Over the last few decades, the awareness that children require subspecialized care by dedicated pediatric neurosurgeons and an interdisciplinary team has been growing worldwide, leading to an increase in pediatric neurosurgeons. Several studies have shown that subspecialized care for pediatric patients is cost-effective and improves outcome. The aim of this survey is to assess the current training of neurosurgical residents in pediatric neurosurgery in Switzerland.

Methods: We conducted an online survey by sending e-mail invitations to all neurosurgical residents in Switzerland. The survey included questions regarding the participants' demographics, current workplace structures, specific pediatric neurosurgical pathologies, and participants' opinions of the Swiss pediatric training program and possible improvement. We defined at the beginning of the survey that a pediatric neurosurgeon is a fully board-certified general neurosurgeon with at least one year of dedicated pediatric neurosurgical fellowship training abroad.

Results: We included a total of 25 residents, of which 20 (80%) were male. Twenty-two participants (88%) worked in an A-clinic at the time of the survey, and four (16%) were interested in pursuing a fellowship in pediatric neurosurgery. Seven residents (35%) feel comfortable taking care on the ward of a patient with craniosynostosis, five residents (25%) feel confident taking care of a hydrocephalus patient younger than 6 months, and 12 residents (60%) feel comfortable taking care of a pediatric brain tumor patient. A majority ($n = 22$, 88%) of all residents agree that a fellowship-trained pediatric neurosurgeon should treat children, while two (8%) residents state that any neurosurgeon interested in pediatric neurosurgery should be able to treat children. All residents ($n = 25$, 100%) agree that pediatric neurosurgery training in Switzerland needs to be improved.

Conclusions: Pediatric neurosurgery training in Switzerland is very heterogeneous, with varying frequencies of children-specific neurosurgical pathologies. Most residents agreed that a subspecialized pediatric neurosurgeon should oversee the care of children in neurosurgery, while all agree that pediatric neurosurgical training should be improved in Switzerland.

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Establishing a Virtual Reality Database of Pediatric Craniosynostosis Cases: An Innovative Approach for Enhanced Teaching and Learning

S Schmid [1], A Saemann [1], M Licci [1], M Zelechowski [2], B Faludi [2], P Cattin [2], J Soleman [1] and R Guzman [1]

[1] Department of Neurosurgery, University Hospital Basel;

[2] Department of Biomedical Engineering, University of Basel, Switzerland

Aims: Due to craniosynostosis's variability and anatomical complexity, three-dimensional visualization is critical for teaching, enabling a thorough understanding of the pathology. We established a VR Database with 3D models of the deformities to depict the individual anatomy. We focused on evaluating teaching and understanding regarding efficiency, motivation, and memorability compared to established non-VR methods such as 2D illustrations.
Methods: All craniosynostosis cases with available preoperative computed tomography (CT) imaging and surgically treated at our institution from 2012–2022 were included. The preoperative CT scans were exported as DICOM data and imported to SpectoVR (Specto Medical, https://spectomedical.com) with a specifically designed function segmenting bony structure. All measurements, sub-segmentation, and anatomical planning were done using a headset system in a full-immersive 3D VR experience. Teaching was performed in group settings with students and medical personnel in a multiplayer view, where the group is simultaneously immersed in one VR setting and can explore and discuss the 3D model under the guidance of a host. Their experience was evaluated through a specifically designed questionnaire, considering different aspects, such as improving understanding, memorization, and motivation, from poor (1) to outstanding (5).
Results: 37 cases with multiple types of craniosynostosis were included in our 3D VR Library. The questionnaire results showed very satisfactory scores (4.5 ± 0.2) across all evaluated qualities. All 17 participants attested an increased understanding (mean 4.3 ± 0.77) and memorization (mean 4.2 ± 0.8) with the 3D VR models compared to standard non-VR methods. Explanations could be followed more easily using 3D VR models (mean 4.6 ± 0.6), and a faster understanding (mean 4.4 ± 0.7) as well as increased motivation to the learning process (mean 4.3 ± 0.9) was reported, resulting in the notion that teaching gets more efficient (mean 4.8 ± 0.6) with 3D VR models.
Conclusions: Establishing a 3D VR database for teaching in craniosynostosis has shown advantages in improving and speeding up the understanding and memorization process and increasing the motivation for the study process, thereby allowing for more efficient learning. Future applications in patient consent and teaching in other medical areas should be explored further.

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Changes in Ventricular Volume after Treating Aqueduct Stenosis through Endoscopic Third Ventriculostomy in Adults

F Ebel, R Guzman and J Soleman

Department of Neurosurgery, University Hospital of Basel, Basel, Switzerland

Background. Endoscopic third ventriculostomy (ETV) is an established neurosurgical intervention for treating aqueduct stenosis. Evaluation of ventricular size often relies on linear measurements and indexes such as the Evans Index (EI), which can be imprecise and subject to interpretation. The aim of this study is to analyze changes in ventricular volume following ETV and evaluate its suitability as a monitoring tool for clinical outcomes.
Methods. We retrospectively analyzed data of consecutive adult patients in whom an ETV has been performed between 2010–2020 for treating obstructive hydrocephalus due to an aqueduct stenosis. Volumetric analysis was performed by a semi-automated segmentation tool (Sectra IDS7 volume measurement tool), employing thin-slice MRI or CT images to measure ventricular volume and the EI. Descriptive analysis was used to analyze changes in lateral and third ventricle (LTV) volume and EI, and correlation with improvement in clinical symptoms was assessed. Preoperative images were used as the baseline for measurements, while the first postoperative image was typically obtained between 1–5 days after surgery. The last follow-up imaging was used for subsequent measurements. Values are reported as mean $\pm$ standard deviation.

Results. Forty-six patients underwent ETV for treating aqueduct stenosis. Postoperatively (3.1 ± 2.5 days), the LTV volume decreased by an average of 21.2 ± 17.7 mL. The relative postoperative decrease in LTV volume (-16.7%) was significantly higher than the reduction observed in the EI (−5.6%; $p < 0.001$). Until the last follow-up (25.6 ± 23.3 months), the LTV volume continued to decrease significantly (15.3%), whereas the EI showed a minor reduction (3%; $p = 0.023$). Clinical symptoms improved in 69.6% of patients at discharge and 78.8% during the last follow-up. There was no association between the amount of LTV volume reduction and clinical improvement during the follow-up period.
Conclusion. The volumetric analysis provides a more accurate representation of ventricular size changes following ETV for aqueduct stenosis and demonstrates a significantly greater reduction in LTV volume postoperatively and during the follow-up period compared to the EI. The rate of volume reduction does not seem to correlate with clinical improvement.

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Single Center Experience on Robotic Biopsy in Pediatric Brain Stem Tumors—A Quality Control Study Regarding Feasibility, Diagnostic Yield and Safety

A Stauffer [1], CM Kuzan-Fischer [1], F von Faber-Castell [2], L Tosic [3] and N Krayenbühl [1]

[1] Universitäts Kinderspital Zürich;
[2] St. Michael's Hospital;
[3] Klinik für Neuro- und Wirbelsäulenchirurgie Zentralschweiz, Switzerland

Aim: Until today, only few pediatric centers carry out robotic stereotactic biopsy, that has first been performed in 1985, and its use has rarely been reported in a pediatric population. We aim at evaluating its feasibility, diagnostic yield, and safety.
Methods: We retrospectively analyze performance and outcome of biopsies carried out with the NeuroMate surgical robot (Renishaw, Gloucestshire, UK) in our clinic from March 2019 to June 2023 in children presenting with brain stem lesions. All patients received preoperative MRI. Neuro Inspire Software is used for planning of the trajectory. The target is based on gadolinum enhancement and/or flair hyperintensity.
Surgical procedure: General anesthesia. Positioning of patient's head in a Leksell frame, that will later be rigidly attached to the NeuroMate base. CT scan and matching with preoperative MRI. Surface registration, automatic adjustment of robotic arm along the planned trajectory. 2.4 mm burr hole trepanation with robotic guidance and puncture of the dura. Performing of biopsy using the robotic arm with a stereotactic needle. Ad hoc histopathological analyzation of first staged biopsy. After receiving confirmation by pathology that tumor content was enough, extraction of further 2–3 samples for definite analysis. Collection of needle wash for further analysis. No regular postoperative imaging in postinterventional neurologically unchanged patients.
Results: 36 patients underwent robot-guided biopsy of a brain stem lesion. Mean age was 7.6 (1–16) years. 21 (58.3%) patients received previous radiation. Definitive histopathological analyzation revealed 31 diffuse intrinsic pons gliomas (DIPG), 3 low grade gliomas, and 1 ganglioglioma. 1 biopsy remained inconclusive. Mean duration of the surgery was 125 minutes. In all but one cases, intraoperative diagnostic of the tissue was conclusive, and congruent with the definitive histopathological diagnosis in 97.2%. A histological diagnosis resulted in 35/36 cases, resulting in a diagnostic yield per biopsy of 97.2%. There was transient worsening of symptoms in 3 patients (hypaesthesia, dysarthria and paresis). No permanent morbidities, and no mortality occurred. Mean length of postinterventional hospital stay was 2.05 (1–4) days, all patients were discharged home.
Conclusions: Robot guided stereotactic biopsy of brain stem lesions is fast, safe, and ensures excellent diagnostic yield. We consider it standard technique in the diagnostic of lesions suspicious of DIPG.

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Feasibility and Accuracy of CARLO© Guided Unroofing of The Optical Canal

M Schicker [1], TT Ha [1], Y Luder [1], D Cordier [1], M Marowska [2] and M Röthlisberger [1]

[1] Universitätsspital Basel;
[2] Advanced Osteotomy Tools AG, Basel, Switzerland

Introduction: The surgical procedure known as optic nerve unroofing plays a vital role in skull base surgery. This critical intervention focuses on relieving pressure and decompressing the optic nerve to safeguard vision, restore optimal nerve function, and enhance the surgical view during aneurysm therapy. Nevertheless, the surgical procedure presents inherent challenges and risks due to factors like limited working space, restricted surgical view, and the proximity to critical anatomical structures, including the optic nerve, carotid artery and oculomotor nerve. Significant advancements in medical robotics technology hold promise for addressing these challenges and potentially enhancing multiple aspects of neurosurgery.
Aims: The objective of this study was to evaluate the feasibility and precision of utilizing CARLO© (Cold Ablation Roboter-guided Laser Osteotome) for delineating the boundaries of the optical canal. Additionally, the investigation involved the insertion of a thermal probe into the optical canal to assess the occurrence of significant heat damage resulting from the removal of the optic roof. Success was defined as the accurate excavation of the optical canal, which was confirmed through post-experimental CT scans and photographic documentation.
Methods: The experiment utilized five fresh frozen skulls, securely fixed in a Mayfield clamp. Prior to the procedure, preoperative planning was conducted using NeuroPlan©, which accurately segmented crucial anatomical structures and devised trajectories with a safety margin of 2 mm from high-risk areas. A navigation system and additional referencing screws were employed to achieve precise bone ablation. The target structure was accessed through a pterional craniotomy and the optical canal was prepared extradurally.
Results and Conclusions: While data evaluation is ongoing, preliminary results indicate a successful delineation of the optical roof without significant heat damage while preserving vital anatomical structures. These initial findings have the potential to stimulate further investigation into the applications of robotic and laser technologies in the realm of neurosurgery. The study emphasizes the feasibility and exceptional precision of robotic technology, which can be utilized to advance the development of additional procedures to improve patient outcomes and reduce perioperative risks in neurosurgical interventions.

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Microsurgical Implantation of a Microprism for High-Resolution Optical Access to the Mouse Anterior Cingulate Cortex

D Kiss-Bodolay [1], K Schaller [1] and A Holtmaat [2]

[1] Hôpitaux Universitaires de Genève (HUG);
[2] Université de Genève, Switzerland

Aims: In vivo high-resolution optical imaging through cranial windows in mice is a powerful method for studying the relationship between neuronal activity, behaviour and learning. However, neurons in the brain's medial prefrontal areas such as the anterior cingulate cortex (ACC) cannot be reached through conventional cranial windows due their deep interhemispheric localization, obscured by the superior sagittal sinus. Angular reflecting micromirrors may provide a means to gain optical access. Using laboratory microsurgical tools and mouse models we aimed at:
1. the surgical implantation of a microprism in the brain's longitudinal fissure along the anterior cingulate cortex, while sparing local vascular and bony microanatomy
2. providing proof of concept for using the implant to gain long-term, high-resolution optical access, and the standardization of a surgical protocol

Methods: Laboratory surgical loop (M80, Leica) and microsurgical instruments were used to examine prefrontal bone and vascular microanatomy, and to stably implant a 1.5 mm microprism attached to a 3 mm glass window, subdurally in the interhemisperic fissure facing the ACC. We combined viral vector-based gene transfer and 2-photon laser scanning microscopy (2PLSM) to monitor neuronal structures and activity.
Results: We succeeded in stably implanting microprisms in the sagittal fissure avoiding detrimental damage to the local bony and vascular structures, as well as to the brain parenchyma. These implants proved suitable for gaining optical access over days to weeks. Using 2PLSM, we repeatedly imaged populations of individual neurons and subcellular compartments thereof in the ACC. We provide proof of concept by imaging dynamic synaptic structures and by showing that neurons are bimodally responsive to environmental stimuli during fear learning.
Conclusions: We developed a novel microsurgical protocol to aid brain researchers in gaining access to the mouse ACC. The protocol includes step by step illustrated explanations, a trouble shooting section, and a proof of concept for high-resolution imaging of ACC. In the future, this protocol may be extended to larger animals and even primates.

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No Correlation of Length of Posterior Rib Remnant with Postoperative Outcome after Supraclavicular First Rib Resection for Thoracic Outlet Syndrome (TOS)

C Bauer

Neurozentrum Oberaargau, Langenthal, Switzerland

Aims: To assess the impact of length of posterior rib remnant on outcome of supraclavicular first rib resection for Thoracic Outlet Syndrome (TOS).
Methods: In a prospective study all patients undergoing supraclavicular first rib resection for TOS since 2016 have been enrolled. Patients had to complete Quick DASH (Disability of the Arm, Shoulder and Hand) and CBSQ (Cervical Brachial Symptom Questionnaire) before and 4 to 24 months after operation and report the percentage of improvement after operation. Length of rib remnant was measured on postoperative routine thorax X-ray from costovertebral joint to resection margin in mm.
Results: 108 supraclavicular first rib resections for TOS have been perfomed in 89 patients (21% bilateral). 74% were female, average age was 38 years (18–66). Patients rated the postoperative outcome as 79% improvement. 13 patients were unable to rate the postoperative improvement in percent or were lost to follow up. Quick DASH scores showed an improvement of 65% (66 preoperative vs. 23 postoperative) and CBSQ scores an improvement of 70% (88 preoperative vs. 26 postoperative). Average length of rib remnant was 21 mm (8 to 38 mm). Analysis of subgroups revealed no correlation of length of rib remnant with postoperative Quick DASH or CBSQ scores respectively, but good correlation of self assessed improvement in percent and percentage of improvement of postoperative scores of Quick DASH and CBSQ.
Conclusions: Quick DASH and especially CBSQ are reliable tools in evaluating outcome after surgery for TOS. Subgroup analysis revealed no correlation of length of posterior rib remnant with postoperative outcome. Supraclavicular first rib resection for TOS can offer consistently good long term results with high patient satisfaction in carefully selected patients.

P55

Directional Recordings of Somatosensory Evoked Potentials from the Sensory Thalamus in Chronic Poststroke Pain Patients

D Zhang [1], A Nowacki [1], PA Alvarez Abut [1], J Wermelinger [1], J Rosner [2] and K Seidel [1]

[1] Department of Neurosurgery, Inselspital, Bern University Hospital, University Bern, Bern, Switzerland;
[2] Spinal Cord Injury Center, Balgrist University Hospital, University of Zurich, Zurich, Switzerland

Background: The aim of this feasibility study was to investigate the properties of median nerve somatosensory evoked potential (SEPs) recorded from segmented Deep Brain Stimulation (DBS) leads in the sensory thalamus and how they relate to clinical and anatomical findings.
Methods: We analyzed four patients with central post-stroke pain and DBS electrodes placed in the ventral posterior nucleus (VPL/VPM). Median nerve SEPs were recorded with referential and bipolar montages. Electrode positions were correlated with thalamus anatomy and tractography-based medial lemniscus. Early postoperative clinical paresthesia mapping was performed by an independent pain nurse. Finally, we performed frequency and time-frequency analyses of the signals.
Results: We observed differences of SEP amplitudes recorded along different directions in the VP thalamus. SEP amplitudes did not clearly correlate to both atlas-based anatomical position and fiber-tracking results of the medial lemniscus. However, the contacts of highest SEP amplitude correlated with the contacts of lowest effect-threshold to induce paraesthesia.
Conclusions: Directional recordings of thalamic SEPs bear the potential to assist clinical decision-making in DBS for pain.

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Model to Simulate Brain Biopsies Using a Navigated Robotic Guiding System and a Bone Cutting Laser

TT Ha [1], Y Luder [1], M Röthlisberger [1], M Schicker [1], M Morawska [2] and D Cordier [1]

[1] Universitätsspital Basel;
[2] AOT Swiss (Advanced Osteotomy Tools), Basel, Switzerland

Brain biopsies are necessary in cases of unclear lesions on imaging studies to establish a treat-ment plan based on the histologic diagnosis. A previous study investigated the potential of lasers to make brain biopsies less invasive, faster and safer. The study demonstrated that lasers can create highly precise burr holes which themselves can act as a sufficient guide for the biopsy needle. Furthermore, lasers can create tangential canals in the bone which allows to biopsy brain regions that are usually impossible or hazardous to access. Building upon the results of the pre-vious study, further research and technological advancements were pursued. This includes a biopsy needle attachment for the robot, which will be used to simulate brain biopsies using CARLO© (Cold Ablation Robot-guided Laser Osteotome) with its Er:YAG laser and navigated robotic guiding system. The study utilizes five freshly frozen skulls, which are immobilized us-ing a Mayfield clamp. Prior to conducting the experiment, the NeuroPlan© software is employed to plan the path and angle of the biopsies. To align the pre-experimental CT with the skull, refer-encing points on the skull and its surface are registered using a pointer. A small skin incision is performed to reach the area of bone where the laser ablates the bone for the biopsy. Preliminary experimental results suggest that the combined use of laser ablation and a guidance device ena-bles precise bone ablation and accurate needle guidance for biopsies. These initial results demonstrate the potential of integrating laser technology and robotics in neurosurgery, potential-ly enabling less invasive, faster and safer biopsies, ultimately leading to better patient outcomes.

P57

Primary Pituitary Germinoma after Resection of a Mature 3rd Ventricular Teratoma: A Case Report and Review of the Literature

TJ Hallenberger [1], E von Seth [2], M Roethlisberger [1], R Guzman [1] and J Soleman [1]

[1] Universitätsspital Basel, Switzerland;
[2] Department of Neuroscience, Kings College London, United Kingdom

Introduction: Intracranial germ cell tumours (iGCTs) are rare and account for approx. 3–4% of all paediatric brain neoplasms. It is even rarer, that a second, completely unrelated, histologically different iGCT occurs in the same patient. We herein report such a case, discuss the literature and potential pathophysiological mechanisms leading to this phenomenon.
Case: A 9-year-old boy presented with new onset impaired balance, headaches, nausea, visual disturbances and left facial paresis. MRI scans revealed a third ventricular mass originating from the pineal gland causing obstructive hydrocephalus. After biopsy, a mature teratoma was diagnosed and resected. Postoperative recovery was good and the patient was able to return to normal daily activities. Three and a half years after initial tumor resection, on follow-up MRI, a new slowly progressive lesion in the suprasellar region was detected and after significant growth a biopsy revealed a de-novo developed pure germinoma. The patient was treated with radio-chemotherapy and remained relapse free at last follow up. We identified 16 other cases reporting a primary mature teratoma with histological different iGCT after surgical removal in the literature. Median time between those lesions appears to be around 5 years and there are three main hypotheses discussed regarding development of this phenomenon, yet none can completely account for the observed phenomenon.
Conclusions: Although rare, treating physicians should be aware of the possibility of recurring or de-novo development of iGCTs after treatment of a primary iGCT. Hence, close image and laboratory follow-up should be recommended while further studies are necessary to describe the exact pathomechanism behind this phenomenon.

P58

Polarimetric Markers for Delineation of Lesional Margins during Brain Tumor Surgery

O Rodríguez-Núñez [1], L Felger [1], R Gros [2], T Maragkou [2], R Mckinley [3], S Moriconi [3], T Novikova [4], A Pierangelo [4] and P Schucht [1]

[1] Department of Neurosurgery, Bern University Hospital, Inselspital Bern, Switzerland;
[2] Institute of Tissue Medicine and Pathology, University of Bern, Bern, Switzerland;
[3] Support Center for Advanced Neuroimaging (SCAN), University Institute of Diagnostic and Interventional Radiology, University of Bern, Inselspital, Bern University Hospital, Switzerland;
[4] LPICM, CNRS, Ecole polytechnique, IP Paris, Palaiseau, 91128, France

Aims: Intraoperative identification of the border between healthy brain and tumor tissue is often difficult for neurosurgeons. Poor delineation of tumor boundaries represents a risk factor for incomplete resection and postoperative neurological deficits. In this study, we evaluated the potential of wide-field imaging Mueller polarimetry (IMP) for the visualization of fiber tracts of healthy brain by measuring the optical anisotropy and scattering properties of brain tissue. Identifying the fiber tracts based on their spatial orientation reconstructed from IMP data during brain surgery would allow the delineation of "fiberless" tumors for safe and complete brain tumor resection.
Methods: We implemented a wide-field IMP system operating in a visible wavelength range to visualize the white matter fiber tracts using the maps of depolarization, scalar linear retardance and azimuth of the optical axis (polarimetric markers) calculated from the recorded Mueller matrix images. The instrument is composed of a white light source, followed by the polarization state generator for modulation of the incident light beam illuminating the sample. Light reflected/scattered by a sample is collected in the detection arm that includes the polarization state analyzer, followed by the spectral filters and a focusing system to generate the image on the camera. We tested our IMP system on two fresh cadaveric calf brain specimens and on one fresh human surgical specimen which featured tumoral as well as non-tumoral tissue.
Results: The acquired polarimetric images of all three specimens showed higher mean values of linear retardance and depolarization for cerebral white matter than for gray matter. The orientation of the fiber tracts is well represented by the azimuth of the optical axis for all brain tissue areas assessed. In the surgical specimen we found a contrast between the

strong orientation of the fiber tracts (tumor-free tissue) and the random orientation (tumor tissue) in the azimuth of the optical axis.
Conclusions: Our results demonstrated that for the assessed thick sections of brain tissue, the presence and orientation of white matter fiber tracts are clearly detectable using polarimetric markers. We showed that the wide-field IMP system is a promising stain-free and non-invasive tool to identify tumor margins (indirectly, by detecting white matter fiber tracts) during brain tumor surgery.

P59

Long-Term Blood Pressure Variability is Associated with White Matter Microstrucutral Injury, Lacunes and Microinfarcts in Cerebral Amyloid Angiopathy

L Sveikata [1], MC Zanon Zotin [2], D Schoemaker [2], Y Ma [3], VP Perosa [2], A Chokesuwattanaskul [2], A Charidimou [2], M Duering [4], EM Gurol [2], F Assal [1], SM Greenberg [2] and A Viswanathan [2]

[1] Department of Clinical Neurosciences, Division of Neurology, Geneva University Hospital and Faculty of Medicine, University of Geneva, Switzerland;
[2] J. Philip Kistler Stroke Research Center, Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States of America;
[3] Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, United States of America;
[4] Medical Image Analysis Center (MIAC AG) and Quantitative Biomedical Imaging Group (qbig), Department of Biomedical Engineering, University of Basel, Basel, Switzerland

Introduction: To determine if blood pressure variability (BPV) is associated with white matter (WM) microstructural integrity and longitudinal cognitive decline, we analyzed data from a prospective memory clinic cohort study in patients with and without cerebral amyloid angiopathy (CAA), a well-characterized small-vessel-disease.
Methods: We included 52 non-demented individuals (mean age 74.2 $\pm$ 7.0) with mild cognitive symptoms and CAA and 50 subjects with cognitive impairment unrelated to CAA (non-CAA mild cognitive symptoms). All participants were evaluated with 3.0 T research MRI at baseline and annual neuropsychological during 2 years, for which standardized z-scores for six cognitive domains were obtained. Visit-to-visit BPV was assessed using a coefficient of variation derived from serial outpatient BP measures spanning over 5 years before baseline. We measured the peak width of skeletonized mean diffusivity (PSMD) as a marker of white matter integrity, as well as other markers of ischemic brain injury, including lacunes and microinfarcts. We evaluated whether BPV was associated with WM integrity, adjusting for age, sex, diabetes, mean BP, and whether the presence of CAA influenced this association. Next, we evaluated whether BPV was associated with common CAA imaging markers and longitudinal domain-specific cognitive decline.
Results: We found a significant association between high systolic BPV (b = 0.49, $p < 0.001$) and loss of WM integrity which remained significant after adjusting for common vascular risk factors. The association between BPV and WM integrity was stronger when CAA was present (P for interaction = 0.023). BPV was also associated with lobar lacunes (OR = 1.62, $p = 0.048$) and cortical microinfarcts (OR = 1.65, $p = 0.045$). Higher long-term BPV was associated with a decline in global cognition (b = -0.24, $p = 0.035$) driven by a decline in processing speed (b = -0.30, $p = 0.022$) which remained significant after adjusting for common vascular risk factors.
Conclusions: Long-term BP fluctuations are associated with WM microstructural injury, lobar lacunes, and microinfarcts. The microstructural ischemic brain injury may underly the domain-specific cognitive decline, independent of mean BP and other common vascular risk factors. Long-term BPV may be a modifiable risk factor for cognitive decline, partly driven by CAA pathology.

P60

Natural History of Dissecting Cervical Artery Aneurysms

VK Steinsiepe [1], H Sarikaya [1], P Mordasini [2], S Jung [1], K Antonenko [1], U Fischer [1], J Gralla [2], RM Umarova [1], B Goeggel Simonetti [1], H Chabriat [3], MR Heldner [1] and M Arnold [1]

[1] Inselspital—Universitätsspital Bern—Universitätsklinik für Neurologie;
[2] Inselspital—Universitätsspital Bern—Universitätsinstitut für Diagnostische und Interventionelle Neuroradiologie, Switzerland;
[3] Groupe Hospitalier Lariboisière-Fernand-Widal-Service de Neurologie, Paris, France

Aim: The natural history of dissecting aneurysms in patients with spontaneous cervical artery dissections has so far been defined as "benign". We aimed to elucidate (1) vascular risk factors, (2) local and ischaemic symptoms and (3) long-term prognosis compared to non-aneurysmal dissections.
Methods: This is a case-control study including consecutive patients with spontaneous cervical artery dissection from three university hospitals in Switzerland and France. They were evaluated at baseline and at 3 months. In addition, 6, 12 and 24 months follow-up was performed at the discretion of the treating physician. Dissecting aneurysms were diagnosed with duplex sonography, magnetic resonance angiography and/or digital subtraction angiography.
Results: Of 1012 patients, 151 (14.9%) presented with 167 dissecting aneurysms at baseline or follow-up. Median follow-up was 2.3 years. Compared with patients without a dissecting aneurysm there were no significant differences in vascular risk factors and local symptoms. Ischaemic strokes at baseline were much less common (29.1% vs. 54.4%; OR 0.41, 95% CI 0.28–0.60) in patients with a dissecting aneurysm, even after correction for degree of stenosis (OR 0.53, 95% CI 0.34–0.81). There was no significant difference in recurrent cerebrovascular events and modified rankin scale at 3 months.
Conclusions: Aneurysmal spontaneous cervical artery dissections differed from non-aneurysmal dissections in the rate of ischaemic strokes at baseline, which may reflect different pathomechanisms. We found no differences in vascular risk factors, local symptoms, recurrent events or functional outcome between both groups.

P61

Hyperthyreodism is Associated with Cardioembolic Stroke Etiology through the Mediation by Atrial Fibrillation: Results from the Biosignal Study

A Zietz [1], T Dittrich [2], M Arnold [3], C Inauen [3], L Westphal [3], V Valerie [3], T Pokorny [1], M Arnold [4], U Fischer [1], L Bonati [5], T Kahles [6], K Nedeltchev [6], C Cereda [7], G Kaegi [2], A Bustamante [8], J Montaner [9], G Ntaios [10], C Foerch [11], K Spanaus [12], A von Eckardstein [12], GM De Marchis [2] and M Katan [1]

[1] Department of Neurology and Stroke Centre, University Hospital Basel and University of Basel, Switzerland;
[2] Department of Neurology, Kantonsspital St. Gallen, St. Gallen, Switzerland;
[3] Department of Neurology University Hospital and University of Zurich, Switzerland;
[4] Department of Neurology, University Hospital Bern, Bern, Switzerland;
[5] Reha Rheinfelden, Department of Neurology, University Hospital Basel, University of Basel, Basel, Switzerland;
[6] Department of Neurology and Stroke Center, Cantonal Hospital Aarau, Aarau, Switzerland;
[7] Department of Neurology, Neurocenter (EOC) of Southern Switzerland, Ospedale Civico, Lugano, Switzerland;
[8] Neurovascular Research Laboratory. Vall d'Hebron Institute of Research (VHIR), Universitat Autónoma de Barcelona, Barcelona, Spain;

[9] Neurovascular Research Group, Biomedicine Institute of Seville, Spain IBiS/Hospital Virgen del Rocío/CSIC/University of Seville, Seville, Spain;
[10] Department of Internal Medicine, Faculty of Medicine, School of Health Sciences, University of Thessaly, Larissa, Greece;
[11] Department of Neurology, Goethe University, Frankfurt am Main, Germany;
[12] Institute of Clinical Chemistry, University Hospital of Zurich, Zurich, Switzerland

Background: We aimed to investigate the association of thyreoid stimulating hormone (TSH) with cardioembolic stroke etiology (CES) and analyze to which extend the effect of hyperthyroidism on CES is attributable to atrial fibrillation (AF).
Methods: The BIOSIGNAL study is multicenter, prospective cohort study that including acute ischemic stroke (AIS) patients. TSH levels were measured within the first 24 h of symptom onset. The TOAST classification was used to classify the stroke etiology. Patients were categorized as hyperthyroid using the standard TSH-cutoff of <0.33 mU/L. We used a mediation analysis framework to estimate the total, direct, and indirect effects of hyperthyroidism on (CES), with AF as the mediator variable. Bootstrapping was used to estimate the standard error and 95% confidence interval for the indirect effect.
Results: Of 1,730 AIS patients, 78 (4.5%) were hyperthyroid. Hyperthyroid patients were more likely to have a CES (48.1% vs. 32.4%, $p = 0.004$; Table 1) and a history of AF (41.0% vs. 24.9%, $p = 0.001$). For the effects of hyperthyroidism on CES, results were significant for the total effect (coefficient: 0.143, $p = 0.008$) and the indirect effect (coefficient: 0.085 [bootstrap 95% CI: 0.018-0.152], $p = 0.006$; Table 2), but not for the direct effect ($p = 0.193$). This indicates the presence of a full indirect mediation with approximately 59% of the total effect of hyperthyroidism on CES being mediated by AF (ratio of indirect to total effect: 0.594).
Conclusions: Our findings suggest that in patients with AIS, the association of hyperthyroidism with CES was mainly mediated by the presence of atrial fibrillation.

P62

The Role of Neuronal Antibodies in Cryptogenic New-Onset Refractory Status Epilepticus

A Eisele [1], M Schwager [1], SY Bögli [1], I Reichen [1], J Dargvainiene [2], K Wandinger [2], L Imbach [3], M Haeberlin [1], E Keller [1], I Jelcic [1], M Galovic [1] and G Brandi [1]

[1] Universitätsspital Zürich & Universität Zürich, Switzerland;
[2] Universitätsklinik Schleswig-Holstein, Campus Lübeck, Germany;
[3] Swiss Epilepsy Center, Klinik Lengg, Zürich, Switzerland

Objectives: To analyse the etiology and clinical features of new-onset refractory status epilepticus (NORSE) and investigate known or potentially novel autoantibodies in cryptogenic NORSE (cNORSE).
Methods: We retrospectively assessed the medical records of patients with status epilepticus at a Swiss tertiary referral center and included adults meeting criteria for NORSE between 2010 and 2021. Demographic, diagnostic, therapeutic and outcome parameters were characterized. We performed post-hoc screening for known or potentially novel autoantibodies including immunohistochemistry (IHC) on rat brain with CSF and serum samples of cNORSE.
Results: We identified 20 patients with NORSE. Etiologies included infections ($n = 4$), Creutzfeld-Jakob disease ($n = 1$), CASPR2 autoimmune encephalitis ($n = 1$), and carotid artery stenosis with recurrent perfusion deficit ($n = 1$). Thirteen cases (65%) were cryptogenic despite detailed evaluation. A posteriori IHC for neuronal autoantibodies yielded negative results in all available serum ($n = 11$) and CSF ($n = 9$) samples of cNORSE. Most surviving patients were seizure-free within one year after discharge (6/8, 75%) with a median modified Rankin Scale of 2.
Discussion: Neuronal antibodies are unlikely to play a major role in the pathogenesis of cNORSE. Future studies should rather focus on other immune (e.g., T-cell) mediated mechanisms of autoinflammation in this devastating disease, which is far too poorly un-

derstood so far. Favorable outcomes may be reached in a large proportion of NORSE cases which should encourage clinicians to maintain treatment despite initial refractoriness of status epilepticus.

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EEG Compatibility with Fitness to Drive—A Survey among Swiss Neurologists

L Spoendlin [1], M Hardmeier [2], R Sutter [2], S Rüegg [2] and U Fisch [3]

[1] Universität Basel;
[2] Universität Basel & Universitätsspital Basel;
[3] Universitätsspital Basel, Switzerland

Aims: The Swiss guidelines for driving with epilepsy require that electroencephalogram (EEG) findings must be compatible with the fitness to drive (FTD) without specifying any criteria. This study investigated how Swiss neurologists implement this requirement in clinical practice.
Methods: A questionnaire, including EEG examples and statements about EEG and FTD compatibility, was distributed to all members of the Swiss Society of Clinical Neurophysiology and Swiss neurological clinics with residency programs.
Results: A total of 107 neurologists (39% female; 57% 35–54 years old; 50% with >10 years of EEG experience) completed the questionnaire. The participants' work settings were: 29% private practice (PP), 57% non-epileptology hospital (HOS) and 14% epileptology unit/center (EPI). When asked about the maximal duration of generalized epileptiform discharges (ED) compatible with FTD, 80% favored a time-threshold (71% PP with mean 2 s [standard deviation (SD) 1.5]; 82% HOS with 1.6 s [1.4], 93% EPI with 2.6 s [1.5]), while 14% opted for reaction-time testing (PP 16%, HOS 15%, EPI 7%) and 6% accepted any ED duration if clinical symptoms are absent (PP 13%, HOS 3%, EPI 0%). For the maximal duration of focal ED compatible with FTD, 55% chose a time-threshold (39% PP with mean 1.6 s [SD 1.2], 61% HOS with 3.6 s [3.8], 67% EPI with 3.5 s [3.6]), 22% favored reaction-time testing (PP 19%, HOS 23%, EPI 20%) and 19% accepted any ED duration if clinical symptoms are absent (PP 38%, HOS 13%, EPI 7%), while 4% (PP 4%, HOS 3%, EPI 6%) gave various answers. Regarding an increase in reaction-time post-ED still compatible with FTD, 64% defined a time-threshold (55% PP with mean 0.1 s [SD 0.2], 65% HOS with 0.2 s [0.3], 80% EPI 0.2 s [0.2]) while 36% had no opinion or suggested patient-individual thresholds. Although 81% agreed that EEG findings should be part of the FTD assessment, only 17% stated that the current requirements are sufficiently defined and 82% affirmed that more research is needed. Detailed analyses of EEG examples are ongoing.
Conclusions: This survey reveals diverse views among Swiss neurologists on the compatibility of EEG findings with FTD. While a majority of participants support the guidelines to consider EEG findings for FTD, they concur that criteria are inadequately defined and more research is needed.

P64

Ataxia and Dysarthria in Deep Brain Stimulation (DBS) of the Centromedian Thalamic Nucleus (CMT) May be Altered by Alignment of the Stimulation Field by Directional Leads: A Case Report

S Neidhart [1], O Kohnen [1], L Stieglitz [2] and L Imbach [1]

[1] Schweizerisches Epilepsie-Zentrum, Klinik Lengg, Zürich;
[2] University Hospital Zurich, Department of Neurosurgery, Switzerland

Background: Lennox-Gastaut syndrome (LGS) is a childhood-onset epilepsy characterized by multiple, often drug-resistant seizure types, severe cognitive impairment and specific EEG patterns. Recent data derived from the prospective ESTEL trial demonstrates reduction in seizure frequency in up to 50% in LGS patients by deep brain stimulation (DBS) of the centromedian thalamic nucleus (CMT). DBS therapy in drug-resistant epilepsy, in-

cluding epileptic encephalopathies such as LGS, is a currently rapidly evolving therapy modality in the field of epileptology and functional neurosurgery.
Case presentation: A 46-year-old male with Lennox-Gastaut syndrome presented with worsening of preexisting ataxia and dysarthria after implantation and activation of bilateral deep brain stimulation electrodes into the centromedian thalamic nucleus (CMT). The patient's ataxia and dysarthria showed marked improvement after establishing a medially directed stimulation paradigm where directional leads allowed for a stimulation geometry where laterally oriented contact segments were deactivated. The patient subsequently demonstrated subjective and objective improvements in dysarthria and ataxia.
Conclusions: This case highlights how advancements in stimulation targeting in DBS can lead to improved outcomes in mitigating adverse stimulation side effects by altering stimulation fields through directional leads. Conceptually, this case also suggests that stimulation induced ataxia and dysarthria in CMT DBS may be improved by reduction of lateral thalamic stimulation.

P65

Tai Chi Training of People with Parkinson's Disease (PD)—Neuropsychological and Electrophysiological Analyses

K Toloraia, U Gschwandtner, M Atanasova, TM Al Tavil, S Elsas and P Fuhr

University Hospital Basel, Basel, Switzerland

Tai Chi training of people with Parkinson's disease (PD)—neuropsychological and electrophysiological analyses Ketevan Toloraia U. Gschwandtner, Mira Atanasova, Tammam Mohamed Al Tail, Siegward Elsas, Peter Fuhr, Departments of Neurology and of Clinical Research, University Hospital Basel, Basel, Switzerland
Aims: To analyze the influence of Tai Chi training on neurological changes, neuropsychology, quality of life (QoL) and EEG in PD patients.
Besides pharmacological treatments there were several training studies analyzing the benefits of physical exercises. Tai Chi training is a combination of cognitive (attention and motor planning) and physical exercise, but it is rarely studied in research (Liu et al. 2019). To our knowledge, this is the first study that intended to study Tai Chi applying EEG.
Methods: N = 28 patients (f = 7, m = 21; median age 63y (59y–75y); n = 15 patients in the Tai Chi group, and n = 13 patients in the control group) diagnosed with idiopathic PD completed a comprehensive neuropsychological test battery and a neurological examination. The Tai Chi group was investigated with Tinetti Mobility Test and Epworth Sleepiness Scale (TMT and ESS). We applied 32-channel dry EEG (power bands: theta 3.5–7.5 Hz, alpha1 7.5–10 Hz, alpha2 10–12.5 Hz, beta 12.5–20 Hz). We analyzed the data with repeated-measures ANOVA, with Bonferroni correction, and Wilcoxon sum rank test, $p < 0.05$ was considered as significant.
Results: Four weeks of Tai Chi training showed significant improvements within the intervention group on Verbal Episodic Memory (Basel Verbal Learning Test): (〚p = .017, ηp〛^2 = 0.34) and visual-construction (Rey Figure Test): (p = 0.003, 〚ηp〛^2 = 0.25). In the training group the Tinetti Mobility Test ($p < 0.001$) and Epworth Sleepiness Scale ($p < 0.01$) were improved, the Tinetti Mobility Test benefit remained significant after 6 months ($p < 0.01$). Initial qEEG analyses for absolute power in theta, alpha and beta bands in 8 patients did not show any obvious changes for before and after Tai Chi training.
Conclusions: In patients with PD, Tai Chi training not only improves balance and gait stability, but may also result in improvements of verbal and visual performance in this relatively small group of patients with PD. No improvement in the EEG power spectrum was observed.
Reference: H.-H. Liu, N.-C. Yeh, Y.-F. Wu, Y.-R. Yang, R.-Y. Wang, F.-Y. Cheng. Parkinson's Disease. 2019:1–8.

P66

Weighing Tremor Reduction and Side Effects: Impact of Efficacy and Safety Outcomes on Patient Satisfaction at 6 Months In MR-Guided Focused Ultrasound Thalamotomy for Tremor Treatment

F Buechele, S Mahendran, M Uhl, C Freudinger, A Maric, A Maric, MF Oertel, C Baumann and L Stieglitz

Universitätsspital Zürich, Switzerland

Aims: MR-guided focused ultrasound (MRgFUS) thalamotomy in the ventral intermediate nucleus (VIM) is known to be highly efficacious for tremor treatment but side effects are relatively common and can be persistent. Thus, patient councelling can be a challenge, weighing the chance of tremor improvement and the risk of side effects. In the present study, we sought to understand how precisely efficacy and safety outcomes contribute to patient satisfaction at 6 months.
Methods: We conducted a retrospective analysis of 52 patients with pharmaco-resistant tremor disorders (32 patients with Essential tremor (plus), 5 with dystonic tremor, 15 with Parkinson's disease), who received first-in-life, unilateral MRgFUS thalamotomy in the VIM at the University Hospital Zurich, Switzerland, between 2017 and 2022 by one neurosurgeon. Standardized video-recorded assessments of efficacy (WHIGET tremor scale) and safety outcomes (standardized grading system based on impact on quality of life) at baseline and at 6 months post-treatment were reviewed. Overall patient satisfaction was evaluated by asking: "Based on what you know today, weighing tremor reduction and side effects, would you undergo the procedure again?" (YES/NO).
Results: At 6 months, there was a significant average tremor reduction of 63% for the treated side, with 21 patients (40%) having an excellent (>75% tremor reduction), 17 (33%) having a good (50–75%), 6 (12%) having a moderate (25–49%) and 8 (15%) having a poor treatment response (<25%). Persistent side effects were reported by 26 patients (50%), of whom 10 patients (19% of the total study population) described moderate severity. Gait impairment was present in 17 patients (33%; 25% mild, 8% moderate intensity), arm ataxia in 8 patients (15%; 2% mild, 13% moderate intensity) and sensory disturbance in 10 patients (19%; 17% mild, 2% moderate intensity). Other persistent side effects included dysarthria (n = 3, 6%), dysgeusia (n = 1, 2%) and dysphagia (n = 1, 2%). Nevertheless, 45 of 52 patients (87%), declared that they would undergo the procedure again, whereas 7 patients (13%) would decline. Of these 7 patients, 5 had poor tremor control (all with Parkinson's disease) and only 2 had side effects which they valued higher than tremor improvement.
Conclusions: Most side effects, even when impacting on quality of life, seem to be well tolerated if tremor control is satisfactory. Thus, while side effects are common (50%), patient satisfaction is high (87%).

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Dysphagia in Parkinson's Disease

E Ardila Jurado [1], F Brugger [2], J Walch [2], M Galovic [3], S Stöckli [2], M Rosenblad [1] and G Kägi [2]

[1] Kantonsspital St. Gallen;
[2] Kantonsspital St. Gallen KSSG;
[3] University Hospital Zurich, Switzerland

Background: Oropharyngeal dysphagia is a common, although underappreciated problem in Parkinson disease (PD), particularly in the more advanced stage (1, 2). Aspiration pneumonia is a severe complication associated with dysphagia and even the most common cause of death in PD (3, 4). Only one third of PD patients claims to be dysphagic, but 4/5 patients are identified to be affected if objective measurements are applied (5-8). Due this discrepancy in reporting dysphagia, valuable screening tools to reliably identify dyphagic patients are therefore urgently needed.

Aims and Methods: We assessed whether bedside screening tests predicted the risk of dysphagia on instrumental testing with fiberoptic endoscopic evaluation of swallowing (FEES) in PD patients. All patients were assessed by swallowing questionnaires (SWAL-QOL and Drooling severity and frequency scale (DSFS)) as well as by a clinical swallowing assessment (150 mL water swallow test, "two out of six" scale (Any2 of Daniels), Parramatta Hospitals' assessment of Dysphagia (PHAD), functional oral intake scale (FOIS)). Patients were classified in PD patients with dysphagia or no dysphagia based on the findings seen on FEES. Severity of aspiration was rated by the penetration aspiration scale (PAS) and the fiberendoscopic dysphagia severity scale (FEDSS).
Results: 34 Patients were included in this study. 9 patients were diagnosed with. Patients with dysphagia were significantly older and scored significantly higher on the UPDRS Part II and III as well as the Frontal Assessment Battery. They had higher Any2, DSFS and FOIS scores and lower PHAD scores along with a longer duration on the 150 mL test. The ROC analysis of the DSFS showed an excellent discrimination power and performs well in distinguishing PD patients with dysphagia with an AUC of 0.833. The Any2 test as well as the duration on the 150 mL water test also showed a good sensitivity and specificity.
Conclusions: Drooling severity as assessed by the DSFS (including each subscore) is a valuable tool to predict dysphagia in PD patients. Also the Any2 and the 150 mL water test may be useful tools, whereas the other tests investigated in this study are of less value to distinguish dysphagic from non-dysphagic patients. These study results, however, need to be validated in an independent cohort of PD patients.

P68

To Stimulate or Not to Stimulate? Bilateral Subthalamic (STN) Deep Brain Stimulation (DBS) in Cases of Young-Onset Parkinsonism with Mitochondrial Dysfunction Induced Neurodegeneration

E Efthymiou, B Balint, F Büchele, S Mahendran, CR Baumann and LH Stieglitz

University Hospital Zurich, Switzerland

Objective: To describe two cases of young-onset parkinsonism (YOP; case 1 with mitochondrial membrane protein associated neurodegeneration (MPAN) due to a heterozygous mutation in C19orf12; Case 2 with a heterozygous pathogenic variant in mitochondrial polymerase gamma (POLG; c.2828G > A (p.Arg943His)) treated with bilateral STN-DBS surgery at the University Hospital Zurich.
Background: MPAN or POLG-related YOP is very rare (1,2), and STN-DBS outcomes have not yet been reported. Given the rarity of such conditions, trials are not feasible and case reports are relevant to better understand treatment options.
Methods: Chart review.
Results: Case 1: This Caucasian male developed right-sided tremor and clumsiness at the age of 32. Two years later, he developed attention deficit, slurred speech, and parkinsonism with right-sided resting and postural tremor partly responsive to levodopa. Due to motor fluctuations and psychotic symptoms less than a year later, STN-DBS was performed. 6 years later, levodopa remains markedly reduced, there are no motor fluctuations, and psychiatric symptoms are well controlled. DBS wash-out is currently associated with a 22% worsening in MDS-UPDRS III. However, there is a disease progress with severe myoclonus, and deterioration of parkinsonism, cognition and speech. Case 2: This Caucasian female presented with akinetic-rigid parkinsonism at the age of 42, and had additional features of mitochondrial disease (short stature, external ophthalmoplegia, proximal myopathy). 12 years into the disease course, she had severe motor fluctuations with freezing of gait and dyskinesias, and was treated with STN-DBS. 6 weeks post DBS, levodopa was reduced by 50% and motor fluctuations are no longer present.
Conclusions: To the best of our knowledge, these are the first cases of MPAN or POLG-related disease treated with STN-DBS. In MPAN-YOP, DBS had a favorable effect not only on the severity of motor but also of psychiatric symptoms as it allowed reducing levodopa.

The main limiting factors were, however, overall disease progression with cognitive worsening. In POLG-YOP, there was a favorable response without any adverse effects of STN-DBS in the short term.

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Cranial Myorhythmia as A Novel Clinical Manifestation in Contactin-Associated Protein-Like 2 Antibody Associated Encephalitis

S Crippa [1] and B Florian [2]

[1.] Kantonspital St. Gallen;
[2] Kantonsspital St. Gallen, Switzerland

Aims: Myorhythmia were described in various conditions including autoimmune encephalitis (particularly associated with NMDA- or IGLON5-antibodies), Whipple's disease, ischemic and haemorrhagic strokes (within the Guillain-Mollaret triangle), celiac disease, paraneoplastic conditions or as side effects of medication. Here we describe an intriguing case of cranial myorhythmia as a novel manifestation of a contactin-associated protein-like 2 (CASPR2) antibody associated encephalitis.
Methods: Case report: A 72-year-old man presented due to abnormal movements of the tongue for about 1.5 years. He complained of a salivary accumulation in the mouth and throat, especially when lying down and of a clicking sound in his ears. These symptoms started a few days after his third SARS-CoV19-vaccination.
Results: On clinical examination he presented rhythmic and synchronous movements (myorhythmia) of the tongue, the soft palate, the mimic and jaw muscles, the platysma and the eyes at a frequency of about 1 Hz along with slight dysarthria. A part from mild signs of a length-dependent sensory polyneuropathy (with slight gait ataxia) the remaining neurological exam was unremarkable. A MRI scan of the brain was unremarkable. The laboratory work-up revealed high antibody titers against CASPR2 in the serum and CSF with an otherwise normal CSF cell count (1/μL) and only slightly elevated protein (0.74 g/L). Other autoimmune encephalitis antibodies (including IGLON5, NMDA, LGI1) as well as a screening for celiac disease were negative.
Conclusions: We suggest testing for CASPR2 antibodies should be included in the diagnostic work-up of myorhythmia. Although unproven in this case, a causal association of the CASPR2-autoimmune encephalitis with the SARS-CoV19-vaccination is conceivable due to the close temporal relationship of the vaccination with the onset of the movement disorder.

P70

Serum Glial Fibrillary Acidic Protein (GFAP) is a Longitudinal Indicator of Disease Progression in MS while Neurofilament Light Chain (NfL) Associates with Therapy Response in Patients Under B-Cell Depleting Therapy

A Maleska Maceski [1], P Benkert [2], S Schaedelin [2], E Willemse [1], S Meier [1], L Melie Garcia [3], A Cagol [4], R Galbusera [4], S Subramaniam [2], J Lorscheider [1], B Fischer-Barnicol [1], L Achtnichts [5], O Findlin [5], P Lalive [6], C Bridel [7], S Müller [8], C Pot [9], A Mathias [9], R Du Pasquier [10], A Salmen [11], R Hoepne [11], A Chan [11], G Disanto [12], C Zecca [12], A Orleth [1], M D'Souza [1], O Yaldizli [1], T Derfuss [1], J Oechtering [1], C Gobbi [12], M Khalil [13], A Abdelhak [14], J Oksenberg [14], M Hermesdorf [15], H Wiendl [15], K Berger [15], F Piehl [16], D Conen [17], A Buser [18], L Kappos [1], C Granziera [19], D Leppert [1] and J Kuhle [1]

[1] Department of Neurology, Multiple Sclerosis Centre and Research Center for Clinical Neuroimmunology and Neuroscience (RC2NB), Departments of Biomedicine and Clinical Research, University Hospital and University of Basel, Basel, Switzerland;
[2] Department of Neurology, Multiple Sclerosis Centre and Research Center for Clinical Neuroimmunology and Neuroscience (RC2NB), Departments of Biomedicine and Clinical Research; Departments of Biomedicine and Clinical Research, University Hospital and Unive;

[3] Neurology Clinic and Policlinic, Department of Clinical Research, University Hospital Basel, University of Basel, and Translational Imaging in Neurology (ThINk), Department of Biomedical Engineering, University of Basel, Basel, Switzerland;
[4] University Hospital Basel / University of Basel, Department of Neurology, Multiple Sclerosis Centre and Research Center for Clinical Neuroimmunology and Neuroscience (RC2NB)/Translational Imaging in Neurology (ThINK) Basel, Department of Biomedical Engine;
[5] Department of Neurology, Cantonal Hospital Aarau;
[6] Department of Clinical Neurosciences, Division of Neurology, Geneva University Hospitals, Geneva Switzerland;
[7] Department of Neurosciences, Division of Neurology, University Hospital of Geneva and Faculty of Medicine, Geneva, Switzerland;
[8] Department of Neurology, Cantonal Hospital St. Gallen, Switzerland;
[9] Service of Neurology, Department of Clinical Neurosciences, Lausanne University Hospital (CHUV) and University of Lausanne, Lausanne, Switzerland;
[10] Service of Neurology, Department of Clinical Neurosciences, Lausanne University Hospital (CHUV) and University of Lausanne;
[11] Department of Neurology, Inselspital, Bern University Hospital and University of Bern, Bern, Switzerland;
[12] Multiple Sclerosis Center (MSC), Department of Neurology, Neurocenter of Southern Switzerland, Lugano, Switzerland;
[13] Department of Neurology, Medical University of Graz, 8036 Graz, Austria;
[14] University of California San Francisco, San Francisco, CA, United States of America;
[15] University of Münster, Münster, Germany;
[16] Department of Clinical Neuroscience, Karolinska Institutet, Center for Molecular Medicine, Karolinska University Hospital, Stockholm, Sweden;
[17] Population Health Research Institute, McMaster University, Hamilton, Canada;
[18] Regional Blood Transfusion Service, Swiss Red Cross, Basel, Switzerland;
[19] Department of Neurology, Multiple Sclerosis Centre and Research Center for Clinical Neuroimmunology and Neuroscience (RC2NB), Departments of Biomedicine and Clinical Research, University Hospital and University of Basel, Basel, Switzerland/Department of

Aims: An increasing evidence base links elevated serum neurofilament light chain levels (sNfL) with ongoing neuroaxonal damage in MS. Diffuse, more chronic neurodegeneration is also associated with increased sNfL but levels are closer to normal values. Astrogliosis is a prominent feature of progressive disease biology in MS and is reflected by increased serum levels of glial fibrillary acidic protein (sGFAP), in turn representing a promising progression marker in MS. To model the longitudinal dynamics of sGFAP and sNfL in persons with MS (pwMS) starting B cell depleting therapy (BCDT) in the Swiss MS Cohort (SMSC) and to compare the biomarker profiles between patients with and without progression independent of relapse activity (PIRA) using sGFAP Z scores based on a reference database of control persons.
Methods: To date, sGFAP and sNfL levels were measured using the Simoa Neurology 2-plex B assay in 1029 samples from 228 pwMS under BCDT (31 PPMS, 29 SPMS, 168 RRMS). For sGFAP, age-, sex- and BMI-adjusted Z scores based on healthy controls (485 samples) were calculated as measure of deviation from normal. Multivariable mixed-effects were used to estimate biomarker Z scores longitudinally and to identify covariates, including occurrence of PIRA under treatment.
Results: During BCDT treatment periods of 3–6 years (median [IQR] 4.1 [3.7, 5.3] years) 20.2% experienced at least one PIRA event. On treatment sGFAP Z scores steadily increased by 0.07 Z score units per year ($n = 729$, 0.07 [0.03, 0.11], $p < 0.001$) and were 0.5 units higher in pwMS experiencing PIRA (0.54 [0.15, 0.93], $p = 0.007$) compared with stable pwMS. Longitudinal assessments of sGFAP and sNfL in the entire reference database (> 5000 control persons) and SMSC (>12,000 samples) are under way.

On treatment sNfL Z scores in RRMS decreased with 0.06 Z score units per year (n = 712, −0.06 [−0.10, −0.01], p = 0.01), but did not decrease in progressive MS (n = 307, p = 0.77) and only tended to be higher in pwMS experiencing PIRA (0.44 [−0.02;0.91], p = 0.07).
Conclusions: A continued increase in sGFAP despite BCDT suggests a more limited treatment effect on progressive disease biology. While sNfL is confirmed as treatment response marker in RRMS, its capacity to capture PIRA seems more limited. Increased sGFAP Z scores may serve as a meaningful efficacy measure for novel treatments targeting MS progression.

P71

Investigation of EDSS Functional System Scores and Neurostatus eEDSS Subscores in Secondary Progressive Multiple Sclerosis Patients

M Greselin [1], P Lu [1], S Arnould [2], A Papadopoulou [1], L Kappos [1], N Cerda Fuertes [3], C Granziera [1] and M D'Souza [4]

[1] University Hospital Basel and University of Basel;
[2] Novartis Pharma AG;
[3] Neurostatus-UHB Ltd;
[4] University Hospital Basel, Switzerland

Aim: Neurostatus-EDSS1 is the most frequently used endpoint of disability in patients with Multiple Sclerosis (pwMS). However, the EDSS scale is strongly affected by ambulation and might show low sensitivity to certain Functional System Score (FSS) and Neurostatus subscore changes. Our aim is to investigate the variability of these parameters and their impact on different EDSS steps.
Methods: Our dataset is composed of 1642 patients from the EXPAND trial2, a randomized, double-blind, controlled Phase III study comparing Siponimod versus placebo in patients with secondary progressive MS (SPMS). Each patient had several visits that are considered independently. In accordance with the Neurostatus-EDSS scoring definitions3, the data were subdivided into two groups: (1) EDSS step between 3 and 5 (4.2 ± 0.61), where FSS and Ambulation Score (AS) are jointly considered for the step calculation (2) EDSS step between 5.5 and 8.5 (6.2 ± 0.4), that is based only on AS. Three analyses were conducted: (1) the importance of FSS and AS in the first group, was assessed using a Random Forest Regression model (2) K-means clustering was used to detect subgroups within the second group in terms of FSS (3) The upper and lower extremities were defined as combined subscores that measure signs and symptoms for different FSS. K-means clustering was then applied to determine the extremities impairments in data belonging to the same EDSS step. A z-score normalization was performed before clustering, and the Elbow method was used to define the best number of clusters.
Results: The Pyramidal, Cerebellar and Sensory FSS had the highest impact (71.2%) on the EDSS step in the low-EDSS group. In the high-EDSS group, subgroups were defined at different EDSS steps and two distinctive patterns were found: one with high, and the other with low scores in the Visual, Brainstem, Sensory and Cerebral FS. Pyramidal and Cerebellar FS were similar across these two subgroups, their values increasing with EDSS steps. Within the same EDSS-step, subgroups showed a high variability regarding upper and lower extremity impairment. The cluster allows to identify some patterns that are valid for all the EDSS classes.
Conclusions: Within the same EDSS step, pwMS showed distinct subgroups in terms of FSS and subscores for upper and lower extremity impairments. These differences might have an impact on recruitment strategies. Future work will aim at performing a machine-learning model to predict the progression of EDSS.

P72

Don't Forget Primary Progressive Aphasia for Anti-amyloid Drugs: An Estimation of Eligible Patients from the Lausanne Memory Center Registry

P Salvioni Chiabotti, A Hausmann, M Nasuti, O Rouaud and G Allali

Centre Leenaards de la Memoire, Lausanne, Switzerland

The study recently published on the clinical effect of lecanemab in early Alzheimer's disease (AD) only includes patients with amnestic presentation. However, a significant portion of AD patients presents a non-amnestic phenotype of AD, such as primary progressive aphasia (PPA) and could also benefit of lecanemab. Therefore, we conducted a 10-year retrospective study at the Leenaards Memory Center in Lausanne (Switzerland) to identify how many PPA patients would be eligible for lecanemab. Among 54 patients with PPA, we identified 11 (20%) eligible patients. Furthermore, almost half of the 18 patients with logopenic variant (lvPPA) would be eligible for lecanemab treatment.

P73

The German Version of the Tablet-Based TabcCAT Brain Health Assessment Is Sensitive to Early Symptoms of Neurodegenerative Disorders

G Toller [1], L Stäger [2], D Kumurasamy [2], P Callahan [3], F Köhn [4], T Münzer [4], U Kunze [5], AU Monsch [5], KL Possin [3], KP Rankin [3] and A Felbecker [2]

[1] Memory Clinic Zentralschweiz, Luzerner Psychiatrie AG, Switzerland;
[2] Kantonsspital St. Gallen, Switzerland;
[3] Memory and Aging Center, University of California San Francisco, USA;
[4] Geriatrische Klinik St. Gallen;
[5] Memory Clinic, University Department of Geriatric Medicine FELIX PLATTER, Basel, Switzerland

Aims: Although primary care physicians are frequently the first to assess individuals with early neurodegenerative disease (NCD)1, cognition often remains unassessed in primary care settings. To improve early diagnosis of NCD in Switzerland, we translated the tablet-based TabCAT Brain Health Assessment (TabCAT-BHA)2 and Brain Health Survey (BHS) to standard high German and investigated whether the German version can distinguish patients with mild and major neurocognitive disorder from healthy controls at high sensitivity and specificity.
Methods: The German versions of the TabCAT-BHA, BHS, and Montreal Cognitive Assessment (MoCA)3 were administered to 67 patients with mild (n = 29) or major (n = 38) NCD and 50 healthy controls. The TabCAT-BHA includes subtests of memory, executive, visuospatial, and language functioning, and the informant-based BHS asks about behavior and motor functioning.4
Results: The complete instrument (TabCAT-BHA+BHS) was most accurate at detecting mild NCD (AUC: 0.95; BHA alone: 0.91; MoCA: 0.89) and mild or major NCD without amyloid pathology (AUC: 0.96), followed by the BHA (BHA alone: 0.92; MoCA: 0.90). All measures were accurate (all AUCs > 0.95) at distinguishing major NCD and NCD with amyloid pathology (AD) from controls.
Conclusions: The German TabCAT-BHA and BHS are more sensitive to mild NCD and non-AD presentations than the paper- and pencil-based MoCA, which confirms two previous studies from high-and middle-income countries (USA2, Cuba5). This study suggests that using the standard high German version of the BHA/BHS instrument in primary care practices may result in a higher number of early and accurate diagnoses of typical and atypical presentations of neurodegenerative diseases, and of referrals to dementia specialist centers. The usability of this new German version of the tablet-based BHA/BHS is not limited to Switzerland, but it can be more broadly used in any German speaking country in Europe, including Germany and Austria.

P74

Creation of a Domain Specific Language for Use in Neurological Scales to Verify the Correctness of Entered Data According to the Rules of Set Medical Scale

M Gamez [1] and M D'Souza [2]

[1] Neurostatus-UHB Ltd;
[2] University Hospital Basel, Switzerland

Aim: To quantify and monitor patients with chronic neurological disorders, specific scales are used. Most of them are available in paper and pencil format. Our goal is to create an intuitive process that translates various medical scales from their traditional pen-and-paper format into a digitized model, leveraging a standardized language that has been specifically crafted for neurological scales. By digitalizing these scales, we unlock a range of benefits, including streamlined data collection, increased accuracy, and broader accessibility. This language simplifies the process of rule specification and data input, offering a versatile solution that simplifies the representation of medical scales. We seek to provide a uniform interface that can be interpreted by machines or rendered into a human-friendly format. We used the Neurostatus-eEDSS as a proof of concept.
Methods: The language was formulated using YACC (Yet Another Compiler Compiler). We employed its Go variant, known as goyacc, for the language's definition. The resulting definitions yielded a functional language parser, proficient in interpreting rules defined within the language.
Results: We have successfully engineered a domain-specific language that functions as a rule engine, capable of validating medical assessments against the rules of specific medical scales. As a proof of concept, the Neurostatus-eEDSS scale has been integrated and effectively implemented with more than 500 distinct rules. In support of the practical application, we have launched a website that provides immediate feedback to the assessor regarding the consistency of the data entered in compliance with the EDSS scale rules.
Conclusion: Our solution provides substantial benefits, most notably through standardizing the saving and processing of input data and rules within a single unified framework. This standardization ensures that the same procedures and protocols are followed, leading to consistent, reliable results. It allows for easy rule additions or modifications, enabling collaboration between technical solutions specialists and medical professionals for rule refinement. Importantly, our system is flexible and adaptable, capable of being efficiently repurposed for new studies and use cases that may emerge in the future. Its lightweight nature and ease of integration with most platforms extend its utility, making it an ideal solution for advancing neurological research.

P75

Towards the Quest of CNS-Reactive Antibodies in Autoimmune-Mediated Neurological Syndromes Using a New Human-Induced Pluripotent Stem Cell-Derived Based Platform

A Mathias [1], S Perriot [1], S Jones [1], R Bernard-Valnet [1], M Canales [1], M Gimenez [1], N Torcida [1], L Oberholster [1], C Deffert [2], PH Lalive [2], M Théaudin [1], C Pot [1] and R Du Pasquier [1]

[1] Lausanne University Hospital (CHUV) and University of Lausanne (UNIL);
[2] Geneva University Hospital, University of Geneva, Geneva, Switzerland

Introduction: The discovery of central nervous system (CNS)-reactive auto-antibodies (Abs) has profoundly changed therapeutic approaches of neurological disorders such as paraneoplastic syndromes, autoimmune encephalitis or neuromyelitis optica. Nevertheless, 7–11% of the patients developing auto-immune limbic encephalitis remain seronegative for all currently known neural antigens.
Aims: To overcome the limitations of current auto-Abs discovery systems, we developed a cell-based assay to screen for the presence of novel CNS-specific Abs in sera and cerebrospinal fluid (CSF) using neurons and astrocytes derived from human-induced pluripotent stem cells (hiPSC).
Methods: Human iPSC-derived astrocytes and neurons were incubated with paired serum and CSF of 282 patients with 229 suffering from inflammatory neurological diseases (IND)

and 53 non-IND (NIND) used as controls. IND group comprises 11 patients diagnosed at the time of blood/CSF draw with CNS-reactive Abs (3 Hu, 1 Ri, 1 AK5, 1 LGI-1, 1 NMDAR, 4 AQP4, 1 GFAP), 54 MS patients, 97 patients with infectious diseases and 67 other IND patients with suspected but not diagnosed CNS-reactive Abs [OIND]. IgG bound to hiPSC-derived CNS cells were detected using a combination of fluorescently labeled Abs. IgG-associated fluorescence intensity (FI) measures and microscopy observations were automated. Serum or CSF were defined as positive using a ROUT test with a FDR at 2–10% on measured FI. IgG reactivity to CNS cells was further analyzed by flow cytometry.
Results: We identified Abs recognizing hiPSC-derived CNS cells in 61/229 IND patients (26.7%) vs. only 3/53 NIND patients (5.6%). Astrocytes or neuron-reactive Abs were detected in 11/11 patients who had known CNS-reactive Abs detected in routine laboratories, validating our new hiPSC-based approach. Interestingly, we further found CNS-reactive Abs in 16/54 pwMS (29.6%); 21/97 patients with infectious disease (21.6%); 14/67 patients with OIND (23.9%). CNS-reactive Abs were found: 1. mostly only in the CSF (54.1%) vs. only in the serum (39.3%) or in both serum and CSF (6.6%) and; 2. only on astrocytes (46%), only on neurons (39%) or (15%) on both cell types. Microscopy and flow cytometry analyses further confirmed these results.
Conclusions: Our hiPSC-based CBA allows for the discovery of CNS-reactive Abs. Such a potent tool opens new perspectives in identifying previously undiscovered CNS antigens targeted in autoimmune antibody-mediated diseases of the CNS.

P76

Personalized Treatment Decision Algorithms for the Clinical Implementation of Serum Neurofilament Light Chain in Multiple Sclerosis: A Modified Delphi Study

P Janiaud [1], P Benkert [1], L Achtnichts [2], A Bar-Or [3], V Bohner Lang [1], C Bridel [4], M Comabella [5], G Disanto [6], O Findling [2], C Gobbi [6], C Granziera [1], M Herwerth [7], R Hoepner [8], D Horakova [9], N Kamber [8], M Khalil [10], P Kunz [1], P Lalive [4], R Linker [11], J Lorscheider [1], S Müller [12], J Oechtering [1], V Pettypool [1], F Piehl [13], C Pot [14], P Roth [7], M Théaudin [14], M Tintoré [15], C Tur [15], D Uffer [12], J Vehoff [12], H Wiendl [16], T Ziemssen [17], C Zecca [6], A Salmen [8], D Leppert [1], T Derfuss [1], L Kappos [1], J Kuhle [1], L Hemkens [1] and Ö Yaldizli [1]

[1] University Hospital Basel and University of Basel, Basel, Switzerland;
[2] Cantonal Hospital Aarau, Switzerland;
[3] University of Pennsylvania, USA;
[4] Geneva University Hospital (HUG), Switzerland;
[5] Hospital Universitari Vall d'Hebron, Universitat Autònoma de Barcelona, Spain;
[6] Neurocenter of Southern Switzerland, Ospedale Regionale di Lugano, Ente Ospedaliero Cantonale, Lugano, Switzerland;
[7] University Hospital Zurich;
[8] Bern University Hospital (Inselspital), Switzerland;
[9] Charles University in Prague and General University Hospital, Poland;
[10] Medical University of Graz, Austria;
[11] University of Regensburg, Germany;
[12] Kantonsspital St. Gallen KSSG, Switzerland;
[13] Karolinska University Hospital;
[14] Lausanne University Hospital (CHUV), Switzerland;
[15] Vall d'Hebron Barcelona Hospital Campus, Multiple Sclerosis Centre of Catalonia (Cemcat), Spain;
[16] University Hospital Münster, Germany;
[17] University Hospital Carl Gustav Carus, Dresden, Germany

Introduction: Serum neurofilament light chain (sNfL) is a sensitive measure of disease activity and predicts disease worsening in multiple sclerosis (MS). sNfL might therefore be

instrumental for a patient-tailored treatment adaptation ensuring disease stability, fewer adverse events and better quality of life. While sNfL is increasingly used as a marker of treatment response, broad consensus on implementation into clinical routine decision algorithms are currently lacking.
Objectives: We aimed to reach a consensus on treatment decision algorithms to facilitate the implementation of sNfL as supporting information for decisions on escalation and deescalation of disease modifying therapies (DMTs).
Methods: Treatment decision algorithms were designed by a non-voting core team based on their expertise and the literature. Ten international and 18 Swiss MS experts, and 3 patient consultants took part in 3 rounds of voting (2 online surveys and 1 in-person meeting). They rated their agreement on a 9-point Likert scale (1—Strongly disagree to 9—Strongly agree) on DMT changes based on high sNfL levels (defined as >90th percentile based on age and body mass index in controls) or normal sNfL (defined as <80th percentile). Consensus thresholds for agreement were defined as 50 to 80% (moderate consensus), 80 to 95% (broad consensus), >/= 95% (strong consensus), and 100% full agreement. Decision algorithms without a majority agreement (< 50% agreement) were excluded.
Results: The Delphi process resulted 9 treatment escalation algorithms (2 full; 3 strong; 2 broad; 2 moderate consensus) e.g., initiating treatment based on high sNfL, 11 switch algorithms (9 broad; 2 moderate consensus) e.g., switching natalizumab for another high efficacy DMT based on high sNfL, and 3 de-escalation algorithms (1 broad consensus; 2 moderate) e.g., stopping DMT or extending interval in B cell depleting therapies based on normal sNfL. Consensus was also found on DMTs classification into low, medium, high efficacy.
Conclusions: Within a group of experts we reached consensus on a set of treatment decision algorithms for frequent clinical scenarios. They allow informed shared decision-making between patients and physicians, and may represent a step towards more precise and personalized treatment choices. They will now be implemented in a pragmatic randomized clinical trial embedded in the Swiss MS Cohort assessing the superiority of 6-monthly sNfL monitoring compared with usual care.

P77

Clonal Expansion of CD8+ T Cells from Autoimmune Encephalitis Patients after Co-Culture with Autologous Neurons or Astrocytes

S Jones [1], S Perriot [1], R Genolet [2], M Canales [1], L Oberholster [1], M Gimenez [1], L Queiroz [2], M Théaudin [3], A Harari [2], C Pot [1], A Mathias [1] and R Du Pasquier [1]

[1] Laboratories of Neuroimmunology, Neuroscience research Centre, Department of Clinical Neurosciences, Lausanne University Hospital (CHUV) and University of Lausanne, Lausanne, Switzerland;
[2] Ludwig Institute for Cancer Research, Lausanne Branch, University of Lausanne and Lausanne University Hospital, Lausanne, Switzerland;
[3] Service of Neurology, Department of Clinical Neurosciences, Lausanne University Hospital (CHUV) and University of Lausanne, Lausanne, Switzerland

Introduction: Antibodies targeting brain surface, synaptic or intracellular antigens are an essential hallmark for the diagnosis of autoimmune encephalitis (AIE). Unlike CNS cell surface antibodies, intracellular brain-targeting antibodies are probably not key effectors of disease as they are unable to reach their antigen. Importantly, AIE linked with intracellular antigens (I-AIE) (e.g., Hu, Ri or GFAP AIE) appear with a concomitant cytotoxic CD8+ T cell response which is thought to be responsible for disease development. Our objective here, is to screen patients with I-AIE for the presence of brain-reactive CD8+ T cells.
Method: To expand and detect brain-reactive CD8+ T cells, we have developed a co-culture assay between peripheral blood mononuclear cells (PBMC) and autologous human-induced pluripotent stem cell (hiPSC)-derived neurons and astrocytes. First, an expansion step is initiated where ex vivo PBMC and autologous HLA-I-enhanced neurons or astrocytes are cultured together for 14 days. Second, expanded CD8+ T cells are isolated and incubated

overnight with fresh HLA-I-enhanced neurons and astrocytes and reactive CD8+ T cells are detected by secretion of IFN-gamma. Finally, if an IFN-gamma production is present, CD8+ T cells undergo bulk TCR sequencing to assess for clonally expanded TCR-alpha and TCR-beta chains.

Results: First, we have generated hiPSC-derived neurons and astrocytes from 6 healthy donors (HD) and 3 patients with I-AIE (1 Hu AIE, 1 Ri AIE and 1 GFAP AIE). Second, we demonstrate that hiPSC-derived neurons and astrocytes upregulate HLA class I expression upon exposure to IFN-gamma and TNF-alpha. Third, we are able to detect neuron or astrocyte-reactive CD8+ T cells in our cohort after co-culture with autologous target cells. Finally, in I-AIE patients we identify TCR-alpha and TCR-beta chains that are present at a high frequency ex vivo and then clonally expanded after co-culture with autologous neurons or astrocytes.

Discussion: Overall, our co-culture system allows to successfully identify neuron and astrocyte-reactive CD8+ T cells from virtually any donor. We are currently performing TCR-specificity validation assays from identified clonally expanded TCR-alpha and TCR-beta chain sequences of I-AIE patients. The identification of pathogenic TCRs implicated in I-AIE is essential for the identification of antigens implicated in disease development and will undoubtedly deepen our understanding of this poorly treatment-responsive disease.

P78

Effectiveness of Individualized Ocrelizumab Treatment in Multiple Sclerosis during and after COVID-19 Pandemic: Clinical, Radiological and Laboratory Prospective Study

R Sacco [1], D Meng [2], G Disanto [2], C Gobbi [2] and C Zecca [2]

[1] Neurocenter of Southern Switzerland;

[2] Neurocenter of Southern Switzerland

Aim: Ocrelizumab (OCR) is an anti-CD20 monoclonal antibody approved for the treatment of relapsing-remitting (RR) and progressive (P) multiple sclerosis (MS). To evaluate effectiveness of individualized OCR extended interval dosing (EID, 600 mg following repopulation of CD19+27+ memory B-cells) after switching from standard interval dosing (SID, OCR 600 mg every 6 months).

Methods: This is a prospective observational, single-center study including MS patients regularly followed at the MS center of the Neurocenter of Southern Switzerland in Lugano, who switched from OCR SID to EID. Relapses, disability progression, occurrence of new/enlarging T2 brain or spinal MRI lesions and/or gadolinium-enhancing lesions, and IgG/IgM concentrations were assessed.

Results: 113 (88.3%) of 128 MS patients included [89 (69.5%) RR, 39 (30.5%) P] switched from SID to EID. Median follow up after switching to EID was 18.1 (IQR 9.3–27.8) months. Median time between the last SID and the first EID infusion was 9.8 (IQR 8.3–11.5) months. Three (2.3%) RRMS patients experienced a clinical relapse and 8 (6.3%) an EDSS progression (4 RRMS and 2 PMS) during SID regimen. Under EID regimen, no clinical relapses occurred and 2 (1.8%) patients showed disability progression. Twenty-one (17.2%) and nine (7%) patients had at least one new T2 brain and spinal lesions respectively under SID while 3 (2.7%) and 2 (1.8%) experienced new T2 brain and spinal lesions under EID. Four patients (3.1%) under SID and none under EID had at least one brain Gadolinium enhancing lesion. No Gadolinium enhancing lesions were detected in the spinal cord. IgG and IgM serum concentrations tended to steadily decrease over time, in both SID and EID. IgG reduction was associated with age (beta: −0.04648, $p = 0.00672$) and both IgG (beta: −0.23145, $p = 0.00115$) and IgM (beta: −6.78E-02, $p = 9.08E-11$) reduction was associated with time since the first OCR infusion. IgM serum concentration was negatively associated with the previous use of DMTs (Other Monoclonal Antibobodies [beta:-5.86E-01, $p = 0.011091$]). OCR EID regimen was associated with a reduction of 40% of drug's costs.

Conclusions: EID based on CD19+27+ memory B cells count was associated with maintained clinical and radiological efficacy over more than one year, reducing the cost of treat-

ment. IgG and IgM reduction remained stable under the EID regimen and was related to the time since the first OCR infusion and the exposure to previous immunosuppressive drugs.

P79

A Case of Acute Hemorrhagic Leukoencephalitis: Expanding the Clinical Spectrum of MOGAD

L Skarsta [1], T Nicoletti [1], K Frick [2], V Kana [1], AJ De Vere-Tyndall [3], M Weller [1], P Roth [1] and M Herwerth [1]

[1] Department of Neurology, University Hospital Zurich and University of Zurich, Zurich, Switzerland;
[2] Institute of Intensive Care, University Hospital of Zurich, University of Zurich, Zurich, Switzerland;
[3] Department of Neuroradiology, University Hospital and University of Zurich, Switzerland

MOGAD, a recently identified autoimmune disease of the central nervous system, presents a notably heterogeneous spectrum. It encompasses cases of cerebellitis, autoimmune encephalitis, and a syndrome of encephalitis with steroid-responsive seizures, known as FLAMES (FLAIR-hyperintense lesions in anti-MOG-associated encephalitis with seizures). Here, we present a new possible manifestation of MOG antibody-associated disease (MOGAD) in a case that progressed to acute hemorrhagic leukoencephalitis (AHLE). The patient initially presented with bilateral optic neuritis. Blood tests showed mild CRP elevation and mild leukocytosis. CSF analysis revealed pleocytosis (77 cells/μL, 55% lymphocytes, 35% neutrophils) and elevated protein (750 mg/L). Oligoclonal bands were not detectable. Brain MRI revealed bilateral T2/FLAIR hyperintense signal alterations of optic nerves with contrast enhancement and small infra- and supratentorial subcortical, periventricular and pontine T2/FLAIR hyperintense lesions. After initial response to intravenous steroid treatment, the patient's condition deteriorated later despite escalation therapy with methylprednisolone 2 g/day and plasma exchange. A second lumbar puncture revealed massive increase of cell count (887 cells/μL, 80% neutrophiles). Bacterial, viral and fungal multiplex-PCR was negative. Extensive evaluation of collagen vascular disease and autoimmune encephalitis antibodies was negative. Testing for serum AQP4-IgG and MOG-IgG in a cell-based assay revealed a marked titer positivity for MOG-IgG of 1:320 (cut-off 1:10). A new MRI scan revealed new and size-progressive lesions with hemorrhagic and necrotic areas as well as an expansive effect in the brainstem, indicating a progression to AHLE. AHLE, also known as Weston-Hurst disease, is considered a variant of ADEM. Both typically present with acute encephalopathy and multifocal neurological deficits due to multiple inflammatory demyelinating lesions in cerebral hemispheres, brainstem, and spinal cord. Overall, the presented case expands our knowledge about the heterogeneous manifestation of MOGAD and suggests a putative role of MOG-Ab in the pathophysiology of AHLE. Future studies are warranted to further investigate the association between MOG-Ab and AHLE.

P80

Clinical Presentation and Outcome of S1PR-Modulators and Natalizumab-Associated-Progressive Multifocal Leukoencephalopathy: A Retrospective Multicenter Cohort

J Blant [1], N De Rossi [2], C Schroeder [3], A Maurousset [4], M Kraemer [5], K Kume [6], T Misu [7], J Ouallet [8], M Pallix-Guyot [9], S Gerevini [10], C Bakirtzis [11], R Piñar Morales [12], B Vlad [13], P Karypidis [14], I Ayzenberg [3], X Moisset [15], T Derfuss [14], I Jelcic [13], G Martin-Blondel [16], R Du Pasquier [1] and R Bernard-Valnet [1]

[1] Department of Clinical Neurosciences, Lausanne University Hospital (Centre Hospitalier Universitaire Vaudois) and Lausanne University, Switzerland;
[2] Regional Multiple Sclerosis Center, ASST–Spedali Civili di Brescia;
[3] Department of Neurology St. Josef-Hospital, Ruhr University Bochum, Germany;

[4] Centre hospitalier régional universitaire de Tours, Hôpital Bretonneau, Service de neurologie, France;
[5] Department of Neurology, Alfried Krupp von Bohlen und Halbach Hospital, Essen, Germany;
[6] Department of Epidemiology, Research Institute for Radiation Biology and Medicine, Hiroshima University, Japan;
[7] Department of Neurology, Tohoku University Hospital, Japan;
[8] Service de Neurologie, Pôle des Neurosciences Cliniques, CHU de Bordeaux Pellegrin Tripode, France;
[9] Service de Neurologie et Unité Neurovasculaire, Centre Hospitalier Régional d'Orléans, France;
[10] Unit of Neuroradiology, Papa Giovanni XXIII Hospital, Italy;
[11] Multiple Sclerosis Center, Second Department of Neurology, Aristotle University of Thessaloniki, Greece;
[12] Servicio de Neurología, Hospital Clínico Universitario San Cecilio, Spain;
[13] Department of Neurology, University Hospital Zurich and University of Zurich, Switzerland;
[14] Neurologic Clinic and Policlinic and Research Center for Clinical Neuroimmunology and Neuroscience, Departments of Medicine, Biomedicine, and Clinical Research, University Hospital Basel, University of Basel, Switzerland;
[15] Service de Neurologie, Université Clermont Auvergne, CHU de Clermont-Ferrand, Inserm, Neuro-Dol, France;
[16] University Hospital of Toulouse, Infectious and Tropical Diseases Unit, France

Background and Objectives: Progressive multifocal leukoencephalopathy (PML) is a severe neurological disease caused by JC virus reactivation in immunocompromised individuals. Several multiple sclerosis disease-modifying therapies (DMT) have been associated with the risk of developing PML including natalizumab and to a lesser extent sphingosine-1-phosphate receptor modulators (S1PRM) (fingolimod, siponimod, ozanimod). Although the course and management of natalizumab-associated-PML have been largely described, information on S1P1RM-associated-PML remains scarce. We aimed to compare the clinical presentation and outcome of S1PRM and natalizumab-associated-PML.
Methods: We conducted a retrospective multicenter cohort study. Patients admitted at participating centers between 2009 and 2022 for PML related to S1PRM or natalizumab were included. We collected information on the clinical and radiological presentation. We also analyzed the outcome of PML, namely the occurrence of an immune reconstitution inflammatory syndrome (IRIS), the survival and disability (measured by modified Ranking Scale–mRS) at 12 months, and the occurrence of multiple sclerosis (MS) relapses within the first year following PML.
Results: 84 patients were identified and 82 were included in the final analysis (17 on fingolimod and 65 on natalizumab). Fingolimod-associated PML occurred in older patients (median (IQR25-75): 51 (44 60.5) vs. 44 (38–47) years, p = <0.001) and after a longer treatment duration (median (IQR25-75): 53.8 (45.5–86.2) vs. 41.5 (26.8–52) months, p = 0.003). PML presentation was similar in the two groups. For initial management, most natalizumab-associated-PML received plasma exchange (80 vs. 29.4%, p < 0.001) but there was no difference for the use of antiviral therapies. PML in natalizumab-treated patients- was more prone to develop immune reconstitution inflammatory syndrome (92.2% vs. 58.8%, p = 0.002). However, in most patients, fingolimod withdrawal was associated with new MS activity (75% vs. 31.3%, p = 0.003). Overall, the outcome was similar in the two groups for the 12 months disability (median mRS (IQR25-75): 3 (2–4.7) vs. 3 (2–4), p = 0.542).
Discussion: Our study shows that fingolimod-associated PML is associated with a reduced risk of IRIS but a higher rate of early MS activity after fingolimod cessation. Considering these differences clinicians should adapt their post-PML treatment strategy according to the pre-PML medication.

P81

Challenges in Establishing Diagnosis of GFAP Astrocytopathy Based on a Case Report of A 73-Year-Old Man

J Deppe [1], B Wagner [1], C Hader [2], K Boggian [3], U Pietsch [4], F Brugger [1] and J Vehoff [1]

[1] Department of Neurology, Cantonal Hospital St. Gallen, Switzerland;
[2] Department of Radiology, Cantonal Hospital St. Gallen, Switzerland;
[3] Department of Infectious Diseases and Hospital Epidemiology, Cantonal Hospital St. Gallen, Switzerland;
[4] Department of Anaesthesiology and Intensive Care, Cantonal Hospital St. Gallen, Switzerland

Autoimmune glial fibrillary acidic protein (GFAP) astrocytopathy was first described in 2016 as an antibody-derived meningoencephalomyelitis with mainly monophasic course, often accompanied by fever, marked pleocytosis in cerebrospinal fluid (CSF) and a wide range of possible neurological manifestations. Linear radially-oriented periventricular enhancement is a characteristic radiological sign, but in many patients, brain imaging findings are rather unspecific. Besides, GFAP astrocytopathy is often accompanied by malignancies or other autoimmune disorders and is often preceded by symptoms of an infection, overall making diagnosis challenging. Here, we report a case of a GFAP astrocytopathy in a 73-year-old man who initially presented with isolated meningitis progressing to paraparesis and dysautonomia, requiring intubation due to respiratory failure. There were no clinical or radiological signs beyond meningitis and CSF analysis revealed marked pleocytosis, elevated lactate and low glucose, prompting treatment for suspected cerebral infection. Exhaustive work-up including brain biopsy did not reveal any conclusive etiology. After having excluded an underlying infectious disease or malignancy, treatment was switched to high-dose steroids, leading to remarkable improvement in terms of wakefulness and dysautonomia, but with persistence of paraparesis. Eventually, anti-GFAP-IgG antibodies were detected in the CSF, confirming the diagnosis of autoimmune GFAP astrocytopathy. In conclusion, GFAP astrocytopathy is an uncommon cause of meningoencephalitis, characterized by marked pleocytosis and detection of anti-GFAP-IgG in the CSF. Establishing the correct diagnosis can be challenging as both clinical and radiological findings are heterogeneous, with standardized diagnosis criteria and treatment protocols still missing. Including GFAP astrocytopathy in differential diagnosis in patients with non-infectious meningoencephalitis is crucial, as early treatment with steroids or other immunosuppressants can yield good clinical response.

P82

Patient Support Programs for Multiple Sclerosis Patients Treated with Interferons or Dimethyl Fumarate in Switzerland and the Principality of Liechtenstein

H Hammer [1], T Ludersdorfer [2], S Chen [2], GC Duiker [3], U Mai [3], M Stürchler [3] and A Le Coz-Iffenecker [2]

[1] Inselspital—Universitätsspital Bern—Universitätsklinik für Neurologie;
[2] Biogen Switzerland AG;
[3] MediService AG, Switzerland

Patient Support Programs (PSPs) for disease modifying treatments (DMTs) in multiple sclerosis (MS) are in place to ensure optimal patient management including training of product application, therapy support and reporting/managing of potential adverse events. Thereof, PSPs can have a positive impact on patients' adherence1. However, there is limited knowledge about the use of PSPs, how patients perceive PSPs and what drives patient satisfaction. Here we describe two PSPs for MS patients prescribed with interferons (IFNs) or dimethyl fumarate (DMF). To provide an optimal patient-centric service, competent and experienced nursing specialists provide well-founded advice and instructions via telephone, video calls and personal visits. The service is voluntary and has no influence on any treatment decision by the patient's treating physician. Patients are registered by

their treating physician. The PSPs are set up for a period of 12 months and carried out by MediService AG. Enrolled patients are contacted by nursing specialists according to a pre-defined time schedule. If needed, patients have the option to contact the nursing specialists via telephone between the planned contacts.
Aims: To better understand and evaluate the patients' unmet needs and satisfaction with the PSP, a patient satisfaction survey was implemented in the PSP setting.
Methods: Patients received in total 3 surveys, the first during month 1–3, the second during month 5–7 and the third at month 9–12. Survey data was collected for 4 years.
Results: From April 2019 to May 2023, 167 patients were enrolled for the DMF PSP and 152 patients were enrolled for the IFN PSP. During the 12 months, 9 contacts with the patient are pre-planned for the IFN PSP and 8 contacts for the DMF PSP. Personal visits took on average 65 min, video calls 38 min and telephone calls 17 min.
Overall, 8 out of 10 patients would recommend the PSP to other patients. The recommendation rate was similar between the IFN PSP and the DMF PSP.
Conclusions: The data from the surveys demonstrate that PSPs support the patients to better understand how their prescribed MS medication works and helps them to manage their MS therapy independently. In addition, patients appreciate the PSP services, independent of whether they were on injectable or oral drugs.

P83

Effectiveness, Safety and Patients' Satisfaction of Nabiximols (Sativex®) on Multiple Sclerosis Spasticity in A Real-Life Swiss Multicenter Study

R Sacco [1], GC Riccitelli [2], G Disanto [3], C Gobbi [4] and C Zecca [4]

[1] Neurocenter of Southern Switzerland, Ospedale Regionale di Lugano, Ente Ospedaliero Cantonale, Lugano, Switzerland;
[2] Neurocenter of southern Switzerland, Department of Neurology, Regional Hospital Lugano (EOC);
[3] Neurocenter of southern Switzerland, Department of Neurology, Regional Hospital Lugano (EOC), Lugano, Switzerland;
[4] Ospedale Civico di Lugano, Neurocenter of Southern Switzerland (NSI), Faculty of Biomedical Sciences Università della Svizzera Italian (USI)

Background: Nabiximols, a cannabinoid-based oromucosal spray, is approved for patients with moderate to severe multiple sclerosis spasticity (MSS) resistant to other antispastic medications. No data on effectiveness, safety and patients' satisfaction in Swiss MS patients, treated with nabiximols alone or as add-on, have been reported so far.
Objective/Methods: To investigate the effectiveness, tolerability and satisfaction of nabiximols in a real-life multicentric Swiss cohort. The following data were collected at treatment start (baseline) and 12 weeks thereafter: Modified Ashworth scale (MAS), scores at numerical rating scales ranging from 0 (absent) to 10 (considerable) for effect on spasticity (sNRS), pain (pNRS), gait (gNRS), urinary symptoms (uNRS), tolerability (tNRS) as assessed by the treating neurologist and overall treatment satisfaction (TsNRS) and tolerability (tNRS) as assessed by the patient.
Results: Ninety-five patients (44 relapsing remitting, 37 secondary progressive and 14 primary progressive MS; median age = 53 [IQR 44–62]; female 69%; median EDSS 6 [4–6], concomitant antispastic treatments in 54% of patients) were included. From baseline to week 12, median MAS score decreased from 3.0 to 2.0 ($p < 0.001$). Median scores of each NRS also significantly decreased ($p < 0.001$ for all comparison). At week 12, the median TsNRS and tNRS scores were 8/10 (IQR: 6–9) and 9/10 (IQR: 7–10), respectively, and 93.7% of patients continued to use nabiximols at the average dose of six sprays/day. Nine of 95 patients (9.5%) reported side effects and 5 (5.3% of the overall patients) of these stopped Nabiximol administration. No serious advers event were recorded.
Conclusions: Our first Swiss, multicentric, observational, real-life study supports and enhances previous finding of nabiximols use as monotherapy or in combination with other

spasmolytic drugs being an effective, safe and well-tolerated treatment option for resistant MS spasticity and spasticity-related symptoms (pain, bladder dysfunction and gait).

P84

Neuromuscular Ultrasound Changes in Unilateral Symptomatic Subacute Lumbosacral Radiculopathy: A Prospective Blinded Case-Control Study

D Cuendet [1], D Valsecchi [1], H Najberg [2], G Maestretti [1] and F Medlin [1]

[1] Hôpital Cantonal Fribourg HFR—Université de Fribourg, Medical School;
[2] UNI FRIBOURG, Switzerland

Introduction: Lumbosacral radiculopathy (LR) is a major cause of disability. Electroneuromyography has limited sensitivity in diagnostic accuracy. Neuromuscular ultrasound (NMU) has recently become an established and emergent technique for the investigation of peripheral nerve and muscle disorders, but studies on NMU in LR are lacking.
Aims: The aim of the present study is to describe ultrasonographic neuromuscular changes in patients with subacute compressive LR with motor impairment.
Methods: Patients with unilateral magnetic resonance imaging (MRI) confirmed compressive L4, L5 or S1 radiculopathy with motor impairment were included. The cross-sectional area (CSA) of the sciatic and femoral nerves, the muscles innervated by the affected motor root and unaffected lower limbs muscles and muscle fasciculation detection rate were assessed using a pre-specified neuromuscular ultrasound evaluation with blinded side-to-side comparison.
Results: Of the 18 included patients, 66% were male and the mean age was 51 years. Overall, 56% had L5 radiculopathy, mostly due to disc herniation (83%). Sciatic nerve CSA of the symptomatic side was increased (Cohen's d = 0.78, $p = 0.001$) and the fasciculation detection rate was higher in the affected muscles (delta = 13%, $p = 0.007$). Muscle CSA of the symptomatic side in affected and non-affected muscles was decreased; however, this was not only due to the radiculopathy, contrary to our expectation ($\eta G^2 = 0.087$, $p = 0.005$).
Discussion: NMU evaluation in patients with symptomatic subacute to chronic LR showed significantly larger sciatic nerve CSAs on the symptomatic side and a higher fasciculation detection rate in affected muscles.

P85

Characteristics And Evolution of CIDP Patients According to Their Electrodiagnostic Certainty Based on the 2021 EAN/PNS Criteria

V Loser, K Staedler, A Vicino, T Kuntzer and M Théaudin

Department of Clinical Neurosciences, CHUV, Lausanne University Hospital, Switzerland

Aims: CIDP is a presumed immune-mediated neuropathy with heterogeneous presentation and clinical course. The aim of this study was to describe the characteristics and determine if there was a difference in evolution of patients who were categorized as having a CIDP or a possible CIDP according to the European Academy of Neurology/Peripheral Nerve Society (EAN/PNS) 2021 criteria.
Methods: In this retrospective observational study, we selected 50 adult patients, 29 CIDP and 21 possible CIDP. We reviewed the clinical data, which included the neuropathy impairment scale (NIS) and modified Rankin Scale (mRS), cerebrospinal fluid examination, and nerve conduction studies (NCS) parameters. Those data were assessed during the first evaluation of the patient (T0), after one year (T1), two years (T2) and three years (T3).
Results: At baseline, CIDP patients had a higher NIS score (median NIS score of 38 versus 20.5, $p = 0.03$), suggesting a more severe neuropathy, and were more associated with a typical CIDP phenotype ($p = 0.02$) than possible CIDP patients. Other variable did not differ significantly. CIDP patients tended to have a better objective response to immunotherapy (19 responders, 65%) than possible CIDP patients (9 responders, 42%), but difference was not significant ($p = 0.15$). Between baseline and T1, there was a median Δ NIS of -8 (IQR

−36, 0) for CIDP patients and 3 (−10, 5) for possible CIDP patients ($p < 0.01$), and a median (IQR) Δ mRS of −1 (−1, 0) for CIDP patients and 0 (−1, 0) for possible CIDP patients ($p = 0.05$). Between baseline and T2, there was a median (IQR) Δ mRS of -1 (−1, 0) for CIDP patients 0 (−1, 0) for possible CIDP patients. ($p = 0.04$). In a multivariate linear regression analysis (exploring other confounding factors), a diagnostic certainty of CIDP was associated with a tendency of a decrease of 3.193 in the NIS score at T3 and of 0.355 in the mRS score at T3, although not significant ($p = 0.6$ and $p = 0.34$ respectively).
Conclusions: Excepting for a more severe neuropathy in CIDP patients, estimated with the NIS score, and a more typical phenotype, CIDP and possible CIDP patients had similar electroclinical characteristics. With a follow-up up to 3 years after diagnosis, our data suggest that clinical evolution and prognosis of patients is better for CIDP patients than possible CIDP patients. Fulfillment of the EAN/PNS 2021 criteria for CIDP therefore probably provides an additional prognostic value.

P86

GLUGLIO—A Phase Ib/II Randomized Drug Repurposing Trial of Glutamate Signaling Inhibitors in Combination with Chemoradiotherapy in Patients with Newly Diagnosed Glioblastoma (NCT05664464)

H Wirsching [1], P Roth [1], A Fischer [2], T Hundsberger [3], D Migliorini [4], A Ochsenbein [5], H Läubli [6], K Seystahl [7], L Imbach [8], T Hortobagyi [1], L Held [9], A Bink [1] and M Weller [1]

[1] UniversitätsSpital & Universität Zürich;
[2] Kantonsspital Graubünden;
[3] Kantonsspital Sankt Gallen;
[4] HUG Hôpitaux Universitaires de Genève;
[5] Insel Spital Bern;
[6] Universitätsspital Basel;
[7] Luzerner Kantonsspital (LUKS);
[8] Schweizerische Epilepsie-Klinik;
[9] Universität Zürich, Switzerland

Background: Glioblastoma synthesizes and secretes large quantities of the excitatory neurotransmitter glutamate, driving epilepsy, neuronal death, tumor growth and invasion. Several brain-penetrating drugs that have obtained clinical approval in other pathologic conditions can inhibit glutamate synthesis, secretion and signalling, respectively, including (i) the anti-seizure drug gabapentin, which inhibits the glutamate synthesis enzyme, branched chain amino acid transaminase 1, (ii) the anti-inflammatory drug sulfasalazine, which inhibits glutamate secretion by blocking the cystine-glutamate exchanger system Xc, and (iii) the cognitive enhancer memantine, which can prevent glutamate-driven, calcium-induced neuronal death and tumor cell invasion by blocking N-methyl-D-aspartate (NMDA) type glutamate receptors.
Methodology: The multi-centre, open-label, parallel-group, two-arm, 1:1 randomized, phase Ib/II trial GLUGLIO explores the efficacy of a triple-combination of daily oral gabapentin, sulfasalazine and memantine in combination with standard chemoradiotherapy compared to chemoradiotherapy alone. Dosing of either drug will be sought up to the maximum approved dose and will be reevaluated in an interim safety analysis after 20 patients have been randomized into the experimental arm. The primary endpoint is progression-free survival at 6 months (PFS-6). The sample size of N = 120 patients was calculated to detect an increase in PFS-6 from 50% to 70% with a power of 80% performing exploratory hypothesis testing at a one-sided significance level of 10%. Secondary endpoints include progression-free, overall and seizure-free survival, response rate, quality of life of patients and caregivers, symptom burden, cognitive functioning, tumor glutamate levels by magnetic resonance spectroscopy as well as anti-convulsant and steroid use. Surgical tissues as well as peripheral blood and electroencephalography recordings will also

be sampled longitudinally for translational analyses. Recruitment is ongoing and foreseen to be completed by mid 2026.
Conclusions: The simultaneous targeting of glutamate synthesis, secretion and signalling will clarify whether glutamate should be further explored as a clinical target in glioblastoma patients.

P87

Glioblastoma in Geriatric Patients: Presentation, Treatment and Survival in Patients Above 80 Years

C Stadler [1], D Gramatzki [1], E Le Rhun [1], A Hottinger [2], T Hundsberger [3], U Roelcke [4], H Läubli [5], S Hofer [1], K Seystahl [1], H Wirsching [1], M Weller [1] and P Roth [6]

[1] USZ, Zürich, Switzerland;
[2] CHUV, Vaudois, Switzerland;
[3] Kantonsspital St Gallen;
[4] KSA, Aarau, Switzerland;
[5] USB, Basel, Switzerland;
[6] Universitätsspital Zürich, Switzerland

Aims: While numbers of very old geriatric patients affected by Glioblastoma are increasing, there is limited guidance on treatment strategies and clinical outcomes remain poor. The aims of this study were to get an overview of current therapeutic approaches, as well as, to identify possible predictors of survival.
Methods: Data of patients diagnosed with Glioblastoma at the age of 80 years and above were collected retrospectively from six clinical centers in Switzerland and France. Clinical presentation, demographics and treatment strategies were assessed. To investigate for predictors of survival, cox proportional hazard modelling was performed.
Results: 45 of the 107 patients underwent biopsy only, 30 had subtotal and 25 had gross total tumor resection. The extent of resection was not known in 7 cases. 34 patients did not receive any post-operative treatment. 12 patients underwent radiotherapy with concomitant Temozolomide, however, only two continued with maintenance Temozolomide. 14 patients were treated with Temozolomide only, 35 with radiotherapy only and one with bevacizumab. Another patient was treated within a clinical trial. Median overall survival (OS) for the whole cohort was 4.2 months and median progression free survival (PFS) was 3.3 months. In contrast, median OS was 7.2 months and median PFS was 3.9 months among patients receiving post-operative treatment. Clinical features associated with beneficial outcomes were Karnofsky performance status (KPS) >/= 70%, gross total resection and combined treatment. Patients spent a median of 30 days hospitalized, making up for 23% of the OS. Palliative care was mostly provided by nursing homes (32%) and palliative care wards (26%).
Conclusions: Although associated with longer overall survival, only a small proportion of patients received post-operative, and combined modality treatment in particular. Selected patients might therefore qualify for tumor specific therapies despite their higher age.

P88

Immunotherapeutic Targeting of Fibroblast Activation Protein (FAP) in Treatment Refractory Glioblastoma Using Novel CAR-T Cell Therapy

N Tatari [1], H Mohamed Seid Hedad [1], A Zingg [2], E Bartoszek [3], V Tschan [1], T Schenker [1], M Ritz [1], P Miletic [4], C Venugopal [4], M Etter [1], S Singh [4], H Laeubli [2] and G Hutter [1]

[1] University Hospital Basel, Brain Tumor Immunotherapy and Biology Laboratory, Department of Biomedicine;
[2] University Hospital Basel, Cancer Immunotherapy Laboratory, Department of Biomedicine;
[3] University of Basel, Microscopy Core Facility, Department of Biomedicine;
[4] McMaster University, Department of Surgery

Aims & Background: Glioblastoma (GBM) is the most common malignant primary adult brain tumor, characterized by extensive cellular and genetic heterogeneity [1–3]. The Standard of Care (SOC) therapy and clinical trials have not been successful in improving patients' survival which underscores an urgent need for developing new effective therapies for this treatment refractory disease.
Methods: In silico and in vitro analysis have revealed high level of Fibroblast Activation Protein (FAP) expression in GBM tissue by multiple cell populations including endothelial cells, fibroblasts, stromal and tumor cells, but not normal brain tissue, making FAP a safe and suitable therapeutic target as it allows for destruction of tumor cells as well as effective elimination of their supporting microenvironment [4,5]. As chimeric antigen receptor (CAR) expressing T cells have shown promising results against multiple cancers [6–9], we aimed to target FAP in GBM by FAP specific CAR-T cells generated using a novel GMP-ready FAP-CAR construct produced based on a virus-free CAR gene transfer using advanced sleeping beauty transposon technology and preclinically test their anti-tumor efficacy against GBM at in vitro and in vivo level.
Results: Our data revealed that co-culturing CAR-T cells with FAP+ GBM cells (U87) results in increased surface expression of T-cell activation markers. Moreover, FAP CAR-T mediated cytotoxicity against FAP+ GBM cells was also observed in the co-culture of GBM and CAR-T cells. For further validation, the effect of FAP CAR-T cells will be tested on patient-derived GBM organoids. The in vivo efficacy of FAP CAR-T cells is currently under investigation and we anticipate that the treatment of GBM tumor-bearing mice with FAP CAR-Ts results in extended survival and reductions of tumor burden.
Conclusions: These rigorously obtained data show high level of efficacy for FAP-specific CAR-T cells against GBM suggesting that clinical development of this therapeutic modality can provide a novel therapeutic strategy for GBM patients that can be used in combination with SOC or other immunotherapeutics. Therefore, upon successful completion of the preclinical study, we plan to conduct a phase I dose-escalation trial of autologous FAP-CAR T cells for patients with recurrent Glioblastoma.

P89

Tumor Compression of the Middle Cerebellar Peduncle is Associated with Worse Facial Nerve Outcomes and Lower Degrees of Resection for Medium Sized Vestibular Schwannomas

D Croci, A Tai, J Kim, R Mhaskar, C Danner, K Boyev, H Van Loveren and S Agazzi

University of Southern Florida, Tampa, FL, USA

Introduction: Optimizing the degree of resection (DOR) and facial nerve outcomes (FNO) remain a challenge in vestibular schwannoma (VS) surgery. Currently, tumor size has been the only consistently reported factor predicting FNO and DOR.
Objective: To evaluate whether the degree of the tumor's compression on the middle cerebellar peduncle (peduncular compression, PC) is associated with FNO and DOR in medium to large VSs.
Methods: 99 patients who underwent surgical resection of their VSs were included in this retrospective study. Preoperative MR imaging was used to measure the degree of PC. Patient medical records were queried to determine the DOR and FNO.
Results: Patients with unfavorable FNO (HB 3+) immediately post-op had significantly greater PC than those with favorable FNO (19.9 vs. 15.4 mm, $p = 0.047$). This significance was not observed at last follow-up but there was a trend. When medium sized tumors (15–30 mm) were analyzed separately, patients with unfavorable FNO at last follow-up and immediate post-op had significantly greater PC compared to their favorable counterparts (14.1 vs. 8.7 mm). Significantly greater PC was also observed in patients who underwent subtotal resection (20.7 mm) compared to near (14.3 mm) and gross total resection (10.8 mm). This significance persisted in medium sized but not large sized tumors (>30 mm) when they were analyzed separately.

Conclusions: The degree of PC as measured on preoperative imaging can predict short and long-term facial nerve outcomes as well as the degree of resection in medium sized vestibular schwannomas. Aggressive resection of medium sized vestibular schwannomas with significant PC may be more difficult and associated with worse facial nerve outcomes.

P90

Prognostic Associations of Steroid Use in Glioblastoma: A Population-Based Study

Y Abdel Moneim, P Roth, M Weller and D Gramatzki

University Hospital and University of Zurich, Switzerland

Background and Aim of the Study: Steroids are widely used in brain tumor patients to control symptoms related to tumor and cerebral edema. A possible detrimental effect of steroid treatment on prognosis in glioblastoma patients, the most malignant primary brain tumor (1) with poor overall survival despite extensive treatment (2), has been proposed (3, 4). Whether this represents a negative patient selection due to the potential confounding factor of steroid treatment or whether glucocorticoid use per se causes a worse prognosis remains a matter of debate. The aim of the study was to assess the extent of steroids use in patients with glioblastoma in the Canton of Zurich, clinical outcome and survival.
Methods: We reviewed retrospective data of 225 patients diagnosed with isocitrate dehydrogenase (IDH)-wildtype glioblastoma from 2010 to 2014 in the Canton of Zurich, Switzerland. We assessed clinical data and the use of steroids at different time points. Survival data were analyzed with the Kaplan-Meier method, and corrections for known prognostic or predictive factors were performed with Cox regression analyses. Correlations were determined with Spearman's correlation coefficient.
Results: Most patients (N = 203, 95%) received steroids at least once in the first year after diagnosis, the majority (N = 153, 69%) in the perioperative setting (defined at the time of hospitalisation for the surgery $\pm$7 days), and 94 patients (62%) in the first three months. Among the 67 patients for which an infection at any time was reported, 45 (67%) were under steroid treatment when the infection was diagnosed. Among all infections (n = 85), 53 (62.3%) were reported under dexamethasone. Steroid use at three months after surgery was associated with steroid treatment at six months, too ($p < 0.01$). The latter was associated with inferior overall survival in a multivariate analysis after correction for known prognostic and predictive factors ($p = 0.006$).
Conclusions: Use of steroids at six months after diagnosis was associated with inferior survival in glioblastoma even when controlling for confounding factors. The precise mode of action of steroids in this setting remains to be identified, but cytoprotective effects of tumor cells versus radiotherapy and chemotherapy as well as decreased immune function of the host are potential mechanisms.

P92

Mortality in Acute Ischemic Stroke Patients with a New Diagnosis of Cancer during the Index Hospitalization versus after Discharge

J Göcmen [1], F Steinauer [1], M Kielkopf [1], C Kurmann [2], A Mujanovic [2], L Clénin [1], N Silimon [1], A Boronylo [1], T Meinel [1], J Kaesmacher [2], P Bücke [1], D Seiffge [1], G Costamagna [3], G Costamagna [3], P Michel [4], U Fischer [5], M Arnold [1], B Navi [6], T Pabst [7], M Berger [7], S Jung [1] and M Beyeler [1]

[1] Department of Neurology, Inselspital, Bern University Hospital, and University of Bern, Switzerland;
[2] Institute for Diagnostic and Interventional Neuroradiology, Inselspital, Bern University Hospital, and University of Bern, Switzerland;
[3] Stroke Unit, Neurology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, 20122 Milan, Italy;
[4] Stroke Center, Neurology Service, Department of Clinical Neurosciences, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland;

[5] Department of Neurology, University Hospital of Basel, University of Basel, Basel, Switzerland;
[6] Clinical and Translational Neuroscience Unit, Feil Family Brain and Mind Research Institute and Department of Neurology, Weill Cornell Medicine, New York, New York, USA;
[7] Department of Medical Oncology, Inselspital, Bern University Hospital, and University of Bern, Switzerland

Background and purpose: Early diagnosis of previously unknown cancer (termed occult cancer) in patients with ischemic stroke could result in faster initiation of cancer therapy and potentially improve overall outcomes. The present study aimed to compare mortality rates of ischemic stroke patients with occult cancer diagnosed during the index stroke hospitalization versus those diagnosed after discharge.
Methods: Among consecutive acute ischemic stroke patients treated at our stroke center from 2015 through 2020, we identified new diagnoses of cancer made during the index hospitalization or in the year after discharge. Patient characteristics, cancer profiles, and long-term mortality rates were compared. Covariates influencing overall mortality were calculated and reported using adjusted Hazard Ratios (aHR) and their associated 95% confidence interval (CI) in a multivariable Cox regression analysis. Covariates included in the regression analysis were age on admission, female sex, NIHSS on admission, multiterritory infarctions, leukocyte count in G/L, low hemoglobin in g/L, D-dimer in μg/L, cancer diagnosis after discharge from stroke hospitalization, cancer histological type (as categorical variable), presence of local invasion or metastasis at the time of diagnosis and overall cancer treatment.
Results: Among 3894 patients without known active cancer and available long-term follow-up (median [interquartile range] 1150 [561–1782] days), 59 (1.5%) had cancer diagnosed within one year after index stroke, of which 27 (45.8%) were diagnosed during hospitalization and 32 (54.2%) after discharge. The median time between stroke and cancer diagnosis in patients diagnosed during the index hospitalization was 1 (IQR: 0–6) day. In patients with cancer diagnosis after discharge, the median time to cancer diagnosis was 49 (IQR: 15–139) days. In multivariable analysis, cancers diagnosed after discharge versus those diagnosed during hospitalization were associated with an increased risk of death (aHR 3.25, 95% CI 1.20–8.81, P = 0.021).
Conclusions: A missed diagnosis of occult cancer during initial stroke hospitalization could negatively impact overall long-term mortality. Among stroke patients, studies are needed to hasten the detection of underlying occult cancer when present.

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COSIMO: Paving the Way for Social Cognition in Screening Diagnostics

R Johannessen [1], M Eicher [2] and H Jokeit [1]

[1] Swiss Epilepsy Center, Klinik Lengg;
[2] Universität Zürch, Switzerland

Social cognition is essential for quality of life and mental health, but is often neglected in clinical assessment. In neurology, this gap is particularly surprising since DMS-5 recognized social cognition as a core neurocognitive domain to be assessed in neuropsychological assessments of neurological patients close to a decade ago. A lack of well-validated, sensitive and cost-effective tests of social cognition may explain this diagnostic gap. In an attempt to make screening for social cognition easier and more attractive, we have developed COSIMO (Cognition of Social Interaction in Movies), an online screening tool for social cognition that assesses participants' understanding of social interactions in about 5 minutes using 25 short, silent video vignettes of dyadic interactions. One of two test versions was administered to 524 German-speaking participants, including 289 neurotypical individuals and 235 patients with neurological and psychiatric disorders. In line with previous research, patients with temporal lobe epilepsy (N = 32) differed significantly from neurotypical participants (Hedge's g = 0.79, p = 0.006) in terms of social cognition as as-

sessed by COSIMO. A weak correlation was found between COSIMO and the Montreal Cognitive Assessment (N = 86, r = 0.23, $p = 0.03$), suggesting little dependence on general neurocognitive integrity. A moderate to high correlation was found with the Movie for the Assessment of Social Cognition (N = 41, r = 0.66, $p < 0.001$), a video-based test of social cognition with high ecological validity, and a weak, non-significant correlation was found with the Faux Pas Recognition Test (N = 33, r = 0.25, $p = 0.15$), a text-based, more artificial test of Theory of Mind. Preliminary results suggest satisfactory convergent and divergent validity. COSIMO is a sensitive, ecologically valid, user friendly and cost-effective screening tool for social cognition. It is readily available to researchers and clinicians through its web app-based format, and we welcome collaborations and requests for its use.

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Acute Right Opercular Stroke-Associated Polyopic Heautoscopy and Hallucinations Caused by Disconnexion to the Inferior Parietal Lobule through the Superior Longitudinal Fasciculus III: A Single Case Study

M Obrenovic [1], M Mouthon [2], C Chavan [3], A Saj [3], S Dieguez [2], J Aellen [3] and JN Chabwine [3]

[1] Clinique Romande de Réadaptation SUVA Care;
[2] Fribourg University;
[3] HFR—hôpital fribourgeois

Illusory neuropsychiatric symptoms such as hallucinations or the feeling of a presence (FOP) can occur in diffuse brain lesion or dysfunction, in psychiatric diseases as well as in healthy individuals. Their occurrence due to focal brain lesions is rare, most probably due to underreporting, which limits progress in understanding their underlying mechanisms and anatomical determinants. In this single case study, an 86-year-old patient experienced, in the context of an acute right central opercular ischemic stroke, visual hallucinatory symptoms (including palinopsia), differently lateralized auditory hallucinations and FOP. This unusual clinical constellation could be precisely documented and illustrated while still present, allowing a realistic and immersive visual experience validated by the patient. The acute stroke appeared to be their most plausible cause (after exclusion of other etiologies). Furthermore, accurate analysis of tractographic data suggested that disruption in the posterior bundle of the superior longitudinal fasciculus connecting the stroke lesion to the inferior parietal lobule was the anatomical substrate explaining all illusory symptoms, in coherence with existing literature. We could finally elaborate on symptoms taxonomy and phenomenology (e.g., polyopic heautoscopy, hallucinatory FOP, etc.), and on patient's remarkable distancing from them (with some therapeutic implications supported by plausibly engaged mechanisms). This case not only authentically enriched the description of such rare combination of heterogenous illusory symptoms, but disclosed an unrevealed anatomo-clinical link relating all of them to the acute stroke lesion through an association fiber, thereby contributing to the understanding of these intriguing symptoms and their determinants.

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Social Cognition in Neurology: On the Need for Assessment Tools

M Eicher [1], J Bauer [2], R Johannessen [3] and H Jokeit [3]

[1] University of Zurich;
[2] Swiss Epilepsy Center;
[3] University of Zurich, Swiss Epilepsy Center, Switzerland

Impaired social cognition presents significant challenges for individuals with neurological and psychiatric disorders, yet its assessment has been largely overlooked in clinical practice. Our research team at the Swiss Epilepsy Center in Zurich aims to address this gap by developing new assessment tools for emotion recognition (ER) and theory of mind (ToM).

Through a meta-analysis of 53 studies, we confirmed the prevalence of significant social cognitive dysfunction in adults with temporal lobe epilepsy (ER, d = 0.81; ToM, d = 0.92), frontal lobe epilepsy (ToM, d = 1.16), and epilepsy not originating within the temporal or frontal lobes, including idiopathic generalized epilepsies (ER, d = 0.67; ToM, d = 0.53). A narrative review of the assessment tools employed in the primary studies revealed a strong bias toward the use of static photographs of faces for ER and the Faux-Pas Test for ToM assessment. These tools may have limitations in terms of their ecological validity, i.e. artificiality, reiterating the need for novel approaches in the clinical assessment of social cognition. We developed the NEmo battery, which consists of multiple ER and ToM tests focusing on ecological validity and incorporating a wider range of social-cognitive subfunctions using multi-modal, static, and dynamic stimuli. In an exploratory study, the NEmo battery was administered to three incidental clinical samples, including individuals with temporal lobe epilepsy, acquired brain injury, Parkinson's disease, and a healthy control group. The results indicate statistically significant differences between the clinical groups and healthy controls, thereby highlighting both the presence of impaired social cognition in these neurological disorders and the sensitivity of the NEmo battery in detecting social cognitive dysfunction. However, comprehensive batteries like NEmo are time-consuming, limiting their practicality in everyday clinical practice and emphasizing the necessity for cost-effective screening tools. To address this concern, we have developed and are currently validating COSIMO (Cognition of Social Interaction in Movies), a brief, ecologically valid, browser-based, freely available, and user-friendly screening tool for social cognitive dysfunction.

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Pain Thresholds in Patients with Migraine assessed by Quantitative Sensory Testing

K Ebner [1], F Burguet [1], N Cerdá-Fuertes [1], D Ryf [1], T Sprenger [2], A Gantenbein [3], J Kuhle [1] and A Papadopoulou [1]

[1] Universitätsspital Basel;
[2] University Hospital Zürich;
[3] RehaClinic Bad ZURZACH Care, Switzerland

Background: Cutaneous allodynia and hyperalgesia are described in migraine, indicating central sensitization. However, quantitative sensory findings vary widely among studies, stimuli and locations. Moreover, it is unclear if these symptoms might be predictors of treatment response.
Objective: In our prospective study, we aim at characterizing the somatosensory profile in migraine and its potential role in predicting response to calcitonin gene-related peptide (CGRP)-antibodies.
Methods: From our ongoing study, we report baseline data from quantitative sensory testing (QST). Migraine patients (according to ICHD-3) with $\geq$8 monthly migraine days were recruited in Basel. QST was performed according to a standardized protocol on the hand and face at baseline (before treatment initiation; one side per patient). Pain thresholds for: (i) cold, (ii) heat, (iii) mechanical(pinprick-) and (iv) pressure stimuli (PPT), as well as (v) mechanical pain sensitivity and vi) dynamic mechanical allodynia (DMA) were assessed.
Results: 18 patients underwent QST at baseline (14/18 women, 44.2 14.3 y, 10/18 with chronic migraine, 4/18 with aura). All patients had at least one abnormal QST-finding, 14 (78%) on both face and hand, 2 (11%) only on the face and 2 only on the hand. Decreased PPT was the most common abnormal finding (13/18 = 72% face, 9/18 = 50% hand), followed by DMA to light touch (10/18 = 56% face, 11/18 = 61% hand). Thermal pain- and mechanical thresholds were normal in most patients (4/18 and 5/18 with abnormalities, repsectively). So far we collected 6-month data of 3/18 patients, thus analysis for prediction of response is pending.
Conclusions: QST abnormalities—particularly pressure hyperalgesia and allodynia to light touch- are very common in patients with frequent migraine, not only in the trigeminal

area, but also in the hand. Preliminary data on their predictive value in treatment response to CGRP-antibodies will be also available within the next months.

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How Best to Update and Optimize a Company Quality Management System for Improved Organizational Performance: An Analysis and Strategic Approach

S Njuguna [1], C Girardey [2] and M D'Souza [3]

[1] Neurostatus-UHB AG;
[2] Wega Informatik AG;
[3] Neurostatus-UHB Ltd, Basel, Switzerland. Department of Neurology, University Hospital Basel, Switzerland. Research Center for Clinical Neuroimmunology and Neuroscience Basel (RC2NB), University Hospital Basel and University of Basel, Basel, Switzerland

Aims: This study aimed to evaluate and improve the Quality Management System (QMS) of Neurostatus-UHB AG. Objectives included understanding the current state of the QMS, exploring best practices in the field, identifying applicable standards, developing recommendations for QMS updates, examining relevant change management strategies and evaluating the potential impact of updates on organizational performance.
Methods: The research relied on a literature review of peer-reviewed articles and a case study of Neurostatus-UHB ongoing QMS update performed by wega Informatik AG. Tools such as the Maturity Diagnostic Instrument were discussed, while techniques for performance measurement were applied for assessing potential impacts.
Results: Key insights included understanding the essential components of a QMS, including the hierarchy of documents and the importance of the Plan-Do-Check-Act (PDCA) cycle. Successful auditing processes were identified, such as verifying conformance to standards, identifying improvement opportunities and ensuring effective business processes. Relevant ISO standards (ISO 9000:2015, ISO 9001:2015, ISO 13485:2016) and regulatory frameworks (ICH E6 R2, ICH Q9, ICH Q10, 21 CFR part 11, GAMP5, GDPR) were discussed. An in-depth analysis of the current state of Neurostatus-UHB's QMS was conducted, leading to a tailored implementation plan for updating the system. Lastly, insights into change management strategies were offered as well as performance measurement and evaluation techniques to measure the effectiveness of the newly implemented QMS.
Conclusions: The study concludes that systematic auditing, updating of the QMS based on recognized standards, effective change management strategies and continuous performance evaluation can substantially improve the QMS of an institution and thus enhance the overall organizational performance.
Authors: Steven Njuguna(1), Christophe Girardey(2), Marcus D'Souza(1,3,4)
Affiliations

1. Neurostatus-UHB Ltd, Basel, Switzerland
2. Wega Informatik AG, Basel, Switzerland.
3. Department of Neurology, University Hospital Basel, Switzerland
4. Research Center for Clinical Neuroimmunology and Neuroscience Basel (RC2NB), University Hospital Basel and University of Basel, Basel, Switzerland