Oral Presentations

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501. A Different Look: Increased Charge Requirement of Spinal Cord Stimulators

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Introduction: The authors describe a patient with delayed cervical spinal cord compression due to fibrous scar tissue around an epidural electrode used in spinal cord stimulation (SCS). One year after implantation of the system the stimulation became ineffective, and 1 year later the patient developed progressive paraparesis. There was no evidence of device-related complications on plain radiographs and CT scans, so the system was removed to perform MRI studies. These studies showed a dorsal myelopathy secondary to scar tissue around the electrode. At surgery thick scar tissue was resected, and the patient's neurological symptoms improved. The histological examination confirmed fibrosis, and microbiological studies excluded chronic infection. Scarring around SCS electrodes should be considered as a late complication and as a possible cause of the tolerance phenomenon.

Methods: Describe the different types/insertion points of SCS. Description of the different diagnosis/patient conditions that SCS are used to treat.

Objectives: 1. Describe the different types/insertion points of SCS. Description of the different diagnosis/patient conditions that SCS are used to treat. 2. Describe the physiologic changes that occur to make the in patients following successful implantation of SCS. 3. Discuss the special considerations necessary to effectively treat patients that develop peri-electrode lesions, and subsequently have their SCS removed.

Conclusion: Compare and contrast previous radiographic evidence prior to implantation and after. Review patient lab work, looking specifically for elevated c-reactive protein and sediment rate, for possible clues to inflammatory response. Role of other services or traditional methods to treat patients recurrent symptoms.

503. In the United States, Lack of Parent/Caregiver Compliance Interferes with the Pediatric Neurosurgery Patient Care Sequence

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Introduction: We report limitations identified in follow-up care of pediatric neurosurgery patients because of lack of parental/caregiver compliance, unmet educational/cognitive needs, and medical insurance issues.

Methods: Children with neurosurgical conditions and chronic healthcare needs were seen in a comprehensive multidisciplinary clinic with a team consisting of, but not limited to: pediatric neurosurgery, developmental medicine, physical/occupational therapy, and social services. During the initial period of April 2007-June 2009, there were 114 patient visits (88 patients; 25 return visits). We followed this population through August 2012 and address outcomes in reference to educational placement and occupational therapy (OT) consultations; two categories identified as the most frequent areas of need and having potential impact on neurocognitive and educational outcomes.

Results: Of the 88 patients seen, 71 had referrals for a different educational venue and/or OT consultation referral. In follow-up, the parent/caregiver was questioned by the developmental medicine pediatrician and/or occupational therapist. 27 patients were identified as having inappropriate school placement and were given recommendations to change the school

setting, but 70% did not follow through. Relating patient population to health insurance coverage, 55% of the patients with government sponsored insurance (GSI) did not change to the recommended special education venues that were recommended, whereas 20% of those with private insurance (PI) did. Of 21 patients identified as needing an OT evaluation and/or ongoing therapy, 72% did not follow through. In relation to insurance, 58% with GSI did not follow through with the OT recommendations, whereas 50% with PI did.

Conclusion: Compliance was lower in the GSI population, which could probably be related to the different socioeconomic status. This discrepancy could be best addressed by a better link in the multidisciplinary Pediatric Neurosciences Clinic to primary care providers so as to provide family-centered healthcare.

504. A Single Center Experience of Patient Outcomes and Length of Stay Following Endoscopic Assisted, Neuronavigation Guided Evacuation of Intracerebral Hemorrhage using the Apollo Aspiration System

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Introduction: Outcomes from spontaneous intracerebral hemorrhage (ICH) remain poor. Acute management requires lengthy critical care and hospital stays, and nearly 3/4 of survivors remain disabled. Minimally invasive techniques for ICH removal have shown a positive relationship between hemorrhage volume reduction and patient outcome. We describe our experience with minimally invasive, endoscopic assisted, neuronavigation guided evacuation of ICH using the Apollo system and patient outcomes.

Methods: Patients presenting with ICH and treated with the Apollo system since October 2014 were included in this retrospective review. All had a neurovascular study negative for underlying vascular lesion, and were treated using a burr hole approach. Patient demographics, ICH volume, clot reduction, degree of midline shift, ICU and hospital length of stay, discharge disposition and last known functional outcome were assessed.

Results: 39 patients were treated, average age 53.0 ± 15.1 years, and 28% were female. Starting clot volume was 52.9 ± 30.2 cc, reduced to 7.7 ± 9.1 cc post-operatively, for an average reduction of $86.8 \pm 14.6\%$. Midline shift measured at the level of the septum pellucidum improved from 6.3 ± 4.1 mm to 4.0 ± 3.3 mm. Average length of ICU stay was 9.1 ± 5.6 days, with 12.7 ± 10.5 hospital days. Covariate analysis showed that shorter ICU stay was correlated with greater percent reduction in ICH volume ($p=0.027$), and trended with improvement in midline shift. Mortality was 30.8%, with 30.8% returned home after hospital or acute rehabilitation; the remainder going to skilled nursing facilities or still inpatients.

Conclusion: ICH volume can be rapidly reduced using the Apollo system, and greater clot reduction correlated with shorter ICU length of stay. Improvement in midline shift also trended towards shorter length of stay. Patient outcomes were favorable when compared with historical controls, although randomized controlled studies will be required to determine long term clinical benefit.

506. Prospective Study of the Use of Intraoperative Neuromonitoring in Determining Post-Operative Energy Requirements and Physiologic Midline in Spinal Cord Stimulation

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Introduction: Intraoperative neuromonitoring (IONM) through electromyography (EMG) studies has been shown to be a safe, effective way to determine the laterality of the spinal cord and guide electrode placement during spinal cord stimulation (SCS). However, the use of IONM to predict post-operative energy requirements and midline has not been examined and offers a new avenue to streamline programming and device selection. Further, the impact of cerebrospinal fluid (CSF) thickness on intraoperative and post-operative amplitudes has not been assessed.

Methods: A total of 24 patients undergoing SCS for chronic pain had intraoperative EMG studies performed to determine physiologic midline. The intraoperative midline was compared to the midline determined on post-operative day 1 based on paresthesia patterns during programming. For patients who had thoracic leads placed, the amplitudes needed to induce abdominal and extremity lateralization during SCS placement were compared with the intensities needed to induce therapy at post-operative day 1. Additionally, we examined whether CSF thickness, body mass index, diabetes, drug use, and smoking correlated with intraoperative and post-operative amplitudes.

Results: Intraoperative EMG was able to predict post-operative paresthesia-based midline in 70.83% of patients. There was a statistically significant relationship between the intraoperative intensity needed to induce extremity lateralization with the post-operative intensity to induce therapy ($p=0.009$) as well as the intraoperative intensity needed to stimulate abdominals with the post-operative intensity ($p=0.033$). There was also a relationship seen between CSF thickness and the post-operative energy requirements in patients ($p=0.039$).

Conclusion: EMG accurately predicts post-operative energy requirements and midline in SCS patients. While 29.17% of patients did not have a match between their intraoperative and post-operative midlines, EMG testing was still valuable in guiding electrode placement and providing information to predict post-operative intensities. Additionally, CSF thickness correlated with amplitude settings on the first post-operative day.

507. History of Bone Morphogenetic Protein (BMP) and its Application in Spine Surgery

Lee Onn Chieng, BS; Karthik Madhavan; Michael Wang, MD (Miami, FL)

Introduction: Recombinant human Bone Morphogenetic Protein (rhBMP) has been increasingly used in spinal fusion over the past decade. In this abstract, we sought to provide historical vignette that led to the discovery of BMP and its subsequent robust development in the field of spine surgery. In 1889, Senn noted that decalcified bone can induce healing of bone defects secondary to osteomyelitis. His initial intent was to use iodoform as antiseptic and utilized the decalcified bone as a carrier of the iodoform. His method not only reduce infection but also led to osseous regeneration. In 1934, Lacroix reported crude alcohol extract from cartilaginous epiphysis of the long bones of rabbit (which he later called it as osteogenin) induced new bone injection when injected into muscle. These earlier works have led to the discovery of the bone matrix ability to induce new bone formation by Urist in 1965. However it was not until Reddi and Sampath confirmed that BMP from the bone matrix led to ectopic bone formation. They described the fibroblast-chondroblast-osteoblast transformation with BMP in 1972. In 1992, human BMP was successfully purified clinically. It was FDA approved for repair in long bone defect and ALIF since 2002. Today, BMP often combined with allograft for spinal fusion, which has become the standard of care. With reducing trend of autograft, BMP and newer bone grafts able to reduce infection rate and improve bony fusion.

508. Brain repair and neural network remodeling by hematopoietic growth factors in subacute phase of traumatic brain injury in animal model

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Introduction: The objective of this study is to determine the therapeutic role of SCF+G-CSF in subacute phase of TBI.

Methods: After induction of TBI, mice were randomly divided into: a vehicle control group and an SCF+G-CSF treatment group and shams. Treatment was given 2 weeks after TBI, SCF (200µg/kg) and G-CSF (50µg/kg) sq daily for 7 days. Neurobehavioral tests for evaluation of cognitive function (water maze and novel object recognition tests), anxiety (elevated plus maze test), and motor function (Rota-Rod test) were performed during the period of 2 to 9 weeks after treatment. MAP2 antibody to study dendritic density and Fluoro-Jade C test the level of neurodegeneration were performed.

Results: In the water maze test, SCF+G-CSF-treated TBI mice showed a significant reduced latency to find the hidden platform as compared to the TBI vehicle controls ($p<0.05$), while there was no difference between the sham controls and treated TBI mice. Elevated plus maze test displayed a significant reduction of the post-traumatic anxiety and risk taking behavior in the SCF+G-CSF-treated TBI mice when compared to the TBI vehicle controls while no difference was observed between the SCF+G-CSF-treated TBI mice and sham control. Rota-Rod test and NOR did not reveal differences between the treated and non treated animals. MAP 2 testing shows statistical significant increase of dendritic density contralateral $P<0.05$ and a trend of increasing dendritic density ipsilateral to the lesion. Fluoro-Jade C shows statistical significant decrease of neurodegeneration contralateral to the lesion $p<0.05$ to the lesion.

Conclusion: SCF+G-CSF treatment in the subacute phase of TBI shows recovery in spatial learning and memory and the post-traumatic anxiety in mice. The immunohistochemistry indicates that treatment with SCF and G-CSF enhance neural network remodeling through creation of the new synapses and decreased neurodegeneration.

509. Palliative Care and Communication Training in Neurosurgery Residency

Stephen P. Miranda; Kristen Schaefer, MD; George Vates, MD, PhD; William Gormley; Mary Buss, MD, MPH (Rochester, NY)

Introduction: Neurosurgeons care for critically ill patients near the end of life, yet little is known about how well their training prepares them for this role. We surveyed neurosurgery residents nationwide to describe (1) the quantity and quality of teaching activities related to communication and palliative care, and (2) resident attitudes and perceived preparedness to care for seriously ill patients.

Methods: A previously validated survey instrument was adapted to reflect required communication and palliative care competencies in the ACGME Milestones for Neurological Surgery. The survey was reviewed for content validity by independent faculty neurosurgeons, piloted with graduating neurosurgical residents, and distributed online in August 2016 to all North American neurosurgery residents using the AANS/CNS Joint Section on Neurotrauma & Critical Care email listserv. Multiple choice and Likert scale responses were analyzed using descriptive statistics.

Results: 62 responses were recorded between August-October 2016. Most respondents reported no explicit teaching on: explaining risks and benefits of intubation and ventilation (69%), formulating prognoses in neuro-critical care (60%), or leading family meetings (69%). Compared to performing craniotomies, respondents had less frequent practice leading discussions about withdrawing life-sustaining treatment (61% vs. 90%, $p=0.00016$, weekly or more frequently), and were less often observed (18% vs. 87%, $p<0.0001$) and given feedback on their performance (11% vs. 58%, $p<0.0001$). Nearly all respondents (95%) felt prepared to discuss

withdrawing life-sustaining treatments, however half (48%) reported they would benefit from more communication training during residency. Most (87%) reported moral distress, agreeing that they had participated in operations and worried whether surgery aligned with patient goals. **Conclusion:** Residents in our sample reported limited formal training, and relatively less observation and feedback, on required ACGME competencies in palliative care and communication. Most reported preparedness in this domain, but many were receptive to more training, which may improve competency and mitigate moral distress.

510. The Long-Term Outcomes of Octogenarians with Aneurysmal Subarachnoid Hemorrhage: A National Minimum Data Set Analysis

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Introduction: There is a dearth of data evaluating the long-term outcomes of octogenarians with aneurysmal subarachnoid hemorrhage.

Methods: Patients aged at least 80 years who underwent microsurgical clipping or endovascular coiling for SAH were extracted from the Medicare inpatient claims files and linked with the Minimum Data Set (2008-2011). Multivariable logistic regression evaluated predictors of return to home, and multivariable COX proportional hazards analyzed survival two years after SAH. Variables screened included patient demographics (age, sex, race or ethnicity, and socioeconomic status), comorbidities, severity of subarachnoid hemorrhage (measured with the externally validated NIS-SAH severity scale), aneurysm treatment modality, tracheostomy or gastrostomy placement.

Results: Among the 1,298 patients evaluated, 59.6% had died, 34.1% had returned to home, and 4.9% remained in institutional care two years after SAH. Older patient age, male sex, and tracheostomy or gastrostomy placement were associated with reduced two-year survival. Additionally, older age (odds ratio (OR)=0.89, 95% confidence interval (CI)=0.85-0.92), microsurgical clipping (OR=0.72, 95% CI=0.53-0.98), greater severity of subarachnoid hemorrhage (OR=0.85, 95% CI=0.81-0.88), and tracheostomy (OR=0.57, 95% CI=0.35-0.93) were associated with significantly lower odds of return to home. A sensitivity analysis revealed that endovascular coil embolization improved the odds of return to home among good grade patients, but treatment modality did not impact disposition among poor grade patients.

Conclusion: In this national analysis, 34.1% of octogenarian patients return to home two years after treatment of aneurysmal subarachnoid hemorrhage. Coil embolization was a predictor of return to home, particularly among good grade patients, underscoring the benefit to endovascular treatment in this patient population.

511. Diminishing returns in successive thrombectomy attempts for revascularization in acute ischemic stroke

Jennifer Kosty, MD; Andrew Ringer, MD (Cincinnati, OH)

Introduction: In this study, we examined whether successive attempts at thrombectomy for acute ischemic stroke were equally effective in achieving revascularization, and whether complication rate was related to pass number.

Methods: The charts of patients undergoing mechanical thrombectomy for stroke between 2013-present were reviewed. Baseline demographics, number of attempts at thrombectomy, and procedural complications were noted. For each pass, the change in TICl score was determined, with 2a and 2b assigned the values 2.3 and 2.7. The distributions of successful (any change) versus unsuccessful (no change) thrombectomy attempts by pass number were assessed using the Chi Square statistic, $p < 0.05$.

Results: Fifty-four patients were identified. Twenty-nine (52%) were females and the average age was 65 ± 14 years. Sixty-three percent of lesions were located in the MCA, 20% combined ICA/MCA, 13% basilar, and 4% combined ICA/ACA/MCA. In 24 patients (44%), only one attempt

at thrombectomy was necessary; 16 (30%) required 2, 6 (11%) required 3, and 8 (15%) required 4 or more. The average increase in TICl score for the first attempt was 1.7 ± 1.1 ; second attempt 0.7 ± 0.9 , third attempt 0.9 ± 1.2 , fourth attempt 1.2 ± 1.2 , fifth attempt 0.9 ± 1.5 , and sixth attempt 0. The rate of successful revascularization by attempt was 84% for the first, 48% for the second, 38% for the third, 57% for the fourth, and 25% for the fifth and sixth passes. These differences were statistically significant. Three complications (6%) occurred: 2 vessel perforations and 1 catheter tip shearing. The complication rate by attempt was 0% for the 1st and 2nd attempt, 8% for 3rd, and 17% for the 4th or greater attempt.

Conclusion: As successive attempts at thrombectomy are performed, the likelihood of revascularization decreases and the risk of complications rises.

512. A Quantitative Analysis of Craniopharyngioma Cyst Expansion during and after Radiation Therapy and Surgical Implications

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Introduction: When complete resection of craniopharyngioma is unachievable or sequelae prohibitive, adjuvant intensity-modulated radiotherapy (IMRT) has demonstrated excellent disease control. However, residual cysts can expand during IMRT, causing obstructive hydrocephalus and/or visual deterioration. We present a quantitative analysis of cyst expansion during and after IMRT and examine the impact on disease control and further surgical intervention.

Methods: IRB approved retrospective study was performed for craniopharyngioma patients treated from 2000-2015 with surgery and IMRT. Volumetric measurements of cyst contours were generated on serial MRIs postoperatively, during IMRT and up to 12 months post-IMRT. Patient, tumor and treatment-related variables were analyzed.

Results: Twenty-seven patients underwent surgery and IMRT (median dose=54 Gy). Eleven patients (40.7%) demonstrated cystic expansions within a year post-IMRT. All were radiographically Puget Grade 2. Maximum cyst expansion peaked at 4.27 months post-IMRT, with a median growth of 4.1 cc (mean=9.61 cc) above the post-operative volume. Seven patients had spontaneous cyst regression without intervention. One patient returned to his home country within a year post-IMRT and the other three patients experienced MRI-confirmed cyst enlargement during IMRT, requiring adaptive planning to ensure adequate tumor coverage. Two of three patients required ventriculoperitoneal shunt placement and additional intervention. One underwent additional resection and the other had placement of an intracystic catheter for aspiration and interferon delivery within 12 months post-IMRT. These three patients now have stable disease.

Conclusion: Craniopharyngioma cyst expansion occurs in approximately 40% of our patients during/after IMRT. In the majority of patients, cyst expansion was self-limited and did not confer a worse outcome. During radiotherapy, cystic expansion may be apparent on image-guided RT. Adaptive planning may be required to ensure sufficient dose coverage to the tumor volume. The sequelae of cyst expansion includes progressive hydrocephalus. For patients with cyst expansion, cyst aspiration and/or intracystic interferon may result in disease control.

513. T2-Weighted MRI is Superior to Other Sequences to Determine Intratumoral Heterogeneity in DIPG

Samuel Harrison Farber; Steve Harward, MD, PhD; Eric Thompson, MD (Chapel Hill, NC)

Introduction: Diffuse intrinsic pontine glioma (DIPG) remains the main cause of death in children with brain tumors. The purpose of this study was to determine which MRI sequence provides the best discrimination of intratumoral heterogeneity to guide stereotactic implantation of convection enhanced delivery (CED) catheters into the most cellular tumor regions.

Methods: Patients ages 18 years or younger with a diagnosis of DIPG from 2000-2015 were included. Radiographic heterogeneity index (HI) of

the tumor was calculated by measuring the standard deviation of image intensity of the tumor (SDTumor) normalized to the genu of the corpus callosum (SDCorpus Callosum). Four MRI sequences (T2, T1 post-contrast, FLAIR, and ADC) were compared at several time points both before and after radiotherapy. HI values across these MRI sequences were compared and correlated with patient survival.

Results: MRI sequences from 16 patients with DIPG were evaluated. The mean survival was 1.15 ± 1.14 years (SD). T2-weighted MRI had the highest HI (mean $\pm$ SD, 5.1 ± 2.5) followed by T1 post-contrast (3.7 ± 1.5), FLAIR (3.0 ± 1.1), and ADC (1.6 ± 0.4). ANOVA demonstrated that HI values were significantly higher for T2 than FLAIR ($p < 0.01$) and ADC ($p < 0.0001$). HI values largely decreased following radiotherapy. HI values were not predictive of patient survival ($p < 0.05$).

Conclusion: For children with DIPG, T2-weighted MRI demonstrates the greatest signal to noise ratio for determining tumor heterogeneity. T2 hypointensity is known to correlate with increased cellularity. These areas are putative targets for CED catheter placement in clinical trials, particularly prior to radiotherapy.

514. Investigating IGF2BP1 as an Oncogenic Driver in Infant Ependymoma

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Introduction: Despite a paucity of genetic aberrations, infantile ependymomas (Posterior Fossa – Type A, PFA) demonstrate widespread epigenetic alterations, suggesting that the ependymoma epigenetic landscape can reveal novel treatment paradigms. Specialized enhancers, termed super enhancers, demarcate key oncogenic drivers in a variety of cancers. Characterization of the enhancer landscapes and super enhancer (SE) mapping of 30 primary tumors revealed subgroup specific lesions across ependymomas. To identify novel oncogenes of PFA ependymoma, we defined the SE landscapes in 11 PFA ependymomas. Super enhancers regulating the insulin-like growth factor-2 mRNA binding protein (IGF2BP1) locus emerged as the top candidate for PFA tumors. Furthermore, I explored the role of IGF2BP1 as an oncogenic driver in ependymoma and used genetic knockdown studies to examine the significance of IGF2BP1 in cell survival and proliferation.

Methods: Tumor specific SE regulated genes in ependymomas were ranked by regions with the highest density of H3K27 acetylation. Subsequently, shRNA-mediated knockdown of IGF2BP1 were done to evaluate effects upon survival of ependymoma cells.

Results: IGF2BP1 exhibited the highest gene expression in PFA ependymoma as compared to other brain tumor types, and normal brain tissue. Within PFA ependymoma, elevated IGF2BP1 was associated with poor overall and progression-free survival. shRNA knockdown of IGF2BP1 in ependymoma cells led to decreased survival by day 3 as compared to a non-targeting control.

Conclusions: Targeted genomic strategies have been successful in many cancers yet has failed in PFA ependymoma, the patient population with the most common, most aggressive, and most therapy resistant tumors. This represents a novel class of epigenetically guided therapies for a lethal and chemotherapy resistant brain tumor with no targeted treatments currently available for children. Among these, IGF2BP1 is a potential oncogenic driver that maintains the neoplastic phenotype of infant ependymoma and represents a candidate oncogene, prognostic marker and therapeutic target in PFA ependymoma.

515. Phase I Trial of Laser Interstitial Thermal Therapy Treatment for Cerebral Radiation Necrosis

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Introduction: Cerebral radiation necrosis is a known complication of

radiation therapy in up to 5% of patients. Treatment options are limited and include high-dose steroids, bevacizumab, and surgery. This study seeks to determine safety and efficacy of LITT treatment for radiation necrosis.

Methods: In the prospective, phase I trial, patients underwent LITT for tumor treatment at Henry Ford Hospital between November 2013 and January 2016. Patients with biopsy-confirmed radiation necrosis were reviewed with attention to ablation volume, survival, demographic data, steroid dose, and complications. Imaging occurred at set intervals beginning one-two weeks post-ablation.

Results: Ten patients with 11 ablations were evaluated. Four patients had a primary diagnosis of high-grade glioma, while six were metastatic lesions. Immediate ablation volumes increased 220% of initial radiation necrosis volume, rising to 430% at one-two weeks before decreasing to 69% at greater than six months time. No patient had a decline in baseline neurological exam while inpatient. Four patients had a deficit after discharge. Three of those patients had worsening hemiparesis that improved to baseline over time. The fourth had intractable seizures without improvement. The 6-month survival was 77.8% and 1-year survival was 64.8% based on Kaplan-Meier curve estimates.

Conclusion: In this prospective study, LITT was a safe and effective treatment for radiation necrosis with 90% of patients maintaining or returning to baseline neurological function. Despite an increase in ablation volume by 430%, only one patient had a permanent deficit. Further studies are needed to better define the role of LITT in the treatment of cerebral radiation necrosis.

516. Pedicle Screw Placement Accuracy with Ultra-Low Radiation Imaging - a randomized controlled trial

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Introduction: Randomized control trial OBJECTIVE: Compare pedicle screw placement between ultra-low radiation imaging (ULRI) with image enhancement and standard fluoroscopy for patients undergoing single level, minimally invasive transforaminal lumbar interbody fusion (MIS-TLIF).

Background: Previous studies show that ULRI with image enhancement significantly decreases radiation exposure by roughly 75% for both the patient and operating room (OR) personnel during MIS-TLIF ($p < 0.001$). However, no clinical data exists on whether this negatively impacted patient outcomes. Our goal was to see if utilizing ULRI with image enhancement would negatively impact pedicle screw placement.

Methods: An IRB approved, prospective, internally randomized controlled trial was performed to compare pedicle breach rates between ULRI with image enhancement and conventional fluoroscopy. By assigning each side to an imaging modality (right vs left sided randomization for cannulation and screw placement), each patient served as their own control. In addition to standard intra-operative images to check screw placement, each patient received a post-operative CT. Two trained neurosurgeons independently analyzed images, blinded as to what imaging modality assisted each screw placement.

Results: 24 consecutive patients underwent single level MIS-TLIF, and were randomly assigned as to which side utilized ULRI. No patients suffered immediate post-operative complications (neurologic decline, need for hardware repositioning, etc.). By CT scan confirmation, no breach was noted in either imaging group (ULRI breaches: 0%, Standard fluoroscopy breaches: 0%, $p = 1$). Various other radiographic parameters were analyzed (true-ness of fit, screw depth, etc.) with no significant differences between imaging groups.

Conclusion: Ultra-low radiation imaging with image enhancement does not compromise accuracy during pedicle screw placement compared to conventional fluoroscopy, while significantly decreasing radiation exposure to both patient and OR personnel.

517. Effect of Segmental Lordotic Angle after a Single Level Interbody Fusion on Lumbar Lordosis and Development of Adjacent Level Disease

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Introduction: Techniques for lumbar interbody fusion include anterior, posterior, transforaminal, and extreme lateral approaches. Also variation exists in the minimally invasive approaches. This retrospective study evaluates the effect of postoperative lordosis angle at the fusion level on follow up lumbar lordosis and the development of adjacent level disease.

Methods: 1229 patients were identified based on CPT code for interbody fusion(22630) at our institution between 2007 and 2016. Preoperative and postoperative imaging was evaluated obtaining measurements on lordosis, pelvic incidence, and disk height. Patient charts were then reviewed for follow up and evidence of further deterioration.

Results: 428 patients had single level surgery and follow up of at least 36months. 13 patients (3%) required an adjacent level surgery after an average of 34months, all of which were at the rostral level. Pre- and postoperative segmental lordosis was 13.4 and 14 degrees respectively in patients requiring second surgery versus 14 and 17 degrees for patients that did not ($p<0.01$). Average lumbar lordosis was 43 degrees in both groups and did not significantly change after an interbody surgery. PI-LL mismatch and disk height was not associated with adjacent level disease development.

Conclusion: Total lumbar lordosis was not affected by a single level interbody fusion, suggesting that the unfused levels continue to share the burden in order to maintain sagittal balance. If an interbody fusion surgery does not effectively reduce the load on other levels adjacent level disease may develop. Segmental lordotic angle is an important factor in the outcome of interbody fusion surgery.

518. Expandable vs Static Inter-body Grafts Reduce Operative Time, Improve Lordosis and Accelerate Return to Work after Fusion for Lumbar Stenosis and Spondylolisthesis

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Introduction: Inter-body instrumentation (TLIF/PLIF) improves arthrodysis and lumbar lordosis. Static inter-body grafts have become standard of care. Expandable inter-body grafts allow for potential to generate increased lordosis while facilitating less disruptive placement. We set out to determine if expandable inter-body grafts were associated with improved lordosis and outcomes compared to static grafts.

Methods: All TLIF/PLIF cases for lumbar stenosis and spondylolisthesis prospectively entered into the National Neurosurgery Quality and Outcomes Database (N 2 QOD) from our institution between 2011-2015 were analyzed. Patients were stratified based on whether a static PEEK inter-body versus an expandable inter-body graft was used. Post-fusion lumbar lordosis (L1-S1) - pelvic incidence (PI) mismatch was compared between cohorts on standing lateral X-rays. Propensity score matching, Independent t-tests, chi-square tests were used to compare radiographic, peri-operative, and one-year outcomes.

Results: 230 patients with one-year reported outcomes were available for review (188 expandable vs 42 static). In unadjusted comparison, expandable grafts were associated with reduced operative times and a trend of reduced blood loss. For single-level fusion, LL/PI mismatch was similar (+3 vs +5) between cohorts. For two-level (+8 vs +14) and three-level fusion (+8 vs +15), expandable grafts were associated with reduced LL/PI mismatch. After propensity matching, expandable grafts remained associated with reduced operative times and accelerated return to work. Both static and expandable interbody grafts were associated with significant improvements in pain, physical disability, and quality of life 12 months after surgery.

Conclusion: Both static and expandable inter-body grafts provide significant improvements in one-year pain, disability, and quality of life with similar safety profiles. Expandable inter-body grafts may facilitate more efficient graft placement resulting in reduced operative times; and can help achieve more appropriate lumbar lordosis potentially contributing to the accelerated functional recovery and return to work.

519. Using Telomere Length to Help Determine Amygdala Function for potential use in the Setting of Mesial Temporal Sclerosis

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Introduction: When considering surgery for Mesial Temporal Sclerosis, there is neuropathological and electrophysiological evidence for the involvement of parahippocampal structures such as the amygdala in temporal lobe epilepsy, but morphometric measurements have not been reliably correlated to neuropsychiatric performance. Prior to potential resection, amygdala sclerosis or hypertrophy on MRI can complicate diagnosis and surgical planning. DNA telomere length has been associated with the volume of certain subsegmental regions of the brain. Using high resolution MRI, we analyzed volume measurements of the amygdala as well as DNA telomere length. We also conducted the Patient Health Questionnaire (PHQ) on these subjects to determine if we could find a viable, non-invasive test which would correlate with amygdala function.

Methods: Saliva samples were collected from 82 Veterans without history of MTS. Genotek DNA extraction kit was used. Quantitative PCR assay was carried out using 10ng of genomic DNA. The telomere to single copy gene ratio was calculated as described by Cawthon, 2009. Automated MRI volumetric segmentation was performed using the FMRI's Integrated Registration and Segmentation Tool (FIRST).

Results: Telomere length, PHQ2 scores and amygdala volume were measured in Veterans from the War Related Injury and Illness Study Center at the Palo Alto VA. The mean age of participants was 45, twelve percent of whom were women. Telomere length was shown to correlate with amygdala volume ($p < 0.0257$) as well as PHQ2 scores ($p < 0.0279$). Significant association among telomere length, amygdala volume and PHQ mental health screening ($p < 0.0209$) was also shown.

Conclusion: This study could provide Neurosurgeons with noninvasive insight into the complex and subtle clinical implications of amygdala partial or total resection as part of treatment for Mesial Temporal Sclerosis in Temporal Lobe Epilepsy. The next step would ideally involve individuals with TLE to optimize their functional surgical outcome.

520. Military Neurosurgery Socioeconomic Data; Benefits, Challenges, and Opportunities

Richard Menger, MD MPA; William Robbins, MD; Randy Bell, MD (Shreveport, LA)

Introduction: The development of neurosurgery as an independent specialty is intimately linked with Harvey Cushing's military experience. However, studies in 2002, 2011, and 2015 have highlighted consistent unique socioeconomic challenges facing military neurosurgeons. Here we provide objective data from military neurosurgeons surrounding the issue.

Methods: Through the CSNS internet survey responses were solicited from current, separated, and retired military neurosurgeons regarding workforce issues including descriptive data, objective metrics, and subjective responses.

Results: 80.9% (98/121) of those surveyed were pleased with their military experience. Positives included patient population (97.4%), feelings of patriotism (87.4%), development of camaraderie (71.4%), and the experience of deployment (93.8%). However, 76.5% of those surveyed desired in

increase in pay for military neurosurgeons. 37.5% were overwhelmed with administrative responsibilities and over 50% desired more case volume. Multivariate analysis showed those who were not satisfied with their time in the military were those neurosurgeons who did not develop a sense of camaraderie ($p=0.02$). Those still currently serving in the military showed a trend towards increased dissatisfaction compared to those who were retired or separated ($p=0.08$).

Conclusion: Service as a military neurosurgeon is an overwhelmingly positive experience but opportunities exist for policy developments that would increase operative case load, reduce administrative responsibilities, and reduce military-civilian income disparity. This remains salient as current military neurosurgeons were only 0.29 times as likely to recommend military service to another neurosurgeon as compared to those who were retired or separated ($p=0.024$).

600. Four-year Cost Analysis for the Spinal Laminectomy versus Instrumented Pedicle Screw (SLIP) Trial

Vijay Mysore Ravindra, MD; Robert Whitmore, MD; Jill Curran, MS; Ryan Din, MD; Zoher Ghogawala, MD (Salt Lake City, UT)

Introduction: The SLIP trial demonstrated the addition of lumbar fusion to laminectomy was associated with improved HRQOL versus laminectomy alone with a lower re-operation rate (14% vs. 34%); we performed a four-year cost analysis.

Methods: The participants were enrolled in a randomized, controlled clinical trial comparing laminectomy versus laminectomy with fusion for grade I degenerative spondylolisthesis (SLIP) between 2002-2009. Direct costs from the SPORT trial, derived from 2004 Medicare diagnosis related group payments, were applied to the SLIP cohort – and inflation adjusted for 2015. Short Form-6D (SF-6D) utility scores were computed from the SF-36, and gains in Quality-Adjusted Life-Years (QALYs) were calculated by taking the AUC relative to the baseline.

Results: Thirty-five patients underwent laminectomy and 31 underwent laminectomy plus fusion. Fourteen patients (21%) underwent re-operation: 12 patients (34%) in the laminectomy group and 4 (14%) in the laminectomy with fusion group ($p=0.05$). Total costs, including reoperations, were lower for the laminectomy group compared to fusion (\$55,193.88 vs. \$71,904.14). Patients receiving fusion showed greater gain in QALYs at 4 years (0.64 vs. 0.39, $p=0.086$). Cost/QALY ratios were comparable (fusion: \$112,350.22 vs. laminectomy: \$141,522.77). Incremental cost-effectiveness ratio (ICER) of fusion compared to laminectomy alone was \$68,841.04 – below the societal willingness-to-pay threshold of \$100,000.

Conclusions: The four year cost analysis demonstrates that laminectomy with fusion is associated with greater gain in QALYs at 4 years compared to laminectomy alone and is cost-effective for Grade I degenerative lumbar spondylolisthesis given the four-year re-operation rates; further analysis using exact cost data from the Medicare database is necessary.

601. Olig2 as a novel target for IDH1mutant tumors

Mahaley Clinical Award

Matthew Clark Garrett, MD, PhD; Harley Kornblum, MD, PhD; Jantzen Sperry, BS; Linda Liao, MD, PhD; Rob Prinse, PhD; Lea Guo; Rosemarie Tsoa, PhD (Los Angeles, CA)

Introduction: Large scale sequencing of tumor banks has revealed a subset of tumors that have a mutation in the isocitrate dehydrogenase (IDH1) enzyme that leads to very high levels of a compound, 2-hydroxyglutarate (2-HG), which is normally found at vanishingly small levels. While initial studies provided evidence that the 2-HG molecule may be an oncometabolite, more recent studies using pharmacological inhibition of IDH1mutant enzyme have yielded mixed results. Thus we sought to identify a better molecular target to inhibit growth in IDH1mutant tumors.

Methods: We propagated 74 patient-derived in vitro glioma spheres

lines (7 bearing IDH1mutations) and performed expression analysis using U133 Plus 2.0 microarrays. Using both this dataset and the TCGA dataset we identified a list of 6 genes that were differentially over-expressed in IDH1mutant tumors. We used a CRISPR-Cas9 system to knock-down Olig2 expression and determine its effect on growth. We also tested the ability of valproic acid, an HDACi to knock-down olig2 expression and reduce growth in IDH1mutant tumor cells.

Results: In this study, we show that IDH1mutant glioma spheres are a good model for IDH1mutant tumors and phenocopy the expression and methylation patterns of in vivo IDH1mutant tumors. We also show that inhibition of the IDH1mutant enzyme has no effect on the expression pattern or growth of IDH1mutant glioma cells. We identified Olig2 as one of the few molecular targets that is up-regulated in IDH1mutant tumors for evaluation. CRISPR knock-down of Olig2 effectively slowed growth in IDH1mutant lines in vitro. Expression analysis after Olig2 knock-down identified Tet2 as a repressive target of Olig2. HDAC inhibitors effectively down-regulate Olig2 expression and slow growth in IDH1mutant tumors

Conclusion: Pharmacological inhibition of the IDH1mutant enzyme is an ineffective therapeutic strategy. HDAC inhibitors are able to target Olig2 an essential gene for IDH1mutant tumor growth.

602. The utility of platelet function testing prior to Pipeline Embolization Device placement for the treatment of intracranial aneurysms: A multicenter cohort study

Christoph Johannes Griessenauer, MD; Nimer Adeeb; Paul Foreman; Justin Moore; Hussain Shallwani; Rouzbeh Motiei-Langroudi; Abdulrahman Alturki; Raghav Gupta; Adnan Siddiqui; Mark Harrigan; Christopher Ogilvy (Brookline, MA)

Introduction: Thromboembolic complications constitute a significant source of morbidity following neurointerventional procedures. Flow diversion utilizing the Pipeline Embolization Device (PED) for the treatment of intracranial aneurysms necessitates the use of dual anti-platelet therapy to reduce this risk. The utility of platelet function testing prior to PED placement remains controversial.

Methods: A retrospective review of prospectively maintained databases at three academic institutions was performed from the years 2009 to 2016 to identify patients with intracranial aneurysms treated with PED placement. Clinical and radiographic data were analyzed with emphasis on thromboembolic complications and clopidogrel responsiveness. Clopidogrel responsiveness was assessed pre-procedure with commercially available platelet function tests.

Results: A total of 402 patients underwent 414 PED procedures for treatment of 465 intracranial aneurysms. Thromboembolic complications were encountered in 9.2% of procedures and were symptomatic in 5.6%. Clopidogrel non-responders suffered a significantly higher rate of thromboembolic complications compared to clopidogrel responders (17.4% vs 5.6%, $p=0.0002$). This risk was significantly lower in non-responders who were switched to ticagrelor when compared to patients who remained on clopidogrel (2.7 vs 24.4%, $p=0.004$). In patients who remained on clopidogrel, the rate of thromboembolic complications was significantly lower in those who received a clopidogrel boost within 24 hours pre-procedure when compared to those who did not (9.8% vs 51.9%, $p=0.00004$).

Conclusion: Clopidogrel non-responders suffered significantly higher rate of thromboembolic complications when compared to clopidogrel responders. However, this risk appears to be mitigated in non-responders that were switched to ticagrelor or received a clopidogrel boost within 24 hours pre-procedure.

603. Cheating Death: A Neurosurgical History of Human Resuscitation, Reanimation, and the Pursuit of Immortality

Vesalius Award

Michael Bohl, MD; Tyler Steed, MD, PhD; Evgenii Belykh, MD; Nilkolay Martirosyan, MD, PhD; Mark Preul, MD (Phoenix, AZ)

For millennia, adventurers searched for the mythical Fountain of Youth in hopes of achieving immortality. The late European Renaissance, however, saw the emergence of a more practical method for pursuing longevity: evidence-based medicine. This historical analysis details the last 500 years of physician-led efforts to cheat death, and specifically the neurosurgeon's role in the scientific and literary canons of human immortality.

Case reports of hypothermic patients surviving typically fatal circumstances (The Hanging of Anne Green, 1650) prompted early surgical pioneers such as John Hunter to perform the first methodical experiments on human resuscitation. His work with hypothermia and electrical stimulation interested The Royal Humane Society, which years later sponsored an infamous attempt by Giovanni Aldini to reanimate the body of an executed criminal before a crowd of London's social elite. Attending this reanimation was William Godwin, whose descriptions of this event inspired his daughter, Mary Shelley, to write *Frankenstein*. Temple Fay introduced modern medicine to the neuro-protective power of hypothermia. Although his work was derailed by Nazi physicians at the Dachau concentration camp, he successfully inspired a new generation of neurosurgeons such as RJ White. Under hypothermic cerebrovascular arrest, RJ White successfully performed the first primate head transplant, catching the attention of Russian scientists who were hoping to achieve a method for extending life indefinitely via head transplantation. These efforts coincided and prompted the release of numerous literary and visual works depicting neurosurgeons as mad-scientists, and inspired Italian neurosurgeon Sergio Canavero to plan the first human head transplant for 2017.

604. Immune dysregulation has long been implicated in the development of DCI following aneurysmal subarachnoid hemorrhage (aSAH)

DePuy Synthes Cerebrovascular Section Resident/Fellow Award

Fawaz Al-Mufti, MD; Kalina Anna Misiolek; David Roh, MD; Andrew Bauerschmidt, MD; Soojin Park, MD; Sachin Agarwal, MD; Philip Meyers, MD; E. Sander Connolly, MD; Jan Claassen, MD; J. Michael Schmidt (Newark, NJ)

Introduction: Immune dysregulation has long been implicated in the development of DCI following aneurysmal subarachnoid hemorrhage (aSAH). Our objective was to determine the relationship of inflammatory cell biomarkers with delayed cerebral ischemia (DCI).

Methods: We evaluated 849 aSAH patients who were enrolled into a prospective observational cohort study and had a white blood cell (WBC) differential obtained within 72 hours of bleed onset.

Results: After controlling for clinical grade ($p < 0.001$), thick SAH on admission CT ($p = 0.002$), and clipping aneurysm repair ($p < 0.001$), WBC count $< 12.1 \times 10^9/L$ (OR 1.2; 95%CI: 1.1-1.3, $p < 0.001$) was the strongest CBC predictor of DCI followed by a neutrophil-lymphocyte ratio < 10.75 (OR 1.5; 95%CI: 1.1-2.2, $p = 0.02$). A significant interaction between clinical grade and WBC count (OR 1.0, 95%CI: 0.9-1.0, $p = 0.002$) revealed that good-grade patients with elevated WBC counts (49%: 273/558) had increased odds for DCI indistinguishable from poor-grade patients. Multivariable Cox regression also showed that elevated WBC counts in good-grade patients increased the hazard for DCI to that of poor-grade patients (HR 2.1, 95%CI 1.3-3.2, $P < 0.001$). ROC curve analysis of good-grade patients revealed that WBC count (AUC: 0.63) is a stronger DCI predictor than modified Fisher Score (AUC: 0.57) and significantly improves multivariable DCI prediction models ($Z = 2.0$, $P = 0.02$, AUC: 0.73; PPV: 34%; NPV: 92%).

Conclusion: Good-grade patients with early elevations in WBC count have a similar risk and hazard for DCI as poor-grade patients. Good-grade patients without elevated WBC may be candidates to be safely downgraded from the ICU, leading to cost savings for both patient families and hospitals.

605. Radiographic outcomes in patients with Chiari Type 1 malformation and increased pB-C2 distance without fusion

Tanya Minasian, DO; Mark Krieger, MD; R. Aaron Robison, MD; J. Gordon McComb, MD (Los Angeles, CA)

Introduction: The presence of ventral brainstem compression (VBSC) in the setting of Chiari Malformation (CM1) is well-known, but management remains controversial. One measure of VBSC is the posterior displacement of the odontoid from the basion to C2 line (pB-C2) proposed by Grabb and Oakes, who hypothesized that a pB-C2 of $< 9\text{mm}$ requires occipital cervical fusion. We do not routinely instrument these patients at our institution, so we evaluated the outcome of patients with initial pB-C2 $> 9\text{mm}$ undergoing craniocervical decompression without fusion.

Methods: All patients who underwent initial craniocervical decompression for CM1 at our institution between 2003 and 2010 were included. The pB-C2 was measured on the pre and post-operative MRI. The change in mean pre- and post-operative pB-C2 of patients with a pB-C2 greater than or less than 9mm were then compared. Patients were excluded if appropriate imaging was not available.

Results: A total of 102 patients met the inclusion criteria, of which 20 had an initial pB-C2 greater than 9mm. Median follow up was 37.6 months. Mean initial pB-C2 was 6.31mm (5.54 mm in $> 9\text{mm}$ group vs 9.44 mm in $> 9\text{mm}$ group). Mean pB-C2 at last follow up was also 6.56 mm (5.97 mm vs 8.95 mm). The mean change in pB-C2 in the $> 9\text{mm}$ group was +0.43mm (95% CI 0.17mm to 0.69mm) versus mean change of -0.49mm in the $> 9\text{mm}$ group (95% CI -1.21mm to +0.22mm). There was no significant difference in syrinx resolution between the groups.

Conclusion: Performing a fusion on patients with VBSC in CM1 remains controversial. We demonstrate that patients with an initial pB-C2 $> 9\text{mm}$ did not have any significant progression in their pB-C2. This suggests that patients with more severe VBSC can be safely managed initially with decompression alone with close follow up.

606. Current MIS Techniques Fail to Optimize Spinopelvic Parameters in Patients with High Pelvic Incidence

Richard G. Fessler, MD, PhD, FAANS; Gregory Mundis, MD; Robert Eastlack, MD; Praveen Mummaneni, MD; David Okonkwo, MD; Stacie Nguyen; Adam Kanter, MD; Neel Anand, MD; Paul Park, MD; Pierce Nunley, MD; Juan Uribe, MD (Chicago, IL)

Introduction: High pelvic incidence (HPI) demands a larger lumbar lordosis (LL) to achieve ideal spinopelvic harmony. Criticisms of MIS spine surgery (cMIS: MIS ant/lateral with MIS screws) include challenges in adequately matching LL to PI. This study analyzes the radiographic and clinical outcomes of patients treated with MIS with varying PIs.

Methods: Retrospective review of multicenter MIS database was queried for cMIS patients. Patients were grouped as low ($LPI \leq 43$; $n = 14$), mid ($41 < LPI \leq 66$; $n = 46$), and high ($HPI \geq 67$; $n = 17$) pelvic incidence, by 1 standard deviation from the mean. Theoretical LL (tLL) was calculated for all groups based on Schwab PI-LL formula with respect to PI outliers: $tLL = LPI + 10$, $= MPI$, $= HPI - 10$. The offset was calculated as the difference between tLL and pre- or post-LL. Well aligned (WA) patients were classified to Vialle et al. Nonparametric Kruskal-Wallis test was used to assess significant differences between groups.

Results: 420 patients were available for review, 165 patients identified in the database and 77 met inclusion. There were no differences for demographics, levels treated, iliac fixation or presence of lateral interbody. At baseline LPI and MPI had lower PT than HPI (15.7 v 23.5 v 33.6; $p < 0.05$) and preop PI-LL lower for LPI than HPI (9 v 21.9; $p < 0.05$) with no difference

in SVA or max Cobb. Post op both LPI and MPI had improved LL, but HPI did not. The tLL, and offset however, was not different between groups at pre or postop ($p < 0.05$). All groups saw improvement in ODI, VAS back and leg, with no difference in reaching MCID. Complication occurrence was similar between groups.

Conclusion: Minimally invasive techniques for treating this patient population reveal the inability to correct the PI-LL mismatch, likely because of the need for more lordosis. Careful consideration should be given when employing MIS techniques in patients with a high PI.

607. Caudate Stimulation Enhances Human Associative Learning

Philip L. Gildenberg MD Resident Award

Sarah Kathleen Bourne Bick, MD; Shaun Patel, PhD; Husam Katnani, PhD; Emad Eskandar, MD (Boston, MA)

Introduction: Associative learning allows an individual to acquire an association between a sensory cue and an outcome resulting from a specific response. Associative learning plays a vital role in our ability to learn new associations that allow us to optimally respond to the world around us. Research in humans and primates supports an important role for the caudate in associative learning. Our objective was to determine whether caudate stimulation could modulate associative learning in humans and to examine the neural circuitry involved in this process.

Methods: Two subjects who underwent depth electrode placement for monitoring of refractory epilepsy were included in our study. During recording from intracranial electrodes subjects participated in an associative learning task requiring them to learn associate a presented image with a button press. For half of the presented images bilateral caudate stimulation was performed at 2 mA and 200 Hz for 1 second during the feedback epoch after correct responses. We calculated the learning curve for stimulated and non-stimulated images using a state space model. We additionally calculated average power at electrode contacts in different spectral bands during the response and feedback epochs of the task and examined for correlation with the learning curve.

Results: Caudate stimulation during correct feedback significantly improved associative learning. Stimulated image associations were learned more rapidly than non-stimulated image associations. Learning was associated with increased low gamma (30-55 Hz) power in the nucleus accumbens and increased theta (3-8 Hz) power in the dorsolateral prefrontal cortex.

Conclusion: Caudate stimulation during reinforcement of correct association enhances learning and is associated with power changes in both dopaminergic circuitry involved in reward processing and areas involved in associative processes. This supports a role for the caudate in integrating reward information with associations. Furthermore, this suggests a new potential target for neuromodulation in human memory disorders.

608. A Comparison of Digital Subtraction Angiography and CT Angiography for the Diagnosis of Penetrating Cerebrovascular Injury

William J. Ares, MD; David Panczykowski, MD; Gregory Weiner, MD; Nitin Agarwal, MD; Felix Nguyen, BS; Bradley Gross, MD; Brian Jankowitz, MD (Pittsburgh, PA)

Introduction: The current Brain Trauma Foundation guidelines recommend screening for cerebrovascular injury following penetrating neurotrauma, however, it states that insufficient data exists to recommend a vascular imaging modality. Here, we sought to compare digital subtraction angiography and CT angiography for the diagnosis of penetrating cerebrovascular injury (PCVI).

Methods: This study included all patients undergoing evaluation of PCVI at our hospital between October 2010 and June 2016. Clinical data was retrospectively collected. All patients underwent radiographic evaluation consisting of 64-slice multidetector row CT angiography (CTA; 1.25mm slice thickness) and 4-vessel digital subtraction cerebral angiography,

DSA). Primary outcome was evidence of PCVI on DSA. Injuries were defined according to Biffi et al. grading scale for BCVI.

Results: Forty-six patients were available for analysis. Overall, 21 (35%) patients had PCVI on DSA; the injuries consisted of 2 (10%) grade I (intimal irregularity), 2 (10%) grade II (dissection), 4 (25%) grade III (pseudoaneurysms), 4 (25%) grade IV (occlusions), and 8 (31%) grade V (active extravasation or fistula) injuries. Of the 21 cerebrovascular injuries diagnosed on DSA only 13 (61%) were evident on CTA yielding a false negative rate of 37% and a sensitivity of 63%. Of the 21 injuries diagnosed on CTA only 13 were evident on DSA yielding a false positive rate of 37% and a specificity of 63%. CTA demonstrated poor discriminatory ability for prediction of PCVI (AUC 0.63, 95%CI, 50-96%). The negative predictive value of a normal CTA was 76% (95%CI, 55-91%).

Conclusion: This study represents the largest comparison of DSA and CTA in the diagnosis of PCVI following penetrating neurotrauma. In this population, CTA has been demonstrated to be significantly less sensitive and specific than DSA for the diagnosis of PCVI. Consideration should be given to making DSA the initial screening modality for PCVI.

609. Vancomycin And Tobramycin Powder Use In Intrathecal Baclofen Pump Implantation: Reducing Surgical Site Infections

Aria Jamshidi; Mya Abousy; Robert Keating, MD (Potomac, MD)

Introduction: While intrathecal baclofen pumps (IBP) have become a mainstay in reducing spasticity, their use remains plagued by infection. We aimed to reduce our infection rate by employing intraoperative vancomycin and tobramycin powder at the surgical site of baclofen pumps.

Methods: A retrospective review (2000-2016) at Children's National Medical Center evaluated 125 patients (73M, 52F), average age 16.35 years, whom had undergone implantation of an IBP for cerebral palsy (89%), spasticity secondary to TBI (8%), or secondary to other causes (2%). Infection rates were reviewed before and after the use of intraoperative topical vancomycin (1g) and tobramycin (1g) powder (started Oct, 2012). Institutional standards of infection prophylaxis were unchanged throughout the study period. Chi-square univariate analysis with a set significance (p -value) of < 0.05 was used for evaluation of data.

Results: Over the 16-year period 56 infections occurred, at an average of 95.95 days after pump placement. Despite rigorous institutional analysis, infections rates before the use of vancomycin/tobramycin increased from 10 to 37% from 2000 to 2012. Due to this unexplained increase in infection, antibiotic powder was instituted and subsequently associated with significantly fewer surgical site infections (17%) than standard antibiotic prophylaxis alone (37%), $p = .028$. Cumulative infection rate over the 16-year period was 24.88% without vancomycin versus 14.81% with vancomycin/tobramycin, and this continues to fall with the new protocol in place. **Conclusion:** The use of intraoperative topical vancomycin/tobramycin powder in this series has significantly reduced the infection rates in our cohort of baclofen pump patients. Further prospective study of this high-risk patient population is warranted and expected to demonstrate meaningful long-term efficacy.

610. Optical Topographic Imaging for Intra-Operative Three-Dimensional Navigation in the Cervical Spine: Accuracy Validation and Initial Clinical Feasibility

Sanford J. Larson, MD, PhD Award

Daipayan Guha, MD; Raphael Jakubovic, MSc; Shaurya Gupta; Michael Fehlings, MD, PhD; Albert Yee, MD, MSc; Victor Yang (Toronto, Canada)

Introduction: Computer-assisted three-dimensional navigation may guide spinal instrumentation. Current systems are hampered by cumbersome registration and inability to account for intra-operative tissue movement. A novel optical topographic imaging (OTI) system was developed for craniocervical navigation, and has been described previously in the thoracolumbar

spine. Here, we validate its accuracy in the mobile cervical spine.

Methods: Initial validation was performed in four human cadavers. Intra-operative registration was performed to thin-slice preoperative CT imaging. A tracked drill-guide was used to navigate screw tracts at all levels. Lateral mass screws were placed at C1 and C3-6, pars screws at C2, and pedicle screws at C7. Navigation data were compared to screw positions on postoperative CT imaging, and the absolute translational and angular deviations computed. Clinical validation was subsequently performed in six patients undergoing open posterior cervical instrumentation.

Results: 53 cadaveric screws were analyzed; 5 lateral mass screws at C1 and 32 at C3-6, 8 pars screws at C2, and 8 pedicle screws at C7. Absolute translational errors were 1.66 ± 1.18 mm and 2.08 ± 2.21 mm in the axial and sagittal planes, respectively; absolute angular deviations were $4.11 \pm 3.79^\circ$ and $6.96 \pm 5.40^\circ$, respectively (mean $\pm$ SD). In hierarchical linear modelling, adjusting for differences between cadavers, C7 pedicle screws demonstrated decreased axial translational error relative to all other screws (0.51 ± 0.36 mm, $p = 0.001$) (mean $\pm$ SD). 22 clinical screws were analyzed; 2 pars screws at C2, 14 lateral mass screws at C3-5, and 6 pedicle screws at C7. Absolute translational errors were 1.52 ± 1.32 mm and 1.06 ± 0.97 mm in the axial and sagittal planes, respectively; absolute angular deviations were $3.69 \pm 2.63^\circ$ and $2.83 \pm 2.65^\circ$, respectively (mean $\pm$ SD). There were no differences in errors between levels. There were no facet, canal or foraminal violations, and no neurovascular injuries.

Conclusion: Optical machine-vision is a novel navigation technique allowing efficient initial and repeat registration. Accuracy even in the more-mobile cervical spine is comparable to current spinal neuronavigation systems.

611. Reduction in Mortality & Morbidity after Subarachnoid Hemorrhage between 2002-2011: A Nationwide Inpatient Sample Analysis

Hormuzdiyar Dasenbrock, MD; Robert Rudy, BS; William Gormley, M. Ali Aziz-Sultan, MD; Rose Du, MD, PhD (Boston, MA)

Introduction: The goal of this study was to utilize a nationally representative patient population to evaluate trends in mortality & morbidity after repair of ruptured cerebral aneurysms in the United States.

Methods: Patients with aneurysmal subarachnoid hemorrhage (SAH) were extracted from the Nationwide Inpatient Sample (NIS, 2002-2011). Multivariable logistic regression evaluated the association of year of hospital admission with in-hospital mortality, discharge disposition, and of a poor outcome (death, tracheostomy or gastrostomy placement, or discharge to institutional care). Covariates included patient age, sex, comorbidities, NIS-SAH severity scale, and hospital characteristics. Thereafter, subgroup analyses evaluated patients separately who were treated microsurgically or endovascularly.

Results: A total of 18,281 patients were included. The in-hospital mortality rate was 13.4% during the entire study period: 15.3% in 2002 and 10.7% in 2011. In multivariable logistic regression, more recent year of admission was independently associated with significantly decreased odds of in-hospital death, non-routine hospital discharge, and of a poor outcome (all $p < 0.001$). Among patients treated surgically, the in-hospital mortality rate decreased from 15.1% in 2002 to 10.9% in 2011; within patients who underwent endovascular embolization, in-hospital mortality decreased from 21.3% in 2002 to 10.5% in 2011. Both subgroups were associated with significantly decreased odds of in-hospital mortality or of a poor outcome during the study period.

Conclusion: Mortality and poor outcomes after aneurysmal subarachnoid hemorrhage have significantly decreased over the past decade, both among patients treated surgically and endovascularly. Advances in neurocritical care and techniques utilized for aneurysm repair and may explain superior patient outcomes.

612. Contextual Differences in Motor Cortical Neural Firing Patterns When Controlling Multiple Effector Devices Using an Intracortical Brain-computer Interface (iBCI)

Vamsidhar Chavakula, MD; Susan Fasoli; David Brandman, MD; Carlos Vargas-Irwin, PhD; Jad Saab, MS; Thomas Hosman, MS; Brian Franco,

MS; John Simeral, PhD; John Donoghue, PhD; Leigh Hochberg, MD, PhD (Boston, MA)

Introduction: For people with tetraplegia, intracortical brain-computer interfaces (iBCI) provide a promising method for controlling effectors such as prosthetic limbs and computer cursors. However, when changing from one effector to another, a significant degradation in control can occur. We sought to elucidate whether neural firing patterns in motor cortex are contextually altered when controlling a virtual cursor versus a physical robotic arm making the same movements.

Methods: A 52-year-old gentleman with tetraplegia secondary to ALS (ALSFRRS-R=7) had two 96 channel microelectrode arrays placed in the hand-knob area of left precentral gyrus as part of the BrainGate2 pilot clinical trial. He performed a two-dimensional task in which he guided either a computer cursor or robotic arm over one of eight radially arranged targets displayed on a computer screen. Calibration of neural decoders was performed at the start of each research session by having the participant observe the automated movement of one of the effectors and then gain gradual control of the effector. Once the decoder was calibrated, we compared performance as the participant alternated control between effectors using the same decoder. Spike Train Similarity Space (SSIMS) based machine-learning classification analysis was used to evaluate differences in ensemble neural data.

Results: There was significant decrease in accuracy when using a decoder calibrated on the opposite effector for both the cursor (47% decrease, $p < 0.001$, Student's t-test) and the robotic arm (38% decrease, $p = 0.0014$). SSIMS classification revealed the presence of two distinct neural ensemble clusters during device usage—one for each effector, with each cluster further showing a consistent organization of intended movement direction for that effector.

Conclusion: Our findings show that contextual alterations in neural firing patterns occur with respect to the effector being controlled, and highlight the dynamic functional network that exists among neurons in motor cortex.

613. Health Care Disparities in Traumatic Brain Injury: The Effect of Insurance on Severity of Presentation

Mohamad Bydon, MD; Meghan E Murphy; Panagiotis Kerezoudis, MD; Patrick R Maloney, MD; Brandon A McCutcheon, MD; Lorenzo Rinaldo, MD; Daniel Shepherd, MD; Daniel S Ubl, MD; Elizabeth B Habermann, MD (Rochester, MN)

Introduction: Previous literature has described disparities in traumatic brain injury (TBI) outcomes by insurance status, but no study has focused on the disparities in presentation of TBI. We aimed to examine influence of insurance on severity of presentation in TBI.

Methods: In this retrospective cohort analysis the National Trauma Data Bank (NTDB), years 2010-2014, was queried for TBI diagnoses codes. Unadjusted and adjusted analyses were performed with respect to insurance type to evaluate for significant differences in head abbreviated injury score (AIS) ≥ 4 and GCS 3-6.

Results: A total of 664,573 cases were included for analysis. Median age was 31 with 75% of patients ≥ 19 years and 67% Caucasian. African-Americans, Native Americans, and Pacific Islanders had greater proportions of Medicaid patients than Caucasians (29%, 35%, and 22%, respectively vs. 16%, p -value 0.001). African-Americans and Pacific Islanders had greater proportions of self-pay patients compared to Caucasians (25% and 23% vs. 17%, p -value 0.001). Forty three percent of patients insured by Medicaid had a head AIS ≥ 4 , compared to 41% in self-payers, and 40% in the privately insured (p -value 0.001). A greater proportion of Medicaid and self-pay patients were noted to have lower GCS compared to private insurance (GCS 3-6: 13% and 15%, respectively, vs. 11%, p -value 0.001). On adjusted analysis Medicaid was independently associated with head AIS ≥ 4 (OR 1.13, 95% CI 1.12-1.15) and GCS 3-6 (OR 1.29, 95% CI 1.26-1.32) compared to private insurance. Self-pay was also independently associated with GCS 3-6 (OR 1.25, 95% CI 1.22-1.28).

Conclusion: We propose that the previously established effect of insurance status on outcomes may be a reflection of its association with more severe presentations rather than a direct effect on outcomes. In this analysis racial minorities suffering TBI compose a greater proportion of non-private insurance than Caucasians, and those insured by Medicaid or self-pay are more likely to present with serious TBIs.

614. Stimulated Raman scattering microscopy provides histopathologic images for accurate intraoperative diagnosis of pediatric brain tumors

Todd Hollon, MD; Mia Garrard; Balaji Pandian; Hugh Garton, MD; Cormac Maher, MD; Karin Muraszko, MD; Daniel Orringer, MD (Ann Arbor, MI)

Introduction: Accurate intraoperative histopathologic diagnosis is essential for optimal surgical management of pediatric brain tumors. Standard intraoperative histopathology suffers from intensive tissue preparation and processing artifact. Stimulated Raman histology (SRH) uses the intrinsic biochemical properties of fresh surgical specimens to provide label-free histologic images. We aimed to evaluate the ability of SRH to reveal histopathologic features of pediatric brain tumors for accurate intraoperative diagnosis.

Methods: Pediatric and young adult brain tumor patients (≤ 26 years) were prospectively enrolled over 18 months. Fresh surgical specimens were imaged intraoperatively using a clinical fiber-laser-based SRH microscope. Blinded reviewers evaluated SRH images for histopathologic features and diagnostic accuracy was calculated.

Results: Twenty-one patients were enrolled and histopathologic diagnoses included pilocytic astrocytoma(8), gangliogliomas(5), medulloblastoma(4), ependymoma(1), high-grade glioma(1) and germinoma(1). SRH provided rapid histologic images with sub-micron resolution for all specimens without tissue processing artifact. A virtual hematoxylin and eosin color scheme was developed to recreate standard light microscopy conditions. Diagnostic histopathologic features (e.g. pilocytic processes, small round blue cell morphology, etc.) were evaluated in 1,617 400 μ m x 400 μ m fields of view for the above listed tumor types. Using histopathologic features, SRH correctly diagnosed 32/33 (97%) fresh surgical specimens. Additionally, SRH provided unique intraoperative histologic data on immune cell infiltration not detected on standard light microscopy that improved diagnostic accuracy of tumor grade. Macrophage infiltration predicted higher tumor grade with 99% specificity and 100% sensitivity.

Conclusion: SRS microscopy provides rapid, high-resolution, intraoperative images for accurate diagnosis of common pediatric brain tumors. Further investigation in a larger pediatric cohort is currently underway.

615. Laser Thermotherapy for Spinal Metastatic Disease provides Comparable Local Control, Reduced Morbidity and Shorter Delay to Systemic Therapy Compared to Open Surgery

Brian D. Silber Award

Richard Everson; Bruno Fernandes; Scott Zuckerman; Ganesh Rao; Jing Li; Amol Ghia; Behrang Amini; Laurence Rhines; Claudio Tatsu (Houston, TX)

Introduction: Spinal cord proximity limits radiosurgical dosing to epidural compressive metastatic lesions. Open surgery creates a safe margin around the spinal cord at the cost of significant morbidity and delay to further treatments. Spinal laser interstitial thermotherapy (SLITT), a minimally-invasive technique, is well-tolerated and can provide local control. Comparison to standard surgical approaches is necessary to determine the utility of the procedure.

Methods: 147 contemporaneously patients with MESCC treated with

open surgery (n=84) and SLITT (n=63) were selected for study. Medical records and imaging studies were analyzed. Demographics, anatomic location, ESCC scores, histology, morbidity, hospital LOS, delay to treatment, local control and overall survival were retrospectively compared.

Results: Patient demographics and clinical characteristics were similar, except pre-op ESCC was higher in the surgery group. Compared to open surgery, SLITT was associated with smaller post-operative decrease in ESCC (1.3 vs 3.4 $P < 0.0001$), but lower EBL (<100cc vs 1186cc $p < 0.0001$) shorter hospital stay (3.4 vs 12.1 $p < 0.0001$) less morbidity (12.7 vs 28.6% $p = 0.021$), fewer days until treatment with XRT/SRS (1.8 vs 40.2 $p > 0.0001$) and systemic treatment (21.7 vs 62.8 $p < 0.0001$). 1-year local control and overall survival were similar between groups (PFS-1: 77.7 SLITT vs 80.4 open $p = .974$, Median OS: 517 vs 562 days $p = 0.839$).

Conclusion: Compared with open surgery, SLITT offers comparable local control with less morbidity, shorter hospitalization and faster return to oncologic treatment. Additionally, the technique may be applicable to a broader set of patients who would not normally be candidates for surgery. These data provide further justification for a randomized controlled comparison study currently being planned.

616. Alterations in Cerebral Ventricle Size Over Time in Children with Congenital Heart Disease

Laurie Lynn Ackerman, MD, FAANS; Christopher Mastropietro, MD; Zachary Daniels, MD; Stephen Kraljic, MD; Mandy Harris, MD; Anne Farrell, MD; Marcus Schamberger, MD (Indianapolis, IN)

Introduction: We evaluated cerebral ventricle size in two groups of children with congenital heart disease prone to chronically elevated central venous pressure (CVP): children with single ventricle anatomy who undergo superior cavopulmonary anastomoses (SCPA) and children with Tetralogy of Fallot (TOF).

Methods: We retrospectively reviewed records of patients who underwent cranial imaging before or after SCPA or TOF repair surgery from 2006-2014. Frontal-occipital (FO) horn ratios were calculated. Reported mean pediatric FO ratio for normal subjects is 0.37 ± 0.03 , independent of age with high inter-rater reliability. Mean FO ratio before and after SCPA and repair of TOF were compared using paired and unpaired t-tests.

Results: We reviewed 41 patients who underwent SCPA (4 with preoperative imaging, 17 with postoperative imaging, and 21 with both) and 20 patients who underwent repair of TOF (10 with preoperative imaging, 6 with postoperative imaging, and 4 with both). For patients who underwent SCPA, mean preoperative FO ratio was 0.37 ± 0.03 and increased significantly after surgery to 0.41 ± 0.06 ($P = 0.02$). In contrast, patients who underwent repair of TOF, mean preoperative FO ratio was 0.40 ± 0.04 and remained statistically unchanged after surgery at 0.40 ± 0.07 ($P = 0.89$). Similar statistical results were obtained in patients with both preoperative and postoperative imaging.

Conclusion: Cerebral ventricle size in children who underwent SCPA was similar to reported norms preoperatively and then increased after surgery, while cerebral ventricular size in patients who underwent repair of TOF was elevated preoperatively and remained relatively unchanged after surgery. These findings could be explained by alterations in CVP commonly observed in these children and may have implications for initiation of treatment of ventriculomegaly.

617. Assessment of Sagittal Balance Following TLIF - Are We Kyphosing the Lumbar Spine?

Stewart B. Dunsker, MD Award

Karthik Madhavan, MD; Lee Onn Chieng, BS; Alan Shamrock; Michael Wang; Steven Vanni (Miami, FL)

Introduction: Transforaminal lumbar interbody fusion (TLIF) has been the "workhorse" spinal procedure for the past decade. However, there

remains the challenge of suboptimal lordotic interbody cage placement. We propose that adjustment of spinopelvic parameters play an important role in outcome following TLIF.

Methods: 730 patients who underwent TLIF surgery were retrospectively reviewed. Standing X rays were assessed for changes in disc height, lumbar lordosis, pelvic incidence, pelvic tilt, and sacral slope. Reoperation rate was assessed as well.

Results: 730 operations were performed at more than 1000 levels. Mean presenting lumbar lordosis(LL) was 47.0 ± 14.0 . Mean postop LL was 46.5 ± 13.0 . Among 90 patients with kyphosis(12.3%), 45% had restoration of lordosis. Interestingly, among those with normal lordosis, 57% developed kyphosis postoperatively. High pelvic tilt(PT), sacral slope(SS), and pelvic incidence(PI) were observed in 57%, 8.5%, and 24% respectively. However, only 32.1% and 60% of these patients with high PT and SS were successfully corrected with TLIFs while the high PI was remained unchanged as expected. Moreover, 44.5% of the patients had PI-LL mismatch $\geq 11^\circ$ (mean: 22.0 ± 9.1) in which 28% of these remained not corrected (mean: 22.9 ± 8.5). The reoperation rate was 4.1% and reasons included adjacent segment disease and pseudoarthrosis. Factors of reoperation included uncorrected LL (OR: 44.0; 95%CI 2.7, 726; $p < 0.0001$) and uncorrected PT (OR: 4.5; 95%CI 0.6, 36.5; $p = 0.16$).

Conclusion: Several factors influence sagittal balance post TLIF including inherent lordosis of the cage, the expandable nature, anterior position of cage and compression of posterior screws. Spino-pelvic parameters are the foundation of spinal correction and any insufficient correction could leads to inverted pendulum effect where the upper body gradually kyphoses forward leading deformity.

618. Seizure Response after Radiosurgery for Cerebral Arteriovenous Malformations

Ajay Niranjana, MD; Ahmed Kashkoush, BA; Hideyuki Kano; Edward Monaco III; John Flickinger; L. Dade Lunsford, MD, FAANS (Pittsburgh, PA)

Introduction: Seizures are the second most common presenting symptom in patients with lobar arteriovenous malformations (AVMs); however few studies have assessed the long-term benefit of stereotactic radiosurgery (SRS). This study aims to assess the outcome of SRS and to identify prognostic factors associated with seizure control.

Methods: The authors retrospectively assessed patients with AVMs and a history of seizure who underwent SRS at our institution between 1987 and 2012. The total cohort included 164 patients with mean follow-up of 80.6 months (95% confidence interval, 69.0-92.2). Preoperative seizure and AVM characteristics, intraoperative radiosurgical parameters, and postoperative AVM assessment were extracted from patient medical records. Outcomes assessed were seizure frequency and anti-epileptic drug regimen at last-follow-up. **Results:** Seizure-free status was achieved in 68.9% (113/164) of patients at a mean of 62.4 months (46.0-78.8). Median preoperative and postoperative seizure frequencies were 3.5 (range, 0.8-8.6) and 0.2 (range, 0-1.4) episodes/year, respectively ($p < 0.001$, Wilcoxon rank-sum test). The proportion of patients reaching medication freedom increased postoperatively (18.2%, 28/154) compared to the preoperative period (8.5%, 14/164) ($p = 0.013$, chi-squared test), with a mean time to medication freedom of 213.0 months (188.7-237.4). A multivariate logistic regression analysis determined that age < 35 years (odds ratio, 2.1 [1.0-4.4]) and partial-complex seizures (odds ratio, 2.4 [1.0-5.8]) at the time of SRS were the greatest predictors of long-term persistent seizures. AVM obliteration did not correlate with seizure control.

Conclusion: This study suggests that SRS improves long-term seizure control and increases the likelihood of being medication-free, independently of AVM obliteration. Seizure control may be more difficult to obtain in older patients as well as those with partial-complex seizure type.

619. Survival and integration of human stem cell-derived cerebral organoids in rat secondary visual cortex

Han-Chiao Isaac Chen, MD; Dennis Jgamadze, MD, PhD; Nadir Bilici; James Lim, BA; Chris Adam, BA; Clarissa Liu; Diego Contreras, MD, PhD; John Wolf, PhD (Philadelphia, PA)

Introduction: Few interventions exist to restore function in patients with neurological deficits. In cases of significant brain damage, neural substrate expansion may be a viable option for rebuilding brain circuitry. We hypothesize that this neural substrate will most effectively restore network integrity if it mirrors brain architecture. Here, we generated structured neural tissue from pluripotent stem cells and characterized its survival and integration after transplantation into rat visual cortex (V2).

Methods: We grew cerebral organoids from a federally approved human embryonic stem cell line (H9-GFP). Organoid structure was analyzed immunohistochemically. Other organoids were transplanted into adult rats immunosuppressed with cyclosporine. A cylindrical core of V2 cortex was aspirated and replaced with a similarly sized core of organoid tissue. After 2 months, animals were re-anesthetized for electrophysiological recordings of the organoid in response to visual stimulation and lateral geniculate nucleus (LGN)/primary visual cortex (V1) electrical stimulation and/or sacrificed for immunohistochemistry.

Results: Immunohistochemical analysis of the organoids revealed the presence of neural progenitor zones and differentiated neurons. Upper (Satb2+) and lower (CTIP2+) layers formed at later time points. In 8/12 (67%) animals, transplanted organoids survived robustly. Extensive outgrowth of neurites into the adjacent host brain was observed. Evoked field potentials appeared to be present in 2/3 animals in response to stimulation of the contralateral eye and ipsilateral LGN and V1. Average response latencies were 49, 6, and 12 ms for visual, V1, and LGN stimulation, respectively.

Conclusion: Human stem cell-derived cerebral organoids recapitulate early cerebral cortex development, including the development of rudimentary cortical layers. This neural tissue survives after transplantation into rat V2 cortex. Preliminary data suggest potential anatomical and functional integration with the visual network. These results raise the possibility that neural tissue with appropriate cerebral cortex architecture could be used to augment the computational capacity of the brain after injury.

620. Predicting Prognosis of Chronic Subdural Haematoma Patients - A New Scoring System

Churl-Su Kwon; Omar Al-Awar; Oliver Richards (London, United Kingdom)

Introduction: We aimed to identify specific prognostic factors related to developing unfavourable outcomes following burr-hole evacuation of chronic subdural haematoma (CSDH) and devise a new scoring system that is practical and statistically reliable to estimate clinical outcome.

Methods: A cohort of patients undergoing evacuation of CSDH at a single institution was established from 2010-2014. Primary endpoint was the dichotomised score on a modified Rankin scale at 1 year follow-up (favourable outcome score 0-1; unfavourable outcome score 2-6). Logistic regression analyses were performed to model determinants related to outcome. A scoring system was made to predict 'favourable vs. unfavourable' outcomes.

Results: 120 patients were included in the study (mean age 66.1 ± 15.2 years). Logistic regression analysis showed: age < 75 (OR 7.1; 95%CI 1.7-29.0; $p = 0.007$), midline shift 10-20mm (OR 3.4; 95%CI 1.0-11.4; $p = 0.04$), disorientation (OR 24.1; 95%CI 3.1-189.0; $p = 0.002$), motor function deficit (OR 4.9; 95%CI 1.5-15.9; $p = 0.008$) before surgery were unfavourable prognostic factors. Duration of hospital stay, sex, ASA, side of haematoma, coagulation status were not predictive of developing unfavourable outcomes. Using the significant prognostic factors a scoring system was devised. (Age: $< 60 = 3$ points, $60-75 = 2$ points, $> 75 = 1$ point; GCS: $< 8 = 0$ points, $8-13 = 1$ point, $> 13 = 2$ points; Haematoma thickness: $< 3\text{cm} = 0$ points, $1-3\text{cm} = 1$ point,

<1cm=2 points;Midline shift:<2cm=0 points, 1-2cm=1 point, >2cm=2 points;Motor function:Not normal=1 point, normal=2 points;Orientation:D isorientated=1 point, orientated=2 points). ROC curves were constructed to predict favourable vs. unfavourable outcomes. A score of ≥ 9 showed favourable outcome.

Conclusion: Unfavourable outcomes are predicted by age<75, MLS<1cm, drop in GCS on verbal/motor score. A scoring system has been devised to predict outcome which can be used to aid in the necessity of surgery in certain patient demographics.

621. Moderate-Grade Intraventricular Haemorrhage activates Cell Division in the Neonatal Mouse Subventricular one.

William John Dawes; Silvia Marino (Kingston, England)

Introduction: Intraventricular haemorrhage (IVH) in the premature neonate is postulated to impact on the neural stem progenitor cells (NSPC) within the subventricular zone (SVZ) however evidence in support of this is lacking. Manipulating NSPC response to haemorrhage may offer new therapeutic approaches.

Methods: Using a modified Narishige stereotactic-frame we have optimised and validated a mouse model of Papile Grade II/III IVH. A thymidine labelling strategy combined with immunohistochemistry has been used to determine the impact of IVH on NSPC at P4 and cortical development at P21. CD133 MACS sorting with RNA analysis has been used to define the impact of IVH on the molecular characteristics within the ventricular domain of the SVZ with validation of targets using in-situ hybridisation (ISH).

Results: Our mouse model recapitulates key features of the human condition, namely failure to thrive (weight: control 3.101g, IVH 2.775g $\pm$ 0.08, $p=0.002$) and hydrocephalus (ventricular-volume: control 0.054cm³ $\pm$ 0.007, IVH 0.078cm³ $\pm$ 0.005, $p=0.02$) Significantly increased EdU+ve cells are seen within the SVZ at P4 (control 59.73; IVH 160.1 $p<0.0001$) and transcallosal pathway (control 26.98; IVH 43.22 $p=0.0004$) in association with increased markers of transient amplifying cells (MASH1 ($p=0.0009$), GFAP ($p=0.00002$), NG2 ($p=0.0006$) consistent with activation of proliferation. RNA analysis from CD133+ve cells at P4 reveals that IVH downregulates Notch2 expression <25 fold ($p=0.01$), a finding confirmed by Hes5 ISH. GMH at P0 leads to a reduction of EdU+ve and Olig2+ve cells within the neocortex at P21 (Control 9.57, GMH 6.8 $p=0.006$ & Control 12.81: IVH 9.6 $p=0.001$ respectively) **Conclusion:** Moderate grade IVH activates proliferation in the SVZ, we hypothesise that this may be due to a downregulation of Notch2 within the ventricular domain and suggest that quantification of Notch expression as a potential prognostic indicator and therapeutic target warrants further exploration.

622. Prediction of 30-Day Morbidity and Mortality Following Resection of Epidural Tumors of the Lumbar Spine in 300 Patients: An ACS NSQIP Analysis

Christopher Ashot Sarkiss, MD; Travis Ladner, MD; Nathan Lee, BS; Parth Kothari, BS; Nikita Lakomkin, BA; John Caridi, MD (New York, NY)

Introduction: Resection of lumbar spinal tumors is challenging and carries risk. Knowledge of modifiable risk factors are important in minimizing postoperative morbidity and mortality. Here the authors perform an analysis of the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) registry to assess predictors of morbidity and mortality in patients undergoing resection of epidural tumors of the lumbar spine.

Methods: We performed a retrospective study of prospectively collected data utilizing the ACS NSQIP database. Inclusion criteria were adults who underwent laminectomy for excision of lumbar spine tumors between 2011 and 2014. Demographics and medical comorbidities were collected. Major morbidities and mortality within 30 post-operative days were also reviewed. A multivariate binary logistic analysis of these clinical variables was performed to determine covariates of morbidity and mortality.

Results: The database search yielded 300 patients, of which 118 (39.3%) were female. Overall, complications within 30 days of surgery occurred in 102 (34%) patients. Sixty-four (21.3%) patients required blood transfusions. Deep venous thrombosis/pulmonary embolism occurred in 17 (5.7%) patients. Thirty-day mortality occurred in 15 (5%) patients. Three (3.2%) underwent a re-operation and 11 (11.6%) were re-admitted. Preoperative anemia (OR 3.4, 95% CI 1.8-6.5) and operative time < 4 hours (OR 2.6, 95% CI 1.1-6.0) were significantly associated with 30-day mortality.

Conclusion: There is a relatively high complication rate for excision of epidural lumbar spinal tumors. Presence of preoperative anemia and anticipated operative time are essential data points in guiding surgical decision making for these lesions. These may be optimized preoperatively to improve surgical safety.

623. Unplanned Readmission after Craniotomy for Tumor: A National Surgical Quality Improvement Program-Pediatric Analysis

Hormuzdiyar Dasenbrock, MD; Timothy Smith; Lilliana Goumnerova, MD (Boston, MA)

Introduction: Although readmission is a common metric of quality of care, this is the first national analysis to evaluate the rate, predictors, and reasons for unplanned readmission after craniotomy for tumor in the pediatric population.

Methods: Patients who underwent craniotomy for tumor resection were extracted from the prospective National Surgical Quality Improvement Program-Pediatric registry (2012-2013). Multivariable logistic regression with backward, stepwise elimination examined the predictors of an unplanned readmission within thirty days of surgery. Variables screened included patient age; sex; tumor location; American Society of Anesthesiologists class; comorbidities; preoperative laboratory values; preoperative steroid administration; recent oncologic treatment; operative time; length of stay and complications during the index admission.

Results: Of the 1,268 patients included, 11.8% (n=149) had an unplanned readmission. Independent predictors of readmission were age less than four years (odds ratio (OR)=1.98, 95% confidence interval (CI): 1.37-2.86, $p<0.001$), a hematologic comorbidity (OR=2.78, 95% CI: 1.07-7.21, $p=0.04$), preoperative steroid usage (OR=1.58, 95% CI: 1.09-2.29, $p=0.02$), and neurologic complications during the index hospitalization (OR=4.80, 95% CI: 1.83-12.50, $p=0.001$). Longer index hospitalization was protective against readmission (OR=0.55, 95% CI: 0.35-0.86, $p=0.001$). The most common reasons for readmission were a deep or superficial surgical site infection (27.0%), hydrocephalus (16.0%), central nervous system complications (7.0%), seizures (6.0%), and headache (5.0%).

Conclusion: In this national analysis, unplanned readmission was common after craniotomy for tumor resection in pediatric patients, and most frequently due to delayed complications—including surgical site infections, hydrocephalus, and seizures. Younger patients and those with a shorter hospitalization were more likely to be readmitted.

624. Dissociation of Early and Delayed Cerebral Infarction after Aneurysmal Subarachnoid Hemorrhage

Oliver Ayling, MD; George Ibrahim, MD, PhD; Naif AIOtaibi, MD; Peter Gooderham, MD; R. Loch Macdonald, MD, PhD (Vancouver, Canada)

Introduction: Cerebral infarction after aneurysmal subarachnoid hemorrhage (aSAH) is a significant cause of substantial morbidity and mortality. Since early and delayed cerebral infarction after aSAH may be mediated by different processes we evaluated if aneurysm securing methods contributed to these infarcts and whether long-term outcomes differ for patients with early and delayed infarcts.

Methods: A post-hoc analysis of the Clazosentan to Overcome Neurological iSchemia and Infarction Occurring after Subarachnoid hemorrhage (CONSCIOUS-1) study was performed. Using multivariate

logistic regression analysis and propensity-matching, independent clinical risk factors associated with infarctions were identified and the contribution of cerebral infarcts to long-term outcomes was evaluated. Predictive thresholds of infarction volume were defined using Receiver Operator Characteristic (ROC) curves.

Results: Within the cohort of 413 subjects, early infarcts were present in 76 (18%), while delayed infarcts occurred in 79 (19%), and 36 (9%), had new infarctions that were present on both early and delayed imaging. Propensity-score matching revealed a significantly higher proportion of early infarcts after clipping (OR 4.62, 95% CI 1.99-11.57, $p=0.00012$). Multivariate logistic regressions identified clipping as an independent risk factor for early cerebral infarction (OR 0.26, 95% CI 0.15-0.48, $p<0.001$), and angiographic vasospasm was an independent risk factor for delayed cerebral infarction (OR 1.79, 95% CI 1.03-3.13, $p=0.039$). Early infarcts were a significant independent risk factor for poor long-term at 3 months (OR 2.34, 95% CI 1.18-4.67, $p=0.015$). ROC curves demonstrated that an infarct volume of 10 cm³ (sensitivity: 50.0, specificity: 70.3) predicted poor long-term outcomes.

Conclusion: Clipping is an independent risk factor for the development of early cerebral infarcts, while delayed cerebral infarcts are associated with angiographic vasospasm. Early cerebral infarcts are stronger predictors of worse outcome than delayed infarction.

625. Treatment of Chronic Low Back Pain via Ablation of the Basivertebral Nerve: Results of a Multicenter, Randomized, Double Blinded, Sham Controlled FDA IDE Trial (SMART Trial)

Bernhard Meyer, MD; Rick Sasso, MD; Hyun Bad, MD; Christopher Yeung, MD; Alfred Rhyne, MD; Joerg Franke, MD; Peter Vajkoczy, MD; Michael DePalma, MD; Jeff Fischgrund, MD (Munich, Germany)

Introduction: The basivertebral nerve (BVN) is a sensory nerve within the vertebral body, whose role in pain transmission is thought to be a source of chronic low back pain associated with degenerative vertebral bodies and endplates. The use of a novel intraosseous bipolar radiofrequency system for ablation of the BVN was tested in this trial.

Methods: After 2:1 randomization, 225 patients were treated in either the investigational group (147) receiving BVN ablation, or the control group (78), receiving the sham procedure by anchoring the introducer within the pedicles. Patients were evaluated preoperatively and postoperatively at 2 and 6 weeks and 3, 6, and 12 months. The primary study endpoint was the comparison of the mean ODI improvement from baseline to 3 months. Patients were followed through one year.

Results: Results of the primary end point for the per protocol (PP) population showed that the ODI improvement observed in the investigational arm was statistically superior ($p=0.019$) to the Sham arm (LS Mean: 20.5 versus 15.2 points). This result was sustained through one year of follow-up. An analysis of ODI responder rates found that 75.6% of patients in the active arm demonstrated a greater than 10-point improvement. There were no adverse device effects. There were no device related serious adverse events (SAE) and only one procedure related SAE. MRI at 6-week and 6-month follow-up found no evidence of any vertebral body collapse, or accelerated disc degeneration.

Conclusion: Ablation of the BVN is safe and effective, since the analysis of the primary study end point showed a significantly greater improvement in ODI for the investigational arm over the Sham arm in the PP population. The high response rate in the Sham population does not invalidate the conclusion, that BVN ablation may provide a new treatment option for a subset of patients with CLBP.

626. Modulating Large-Scale Epileptic Networks by SEEG Guided-Laser Ablations

Louis Ross; Ahsan Naduvil, MD; Jeffery Mullin, MD; Juan Bulacio, MD; Viktor Jirsa, PhD; Patrick Chauvel, MD; Jorge Gonzalez-Martinez, MD (Shaker Heights, OH)

Introduction: Initially described in 2006, laser ablation under real-time

MRI has had promising results in treating multiple intracranial pathologies, including MRI identifiable lesional epileptogenic foci. However, stereo-EEG (SEEG) guided laser ablation (SGL) of specific epileptic networks in patients with non-lesional MRIs has never been attempted.

Methods: The epileptic networks of 10 patients were mapped and characterized by SEEG. The definition of nodes and pathways within specific networks was based on standard anatomo-electro-clinical correlations. Under robotic assistant, laser probes were placed in strategically defined areas within the mapped networks. Ablations were performed in our intraoperative MRI suite. Seizure outcome and complications were assessed during follow-up visits.

Results: SGL was performed on fifteen regions of epileptogenicity identified amongst ten patients using SEEG monitoring. There was an equal distribution of focal and multifocal regions of epileptogenicity. Mean operative time, including MRI, was 3 hours and 43 minutes. Average lesional volume was 2.46 cc. All patients were discharged on post-operative day one. Average follow-up was 17 months. Four patients (40%) reported complete resolution of seizure activity (Engle I); whereas the remainder were: Engle II (5), Engle III (0) and Engle IV (2). No major complications were reported.

Conclusion: Our experience illustrates the feasibility of combining SEEG and laser methodologies to map and modulate large scale-epileptic networks. While the authors acknowledge that further follow-up is needed, our current success allows for the possibility of a future diagnostic-therapeutic combination that offers unparalleled minimal invasiveness, duration of treatment, and seizure control in patients with difficult to localize epilepsy.

627. Clinical Correlates of Quantitative Cerebral Blood Flow using Xe-CT after Decompressive Craniectomy in Traumatic Brain injury

Aditya Vedantam, MD; Claudia Robertson, MD; Shankar Gopinath, MD (Houston, TX)

Introduction: The effect of decompressive craniectomy (DC) on clinical outcomes after TBI has been the subject of recent randomized controlled trials. Few studies have reported on changes in cerebral blood flow (CBF) after DC, and the impact of these measures on clinical outcome.

Methods: We studied prospectively collected clinical and imaging data for patients who underwent xenon enhanced CT (XeCT) CBF studies after DC for evacuation of a mass lesion and/or to relieve intractable intracranial hypertension. Cerebral hemodynamic parameters prior to DC and at the time of the XeCT CBF study were recorded. Global and regional CBF after DC was measured. Regional CBF was measured in the cortical mantle under the craniectomy flap. Associations between CBF, cerebral hemodynamics after DC and early clinical outcome were assessed.

Results: Twenty-seven patients were included in this study. The majority of patients (88.9%) had an initial GCS $\leq$ 8. The median time interval between injury and decompressive surgery was 9 hours. Primary decompressive surgery (within 24 hours) was performed in the majority of patients ($n=21$, 67%). Six patients died at discharge. XeCT CBF studies were performed at a median of 62 hours after decompressive surgery. The mean global CBF after DC was 49.9 ± 21.3 ml/100gm/min. The mean cortical CBF under the craniectomy defect was 46.0 ± 21.7 ml/100gm/min. Patients who died had significantly lower post-craniectomy CBF under the craniectomy defect (30.1 ± 22.9 vs 50.6 ± 19.6 , $p=0.039$) as well as significantly lower CPP (52 ± 17.4 vs 75.3 ± 10.9 , $p=0.001$). These patients also had lower global CBF (36.7 ± 23.4 vs 53.7 ± 19.7 , $p=0.09$), lower PbtO₂ (6 ± 5.8 vs 24.5 ± 17.3 , $p=0.06$) and higher ICP (33 ± 16.8 vs 16.1 ± 6.4 , $p=0.06$), though these differences were not statistically significant.

Conclusion: Cerebral hypoperfusion after DC was associated with early mortality in TBI patients. These data emphasize the prognostic value of continued multimodal monitoring after decompressive craniectomy for TBI.

628. Potential of human nucleus pulposus like cells derived from human umbilical cord to treat degenerative disc disease

Mick J. Perez-Cruet, MD, FAANS; Naimisha Beeravolu, MS; Jared Brougham; Ifran Khan; Christina McKee; Rasul Chaudhry (Southfield, MI)

Introduction: Degenerative disc disease (DDD) is characterized by the loss of extracellular matrix (ECM) integrity and dehydration of the nucleus pulposus (NP) of intervertebral discs (IVDs). Currently, there is no biologic treatment to cure this debilitating ailment. Recently, stem cell based therapies have gained increasing attention to treat DDD. This study investigated the efficacy of mesenchymal nucleus pulposus (NP)-like cells (MNPCs) derived from human umbilical cord mesenchymal stem cells (UC-MSCs) to restore degenerated intervertebral discs using a rabbit model of disc degeneration.

Methods: UC-MSCs were induced to differentiate into MNPCs by using differentiation medium (DM) for two weeks and characterized for the expression of NP specific markers by polymerase chain reaction (PCR) and immunocytochemical analysis. An in vivo rabbit model of DDD was developed in which medium (sham) or PKH26-labeled MNPCs were injected. After eight weeks post-transplantation, biochemical, immunohistological, and molecular analyses of the harvested IVDs was performed.

Results: UC-MSCs differentiated into MNPCs in the DM and expressed NP specific markers SOX9, ACAN, COL2, FOXP1 and KRT19. The rabbit IVDs punctured by needle stab displayed NP disc degeneration (NPDD) as evident by the loss of structural and cellular integrity determined by H&E staining and was consistent with the in vivo MRI analysis. NPDD cellularity, glucose aminoglycan (GAG), and water content improved with MNPCs injection but not sham. MNPCs transplanted cells survived, integrated, and dispersed in the NP and transcribed NP specific genes, SOX9, ACAN, COL2, FOXP1, KRT19, PAX6, CA12 and COMP.

Conclusion: This study demonstrates the feasibility and efficacy of transplanted human MNPCs derived from human UC-MSCs to regenerate the NP. These findings should spur interest for clinical studies to treat DDD using MNPCs.

629. The Benefit of Radiosurgery for ARUBA-Eligible AVMs: A Practical Analysis Over an Appropriate Follow-Up Period

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Introduction: The ARUBA study has shown that patients receiving interventional therapy for the management of unruptured brain arteriovenous malformations (AVMs) have a higher risk of stroke and death with a mean follow-up time of 2.8 years. Given the latency period required for AVM obliteration after stereotactic radiosurgery (SRS), a study comparing intervention to observation cannot assess the benefit of SRS for unruptured AVMs if the follow-up interval is short.

Methods: The authors reviewed their institutional experience with ARUBA-eligible AVMs treated with SRS from 1987 to 2016. The primary outcomes were defined as stroke (ischemic or hemorrhagic) or death (AVM-related or AVM-unrelated). 233 patients with at least 3 years of follow-up in addition to any who experienced stroke or death during the latency period were included. Secondary outcomes measures included obliteration rates, patients with new seizure disorders and those with new focal deficits without stroke.

Results: During the mean 8.4 year follow-up interval after SRS, 32 (13%) had a stroke or died. Comparing the 10% stroke or death rate at a mean 2.8 year follow-up for untreated AVMs in ARUBA, the rate in our study was significantly lower than that anticipated at 8.4 years follow-up for an untreated cohort (13% vs 30%, $p = 0.0003$). The annualized rates of hemorrhage and stroke or death 3 years after SRS were 0.4% and 0.8% respectively. The overall obliteration rate was 72%; 2% of patients had new

seizure disorders, 2% had temporary new focal deficits without stroke, and 2% had permanent new focal deficits without stroke.

Conclusion: This study indicates that SRS for unruptured AVMs has a significantly lower rate of delayed stroke or death compared to the natural history cohort defined by the ARUBA study.

630. Vascular foramina of the odontoid process: Application to better understanding type II odontoid fractures

Fernando Alonso, MD; Jens Chapman; Rod Oskouian; R. Shane Tubbs (Cleveland, OH)

Introduction: The literature suggests that one reason why type II odontoid fractures are prone to non-union is due to the poor blood supply to its base. The aim of this study was to investigate the presence of vascular foramina to understand this potential relationship.

Methods: Forty specimens of the C2 vertebra (adult 35 and children 5) were studied using 10-x magnification. No specimen had evidence of prior trauma or congenital malformations. Random specimens underwent injection of larger foramina to verify their confluence with the internal aspect of the odontoid process.

Results: Vascular foramina are concentrated posteriorly and anteriorly at the base and neck of the odontoid process. However, the majority were found to have 1-3 large foramina between the medial most aspect of superior articular facet and base of the odontoid process. Vascular foramina ranged in size from 0.25 to 2.2 mm (mean 1.1 mm). Anteriorly, these vascular foramina were found to be primarily concentrated off the midline and inferior to a line connecting the superior most aspects of the left and right superior articular facets. On the posterior aspect, these foramina were concentrated inferior to the lowest edge of groove for transverse ligament. No grossly identifiable foramina were identified on the anterior facet of the dens or at the point of contact of the transverse ligament to this bony part.

Conclusion: A concentration gradient for vascular foramina exists on the odontoid process. These are greatest at its base and decrease toward its apex. The anterior facet and region of contact with the transverse ligament are devoid of grossly visible vascular foramina. Injections into the foramina fill the entire odontoid process internally. Reports that type II odontoid fractures occur most frequently and heal poorly due to a lack of blood supply of its neck are not supported by our findings.

631. A Distinct dorsolateral pre-motor essential language site

Nitin Tandon, MD, FAANS; Cihan Kadipasaoglu, PhD; Matthew Rollo, BS; Thomas Pieters (Houston, TX)

Introduction: Prior studies of population language mapping have some limitations due to the era in which they occurred. Inter-subject data co-registration was crude - achieved using measurements from the tip of the frontal and temporal lobes, not accounting for variations in individual anatomy. Additionally, visual-object-naming commonly used in these studies probes only a few aspects of language function. Lastly, the intra-operative environment generally precludes mapping basal temporal and medial frontal regions engaged in language processes.

Methods: We prospectively collected data from 100 patients undergoing intra-operative ($n=64$) or extra-operative ($n=36$) language mapping using auditory cued naming and repetition, visual naming, and simple overlearned articulation. All patients underwent formal language testing prior to and 6 weeks post-operatively. Stimulation data were represented on subject-specific brain surfaces using a depolarization model to compute a point probability for the presence of linguistic function. A surface-based co-registration algorithm was implemented to co-localize positive and negative language sites across subjects and generate topologically accurate population density map for this large cohort.

Results: 1150 positive and 2133 negative sites were localized across subjects. ($p<0.001$) Distinct regions of essential language were identified in canonical locations: Broca's area, superior temporal gyrus, posterior mid-

temporal gyrus, and basal temporal language area. In addition a prominent locus of critical language was identified in the posterior medial frontal gyrus (x,y,z: 33,-15, 54.5), a dorsal premotor site previously conjectured to be involved in articulation. All 10 patients in whom resection included a part of this site, had significant post-op speech impairment.

Conclusion: We report here a significant evolution in the creation of population-based maps of cognitive functions by cortical stimulation mapping that could be used in a predictive model for identifying the probability of the presence of language function. This approach revealed a distinct, new essential region that is involved in human language production.

632. Discovery of A Novel Integrin/Tyrosine Kinase Complex That Drives Brain Metastases

Stryker Neuro-Oncology Award

Arman Jahangiri; Maxim Sidorov; Ankush Chandra; Patrick Flanigan; Alan Nguyen; William Weiss, MD, PhD; Manish Aghi, MD, PhD (San Francisco, CA)

Introduction: Brain metastases are the most common brain tumors and, as such, represent a major public health problem. Past studies have suggested for $\beta 1$ -integrin and c-Met to have a significant role, but the mechanisms remain to be elucidated. We hypothesized that a c-Met/ $\beta 1$ integrin complex drives breast cancer cells to invade their local parenchyma and metastasize to the brain and other organs.

Methods: We utilized immunoprecipitation, Proximity ligation assays (PLAs), cell-culture biologic assays, general cloning and immunohistochemistry.

Results: MDA231 breast cancer cells were injected in mammary fat pads of athymic mice with 20% developing metastasis while the remainder reached endpoint from primary tumor expansion. Comparison of primary tumors in non-metastatic vs. metastatic xenografts displayed a 10-fold increase in c-Met/ $\beta 1$ complexes. Furthermore, metastatic tumors from brain in addition to other organs (colon, stomach) demonstrated an 18-fold higher complex level compared to the primary tumor. Immunofluorescence-imaging of hybridized complexes at metastatic organs showed clustering of the complexes at the tumor edge, invading into the target organ parenchyma. Inducing the complex through iDimerize in MDA231 cells, in which we tagged $\beta 1$ integrin and c-Met with complementary proteins, binding upon heterodimer addition, increased migration, invasion, with a markedly reduced shape factor ($P < 0.05$). Comparing complex levels in MDA231, MDA-MB-231-BR brain-seeking cells selected for brain metastatic capacity in vivo, showed that MDA-MB-231-BR cells markedly upregulate their c-Met/ $\beta 1$ complex levels similar to the artificial upregulation witnessed in MDA231 iDimerize cells as compared to baseline MDA231. Sequential immunoprecipitation and PyMOL crystallography analysis revealed that c-Met bound $\beta 1$ in the $\alpha 5$ -integrin binding site, displacing $\alpha 5$ -integrin, and that c-Met/ $\beta 1$ -integrin had greater affinity for fibronectin than $\alpha 5\beta 1$.

Conclusion: $\beta 1$ integrin forms a complex with c-Met in metastases invading brain tissue. Cancers co-opt these two natural receptors to form a complex with greater affinity for the natural integrin ligand fibronectin, driving metastases through allosteric cross-activation and altered morphology.

633. Comparison of the Long Term Results of One-Level vs Two-level Cervical Total Disc Replacement vs Anterior Cervical Discectomy and Fusion

Jeffrey Ross McConnell; Jeffrey McConnell, MD; Todd Lanman, MD; Matthew Gornet, MD; J Kenneth Burkus, MD; Randall Dryer, MD; Scott Hodges, DO (Allentown, PA)

Introduction: Cervical total disc replacement (TDR) is as safe and effective as ACDF for treating symptomatic cervical disc disease (SCDD) at one and two levels. The objective of this study was to compare the relation between the number of treated levels and safety and effectiveness at 7-year follow-up.

Methods: One and 2-level FDA IDE clinical trials of the Prestige LP cervical artificial disc were conducted treating a combined 942 patients.

A total of 545 and 397 patients were studied in the 1-level and 2-level trials, respectively; TDR (n= 280, 209), ACDF (n=265, 188). Overall clinical success was compared between 1-level and 2-level TDR and ACDF. Comparisons were done across studies, and a propensity score method was used to adjust for potential confounding effects.

Results: There was no significant difference in overall success between 1 vs 2-level TDR (74.9% vs 78.6% $p=0.312$) or ACDF (63.2% vs 62.7% $p=0.774$). NDI success for 1 vs 2 level TDR (86.1% vs 87.0% $p=0.696$) or ACDF (80.1% vs 75.6 % $p=0.953$) and neurological success for 1 vs 2-level TDR (92.8% vs 91.6% $p=0.987$) or ACDF (79.7% vs 82.1% $p=0.487$) showed no significant differences. Implant/surgical related grade 3 or 4 adverse event rates were 6.1% and 3.2% for 1vs 2-level TDR and 5.6% and 7.2% for 1 vs 2-level ACDF. Subsequent surgeries at the index level were 6.4% and 4.2% for 1 vs 2-level TDR, and 10.9% and 14.7% for 1 vs 2-level ACDF. Adjacent level surgery rates were 9.6% and 6.5% for 1 vs 2-level TDR and 8.3% and 12.5% for 1 vs 2-level ACDF.

Conclusion: One and 2-level TDR appear to be equally safe and effective in the treatment of SCDD at 7-years. Two-level ACDF was equally effective as 1-level, but 2-level ACDF had higher re-operation rates at both the index and adjacent levels.

634. Combinatorial Surgical and Neuroprotective Therapy for Cervical Spondylotic Myelopathy Results in Improved Neurological Function: from Preclinical Proof of Concept to a Phase III Randomized Controlled Trial

Michael G. Fehlings, MD, PhD, FAANS, FRCS; Branko Kopjar; Spyridon Karadimas (Toronto, Canada)

Introduction: Surgical decompression is an effective treatment for cervical spondylotic myelopathy (CSM). However, a number of patients continue to experience substantial neurological impairment post surgery. Riluzole has neuroprotective effects in injuries of the central nervous system. To determine the efficacy of riluzole for promoting neurological improvement in CSM following decompression, we performed a pre-clinical proof of concept experiment and then we translated our work and established a Phase III multi-center randomized controlled clinical trial (CSM-Protect).

Methods: Surgical decompression was performed in a rat CSM model and riluzole, or control, was administered. Spinal cord blood flow (SCBF) was evaluated in all CSM rats, in vivo, before and after decompression using FAIR MRI. The long-term outcomes of decompression with or without riluzole treatment determined using neurobehavioural and neuro-anatomical assessments. Our multi-center double-blind randomized CSM-Protect trial includes a total of 300 CSM patients undergoing decompression surgery and randomized 1:1 to receive riluzole (2x50mg daily for 14 days before and 28 days post surgery) or placebo treatment. MJOA score will determine the effectiveness of the combinatorial treatment at 6 months following surgery. Statistical analysis will be performed as a sequential adaptive trial with interim analysis.

Results: Rats receiving combinatorial treatment displayed long-term significant neurological improvements associated with preservation of motor neurons and corticospinal tracts compared to rats treated with decompression alone. Riluzole also dramatically reduced the extent of ischemia-reperfusion injury post surgical decompression in our animal model. At present, 274 subjects have been enrolled into the CSM-Protect trial. A planned interim analysis using this sample has commenced.

Conclusion: The proposed combinatorial therapy promotes neurological recovery in CSM rats. Confirmation of this proof of concept has been translated from bench to the bedside and we are currently running the CSM-Protect trial to determine the efficacy of this combinatorial treatment option for use in CSM patients.

635. Characterization of synchronization between globus pallidus neurons and motor cortex in Parkinson's disease

Doris Du Wang, MD; Nicole Swann, PhD; Coralie de Hemptinne, PhD; Philip Starr, MD, PhD (San Francisco, CA)

Introduction: Excessive oscillatory neuronal synchronization throughout the basal ganglia-thalamocortical motor loop is a hallmark of the Parkinsonian state. This may manifest as spike-spike correlations, coherence between field potentials, or spike-field interactions between structures in the circuit. Globus pallidus occupies a central role in basal ganglia processing, but neither internal (GPi) nor external (GPe) globus pallidus is monosynaptically connected to motor cortex (M1). Understanding patterns of M1-pallidal synchronization will provide insight into the possible different roles of GPi and GPe stimulation in ameliorating the excessive neuronal synchronization in PD.

Methods: Using subdural electrodes and high resolution electrocorticography (ECoG) contacts temporarily placed over motor cortex during DBS implantation and microelectrode recordings, we evaluate the strength and topography of synchronization between pallidal neurons and cortical ECoG potentials in 16 PD patients.

Results: Recording from 59 GPe and 42 GPi cells with cortical ECoG field potentials demonstrated that 17% of GPe and 12% of GPi neurons showed significant interactions with M1 recording sites approximately 25 mm from midline. For those pairs with significant interactions, peak of the spike-triggered average potentials occurred within 100ms prior to spike time. GPe neurons showed maximum coherence with M1 in the beta (13-30Hz) frequency range while that of GPi-M1 was in the alpha (8-12Hz) range.

Conclusion: Topography of significant M1-pallidal interactions underscores the greater influence of basal ganglia on proximal musculature compared to hand function. The observation that GPe stimulation is more prokinetic than GPi stimulation may be explained by the finding that GPe is more synchronized to the cortex in beta frequencies than GPi, as disruption of beta oscillation is important in ameliorating akinesia.

636. Operative vs Non-operative Management of Civilian Gunshot Wounds to the Spine

Peter T McCunniff; James Ramey; Meredith Scott; Mary Roach, PhD; Heather Vallier, MD; Timothy Moore, MD; Michael Kelly (Cleveland, OH)

Introduction: Surgery for patients with spinal cord injury from gunshot wounds (GSCI) remains controversial. Some studies suggest improvement in functional outcomes with surgery for GSCI, particularly for those patients with incomplete GSCI. Few recent studies provide standardized follow-up and detailed functional outcomes.

Methods: The trauma and rehabilitation registries at an urban level 1 trauma center were queried for all patients who sustained GSCI between 2006 and 2015. GSCI patients were divided into surgical (SX) and non surgical (NSX) groups. Neurological function was measured according to the ASIA impairment scale (AIS) and defined as either complete or incomplete injuries. Outcomes were then analyzed separately for complete and incomplete GSCI groups during hospitalization and acute rehabilitation.

Results: A total of 104 GSCI patients were identified from the trauma registry; 67 with complete GSCI and 37 with incomplete GSCI. For complete GSCI, 16 (24%) patients underwent surgery. Baseline admissions characteristics were similar between SX and NSX groups except for a higher median injury severity score (ISS) in the NSX group (34 vs. 27; $p=0.02$). For complete GSCI, total length of stay (LOS) was significantly longer in the SX group (52 vs. 42 days; $p=0.04$) and no difference was observed in overall FIM scores at discharge from rehabilitation (58 vs. 54; $p=0.7$). For incomplete GSCI, 7 (19%) patients underwent surgery. All baseline admission characteristics were similar between SX and NSX groups. For incomplete GSCI, rehabilitation LOS was longer (35 vs. 21; $p=0.02$) and a trend towards longer total LOS was observed in the SX group (40 vs. 32;

$p=0.07$). No difference was observed in overall FIM scores at discharge from rehabilitation (61 vs. 62; $p=0.9$).

Conclusion: Surgery for patients with GSCI is associated with increased LOS and is not associated with improved FIM scores for patients with either complete or incomplete spinal cord injuries.

637. Detection of wtEGFR Amplification and EGFRvIII Mutation in CSF-Derived Extracellular Vesicles of High-Grade Glioma Patients

Preuss Award

Javier Figueroa, MD; Johan Skog, PhD; Johnny Akers, PhD; Hongying Li, PhD; Ricardo Komotar, MD; Ennio Chiocca, MD, PhD; Xandra Breakefield, PhD; Clark Chen, MD, PhD; Karen Messer, PhD; Fred Hochberg, MD; Bob Carter, MD, PhD (San Diego, CA)

Introduction: RNA within extracellular vesicles (EVs) have potential as diagnostic biomarkers for patients with cancer, and are identified in a variety of biofluids. High-grade gliomas (HGGs) release EVs containing RNA into cerebrospinal fluid (CSF). Here we describe a multi-institutional study of RNA extracted from CSF-derived EVs of HGG patients, for the presence of tumor-associated amplifications and mutations in the epidermal growth factor receptor (EGFR).

Methods: CSF and matching tumor tissue were obtained from patients undergoing resection of HGGs. We determined wild-type EGFR (wtEGFR) DNA copy number amplification, as well as wtEGFR and EGFRvIII RNA expression, in tumor samples. We also characterized wtEGFR and EGFRvIII RNA expression in CSF-derived EVs.

Results: EGFRvIII positive tumors had significantly greater wtEGFR DNA amplification ($p=0.02$) and RNA expression ($p=0.002$), and EGFRvIII positive CSF-derived EVs had significantly more wtEGFR RNA expression ($p=0.001$). EGFRvIII was detected in CSF-derived EVs for 15 of the 25 EGFRvIII tissue-positive HGG patients. Conversely, only one of the 56 EGFRvIII tissue-negative patients had the EGFRvIII mutation detected in their CSF-derived EVs. These results yield a sensitivity of 60% and a specificity of 98% for the utility of CSF-derived EVs to detect an EGFRvIII-positive HGG.

Conclusions: Our results demonstrate CSF-derived EVs contain RNA signatures reflective of the underlying molecular genetic status of HGGs in terms of wtEGFR expression and EGFRvIII status. The high specificity of the CSF-derived EV diagnostic test gives us an accurate determination of positive EGFRvIII tumor status, and is essentially a less-invasive 'liquid biopsy' that can direct mutation-specific therapies for HGGs.

638. Lumbar Spine Surgical Site Infection Prevention with a Systematized Peri-operative Protocol: A Propensity Matched Multidepartmental Multiyear Retrospective Cohort Study

Vijay Yanamadala, MD; Thomas Cha; Brian Nahed; Jean-Valery Coumans; John Shin (Seattle, WA)

Introduction: Surgical site infection (SSI) occurs after approximately 4% of degenerative lumbar spine cases and higher for complex spine surgery, including adult spinal deformity. It remains imperative to develop methods to reduce the incidence of SSI.

Methods: After institutional review board approval, we retrospectively examined 1,089 consecutive lumbar spine surgeries performed between August 1, 2014 and August 1, 2016. Surgeons elected whether or not to use a peri-operative infection control protocol which included: (1) three days of chlorhexidine rinse prior to surgery; (2) chlorhexidine pre-prep scrub of the surgical site; (3) chlorhexidine prep with a 5-minute mandatory wait time; (4) intrawound vancomycin powder; and (5) iodine-impregnated antimicrobial film bandage. Nearest-neighbor propensity matching was performed according to demographic (age, sex, body mass index, co-morbidities, ASA grade, active smoking status) and surgical (operative time, estimated blood loss, number of levels fused) parameters. Statistical significance was $p<0.05$ with two-tailed t-test.

Results: 592 patients underwent surgery with this protocol, while 443 patients underwent only chlorhexidine prep. 446 patients (257 with protocol; 189 without) underwent lumbar decompressions. 589 patients (448 with protocol; 141 without) underwent lumbar fusion, with 54 patients (36 with protocol; 18 without) undergoing lumbar fusion involving six or more levels. Overall SSI rate was 1.1% (0.3%, decompression; 1.6%, fusion; 3.2%, fusion = six levels). SSI rate with the protocol was 0.9% (0.3%, decompression; 1.1%, fusion; 2.1%, fusion = six levels) compared to 1.3% without the protocol (0.3%, decompression; 1.9%, fusion; 4.1%, fusion = six levels). Multivariate regression analysis after propensity matching revealed a statistically significant difference in SSI rates for patients undergoing fusion involving six or more levels ($p < .05$), with a trend towards significance for all lumbar fusions.

Conclusion: A rigorous SSI prevention protocol can reduce infection rates, particularly in complex cases. Multi-institutional assessment will be essential to further corroborate its efficacy.

639. Minimally expensive Neurosurgery. State of the art at the public hospital of a developing country

AANS International Travel Scholarship

Edgar M. Carrasco, MD, IFAANS (Santa Cruz de la Sierra, Bolivia)

Introduction: Around 60% of the population in Bolivia does not have any health insurance and they are treated in public hospitals where all supplies and drugs for surgery are acquired by themselves. The national minimum salary is \$ 208, and the cost of a standard craniotomy is approximately \$ 1,423. Because of these high costs many patients with potentially curable diseases decline surgery. We introduce the concept of minimally expensive neurosurgery as an initiative to reduce the cost of surgery using conventional techniques, homemade or improvised alternative materials in the operating room in order to maintain the state of the art.

Methods: More than 400 patients low-income and non uninsured treated at a public hospital since March 2011. We perform standard craniotomies using Gigli saw, cranioplasty with non-absorbable sutures, burr holes reconstruction with bone dust, alternative handmade surgical patties and polyethylene bags to drape the surgical field and the surgical microscope, low cost virtual craniotomy and clipping and computerized neurosurgical planning were developed. Cost of a surgery with these resources and the rate of postsurgical infections are compared.

Results: We reduce the waiting time for surgery 1 week to 3-4 days if programmed and less than 12 hours in case of emergency surgeries. The rate of infection at the surgical site was 3.1%. We reduced the cost of a standard craniotomy from \$ 1530 to \$ 306 with minimally expensive neurosurgery initiative.

Conclusion: It is possible to reduce the costs of a standard craniotomy up to 80% making the minimally expensive neurosurgery initiative an easy, useful, and reproducible alternative to perform a neurological surgery in current standards with the use of minimal supplies.

640. A Comparison of the Nationwide Inpatient Sample and the MarketScan Databases for Trends and Outcomes of Spine Surgery in Octogenarians

Doniel Gabriel Drazin, MD; Siddharth Bhargava; Carlito Lagman; Joe Dettori; Miriam Nuno; Beatrice Ugiliweneza; Maxwell Boakye (Seattle, WA)

Introduction: Despite an increasing use of national databases to conduct spine research, questions regarding the validity and consistency of these studies remain. This study tested for similarity in reported measures between two national databases commonly used.

Methods: A retrospective cohort study of patients undergoing spine surgery procedures in Thomson Reuters MarketScan database (2000-2012) and National Inpatient Sample (NIS) database (1998-2012) using inpatient CPT coding was performed. Patient baseline characteristics included: age, gender,

race, admission type. Outcome measures included: mortality risk, non-routine discharge, length of stay (LOS), in-hospital and 30-day complication risks. Multivariate analysis assessed the association of baseline and patient characteristics with complications, 30-day complications and mortality.

Results: We analyzed 13,925 and 224,352 patients over age 80 years (mean 83.0) from MarketScan and NIS databases, respectively. Patients in the MarketScan database tended to have fewer comorbidities, receive fusion more often, and have less Medicaid insurance than those in the NIS database. The risk of sustaining one or more complications was lower in the MarketScan database compared with NIS, 116 versus 169 per 1,000. Mortality was also lower in the MarketScan database, 3.3 per 1,000 (95% CI 3.3, 3.1 to 3.5) versus 4.0 per 1,000 (95% CI 3.8 to 4.3). Older age, female and the presence of comorbidity increased the odds of complications in both databases. Females and decompression (versus fusion) was associated with a decreased odds consistently between databases.

Conclusion: As database studies become more prevalent in spine surgery, caution should be taken by authors and reviewers. This study shows that two commonly used databases can identify demographically similar patients undergoing common spine procedures; however, the databases document markedly different rates of comorbidities and inpatient adverse events. Overall, it appears that the patients in the NIS have more complications and comorbidities, likely a sicker population than the MarketScan database.

641. Connectivity Disturbances of the Brainstem Ascending Reticular Activating System in Epilepsy and Implications for Surgical Therapy

Dario J. Englot, MD, PhD; Peter Konrad, MD, PhD; Monica Jacobs, PhD; John Gore, PhD; Bassel Abou-Khalil; Victoria Morgan, PhD (Nashville, TN)

Introduction: Seizures in temporal lobe epilepsy (TLE) disturb brain network physiology and lead to brain connectivity problems. In rats, deep brain stimulation of the brainstem ascending reticular activating system (ARAS) counteracts some of the deleterious effects of seizures, making the ARAS a potential neuromodulation target in human epilepsy. However, no prior human studies of ARAS functional connectivity have previously been reported in epilepsy.

Methods: We used resting-state functional MRI (fMRI) recordings in 27 TLE patients and 38 matched controls to measure functional connectivity (partial correlation) between eight brainstem ARAS structures with 105 cortical and subcortical regions throughout the brain. ARAS structures included: cuneiform/subcuneiform nucleus, dorsal raphe, locus coeruleus, median raphe, parabrachial complex, pontine nucleus oralis, pendunculo-pontine nucleus, and ventral tegmental area.

Results: Across all subjects, regions showing the most positive connectivity to ARAS structures included thalamus, limbic system, and nucleus accumbens/basal forebrain, consistent with prior studies of ARAS projections. Overall ARAS connectivity was significantly lower in TLE patients than controls ($p < 0.05$, t-test), with largest connectivity decreases noted in insular, lateral frontal, posterior temporal, and opercular cortex ipsilateral to the epileptogenic zone. Diminished ARAS connectivity in these regions was related to increased frequency of consciousness-impairing seizures ($p < 0.01$, Pearson correlation), suggesting an association with severity of illness. Furthermore, reductions in ARAS connectivity were significantly associated with impairments in verbal IQ, attention, executive function, language, and visuospatial memory on neuropsychological evaluation ($p < 0.05$, Spearman's rho or Kendall's tau-b).

Conclusion: Functional connectivity of the ARAS is disturbed in TLE, with a quantitative relationship to severity of illness, and may help explain profound neurocognitive problems suffered by these patients. In patients with persistent seizures despite best therapy, ARAS structures may be investigated as potential neuromodulation targets to help prevent the adverse network effects of seizures and their long-term neurocognitive sequelae.

642. Analysis of High-Frequency PbtO₂ Measures: Insights into the Treatment Threshold from "Big Data"

Ryan S. Hirschi; Gregory Hawryluk, MD, PhD, FRCSC; Lara Zimmermann, MD; Rajiv Saigal, MD, PhD; Quan Ding, PhD; Geoffrey Manley (Salt Lake City, UT)

Introduction: Brain tissue hypoxia is a major contributor to secondary brain injury. Current guidelines for the management of severe traumatic brain injury (TBI) recommend maintaining PbtO₂ > 15-20 mmHg, however uncertainty persists as to the optimal treatment threshold.

Methods: PbtO₂ measures were automatically collected every minute from consecutive patients admitted to San Francisco General Hospital over a 6-year period. We analyzed mean PbtO₂ values and the proportion of PbtO₂ values below 75 thresholds from 0 mmHg to 75 mmHg in 1 mmHg increments. Patients were analyzed according to clinical outcome (Glasgow Outcome Scale) over various epochs up to 30 days from time of admission. We analyzed all patients undergoing PbtO₂ monitoring and those specifically recovering from TBI.

Results: A total of 1,737,027 PbtO₂ values were recorded from 231 patients, including 190 with TBI, in the first 30 days following ICU admission. A high proportion of PbtO₂ measures were below treatment threshold irrespective of examined epoch. Time spent below treatment thresholds was more strongly associated with outcome than mean PbtO₂. A treatment threshold of 21 mmHg most robustly distinguished patients by outcome ($p=0.06$, days 3-5, all patients).

Conclusion: Although this study does not provide evidence for a causal relationship, it substantially informs the nature of the relationship between PbtO₂ values and neurological outcome. Moreover, our study supports the concept of PbtO₂ thresholds in TBI recovery. Our results suggest a minimum PbtO₂ treatment threshold of 21 mmHg may be considered and further examined and that values up to 45 mmHg may be beneficial.

643. In Situ Tumor Vaccination Against Melanoma Prevents Intracranial Growth of Melanoma Cells

John S. Kuo, MD PhD FACS; Paul Clark, PhD; Zachary Morris, MD, PhD; Emily Guy; Stephen Gilles, PhD; Hans Loibner, PhD; Alan Korman, PhD; Paul Sondel, MD, PhD (Madison, WI)

Introduction: Over 60% of advanced melanoma patients develop brain metastases with poor prognosis. Recent successful melanoma immunotherapy approaches include induction of memory T-cells against mutated tumor proteins for a protective vaccine. We tested this strategy to prevent intracranial melanoma growth.

Methods: B78-D14 (GD2+) melanoma cells (2x10⁶) were subcutaneously engrafted in C57BL/6 female mice (age 6-8 wks). After tumor growth was confirmed, immunotherapy including immunocytokine hu14.18-IL2 (anti-GD2-IL2 antibody fusion protein), radiation (single dose, 12 Gy), and immune modulation with anti-CTLA-4 (IgG2a) was administered to eliminate flank tumor and create an in situ tumor vaccine (Morris et al, 2016, PMID: 27197149). Tumor immunity was verified by the absence of tumor growth (4-6 weeks post-treatment) via peripheral re-challenge with B78-D14 cells. Then B78-D14 melanoma cells (2x10⁵) were intracranially implanted into the right striatum of treated mice (n=8) and control naïve mice (n=7). All mice were monitored up to 50 days for survival curves. Animals were sacrificed when moribund for brain histology, CD4 and CD8 immunohistochemistry.

Results: In situ vaccinated mice (7/8; 88%) survived intracranial tumor implantation and remained asymptomatic up to 50 days, whereas all naïve mice succumbed to CNS melanomas (mean survival 30±1.0 days; $p=0.001$). H&E histology verified large CNS melanomas in all naïve mice, and showed only inflammatory response in pre-treated mice (no visible melanoma cells). Abundant CD4+ and CD8+ T-cells were identified in the brain implantation region of pre-treated mice, but not found within tumors of naïve mice. In the single pre-treated mouse with detectable intracra-

nial tumor growth, the additional 20 days survival suggests delayed tumor growth compared to naïve mice.

Conclusion: We show that in situ vaccination results in robust mobilization of systemic memory T-cells against brain implanted melanoma cells and significantly improved survival. Therefore, in situ tumor vaccinations developed against primary melanomas could potentially prevent or treat brain melanoma metastases.

644. Treatment of Unstable Thoracolumbar Junction Fractures: Short-Segment Pedicle Fixation with Inclusion of the Fracture Level versus Long-Segment Instrumentation

Maurizio Iacoangeli, MD, IFAANS; Mauro Dobran; Davide Nasi; Lucia di Somma; Alessandro Di Rienzo; Maurizio Gladi; Roberta Benigni; Denise Brunozzi; Alessandra Marini; Massimo Scerrati (Ancona, Italy)

Introduction: The management of thoracolumbar burst fractures frequently involves posterior pedicle screw fixation. The length of instrumentation is still controversial. Few biomechanical studies exist to compare the advantage of including or not the pedicles of fractured vertebra in the posterior construct. The aim of this study was to compare the outcome of the short-segment fixation with inclusion of the fracture level (SSFIFL) versus the traditional long-segment fixation (LSF) for the treatment of unstable thoracolumbar junction fractures.

Methods: From December 2009 to February 2014, 60 patients with unstable thoracolumbar junction fractures (T11-L2) were divided into two groups. Group 1 included 30 patients treated by SSFIFL (six-screw construct including the fracture level). Group 2 was the control group and included 30 patients treated by LSF (eight-screw construct excluding the fracture level). Local kyphosis angle (LKA), anterior body height (ABH), posterior body height (PBH), ABH/PBH ratio of fractured vertebra, and Asia Scale were evaluated.

Results: The two groups were similar. Reduction of post-traumatic kyphosis (assessed with LKA) and restoration of fracture-induced wedge shape of the vertebral body (assessed with ABH, PBH, and ABH/PBH ratio) at post-operative period were not significantly different between group 1 and group 2 ($p = 0.234$; $p = 0.754$). There was no significant difference in term of correction loss at the last follow-up too (LKA was $15.97^\circ \pm 5.62^\circ$ for SSFIFL and $17.76^\circ \pm 11.22^\circ$ for LSF [$p = 0.427$]). Neurological outcome was similar in both groups.

Conclusion: Inclusion of fracture level in a short-segment fixation for a thoracolumbar junction fractures results in a kyphosis correction and in a maintenance of the sagittal alignment similar to a long-segment instrumentation allowing to save two or more segments of vertebral motion.

645. Enhanced Preoperative Prediction of Discharge Disposition for Neurosurgical Patients

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Introduction: Bundled care payments are increasingly being explored for neurosurgical interventions. In this setting, sub-acute nursing facility is less desirable from a cost perspective than discharge to home, underscoring the need for better preoperative prediction of post-operative disposition to allow care providers to selectively increase length of stay (LOS) where a home discharge is possible and reduce LOS where discharge to skilled nursing facility (SNF) or acute rehabilitation facility (ARF) is inevitable. Our objective is to assess the capability of the Risk Assessment and Prediction Tool (RAPT) to determine expected disposition prior to the index admission for neurosurgical intervention.

Methods: Between June 2016 and October 2016, 735 consecutive neurosurgical patients were prospectively enrolled. RAPT Scores and discharge outcomes were assessed. The three possible destinations after discharge were home, ARF, or SNF, with anticipated correlation to a RAPT

Score of 9-12, 6-9, and 1-6, respectively. Non-parametric regression analysis was utilized to determine the accuracy of the RAPT Score to predict the patient's ultimate discharge disposition.

Results: RAPT Score significantly predicted discharge disposition ($p < 0.0001$). Patients with a RAPT score < 6 went to SNF or Rehab 76% of the time while scores of 6-9 and greater than 9 went to SNF or rehab 20% and 8% of the time respectively. RAPT was very successful in correctly rejecting those patients who did not go to SNF (98% specificity).

Conclusion: The RAPT Score was able to accurately predict discharge disposition for neurosurgical patients, who scored a 9 or higher, resulting in a discharge to home. Low scores (< 6) were commonly associated with post-acute care inpatient needs. Middle range patients (6-9) may present a targeted opportunity to increase LOS in order to decrease the potential need for post-acute care admission. In conclusion, there are preoperative parameters that can serve to predict postoperative post-acute care disposition.

646. Connectivity-based parcellation of the anterior limb of the internal capsule: targeting applications in psychiatric neurosurgery

Pranav Nanda; Yagna Pathak; Garrett Banks; Tony Wang; Simon Cheng; Sameer Sheth (New York, NY)

Introduction: The anterior limb of the internal capsule (ALIC) is a promising target for neuromodulation in OCD and other psychiatric disorders. Its fiber organization remains poorly described in humans, despite being important for optimizing neuromodulatory targeting. We sought to subdivide the ALIC based on frontothalamic connectivity using a large MRI dataset.

Methods: Using a diffusion atlas from 842 Human Connectome Project controls, thalamocortical fibers were generated by deterministic tractography with thalamus as seed, ALIC as waypoint, and frontal Brodmann areas as independent terminating regions, normalizing for Brodmann area volumes. Each ALIC voxel was classified by its Brodmann area with maximum normalized tract density. We applied this analysis to understand corticothalamic effects of ventral radiosurgical capsulotomy using an example postop MRI of a patient who had undergone this procedure at our institution for severe, refractory OCD.

Results: Thalamocortical fibers through the ALIC were found for Brodmann areas 6, 8, 9, 10, 46, 47, and 11 and were organized in that order along a posterior-superior to anterior-inferior axis. Of the patient's 232mm³ lesion, 57% of the lesion voxels within the ALIC overlapped with thalamocortical fibers, of which all were maximally connected to Brodmann area 11 (orbitofrontal cortex).

Conclusion: Using a large human imaging database, we demonstrate the corticotopic organization of thalamocortical fibers within the ALIC. The superior-inferior pattern of fibers follows the dorsal-ventral organization of cortex, comparable to results from tract-tracing studies in monkeys. These results highlight the importance of modulation of several cortical areas, especially orbitofrontal cortex, by procedures such as ventral capsulotomy and DBS.

647. The Utility of Preoperative Laboratory Values in Patients Undergoing Craniotomy for Subdural Hematoma

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Introduction: Preoperative labs cost in excess of 2 billion dollars annually and several studies have shown that abnormal values have little impact on perioperative decision making. Patients presenting with subdural hematoma (SDH) frequently undergo a panel of laboratory tests. The purpose of this study was to explore the relationship between abnormal preoperative values and multiple outcome metrics in patients undergoing craniotomy for SDH evacuation.

Methods: The 2008-2014 National Surgical Quality Improvement (NSQIP) database was used to identify all patients that underwent a craniotomy for treatment of subdural hematoma. Twelve preoperative laboratory values were collected for each patient: sodium, creatinine, bilirubin, white

blood cell count (WBC), partial thromboplastin time (PTT), and others. Outcomes of interest included death, major complications (Clavien IV), and prolonged length of stay (LOS). A binary logistic regression model was constructed for each outcome, incorporating the 12 labs, as well as demographics, preoperative comorbidities, bleeding disorders, and perioperative factors including operative time, body mass index (BMI), and American Society of Anesthesiologists (ASA) score. The c-statistic was computed to assess the predictive capacity of the models.

Results: A total of 2997 patients met inclusion criteria. Of these, 549 (18.3%) died within 30 days of surgery. When controlling for patient demographics, comorbidities, and operative variables, no laboratory values were significantly associated with mortality. Abnormal preoperative PTT was an independent predictor of major complications (OR=1.57, $P=0.047$), while WBC was significantly associated with prolonged LOS (OR=1.79, $P=0.013$). The c-statistic values for the models were 0.803, 0.780, and 0.746, respectively.

Conclusion: Abnormal coagulation labs were significantly associated with major complications. However, 10/12 tests, including sodium, were not associated with adverse outcomes. All neurosurgical patients need preoperative sodium testing, but these data suggest that other labs may not be as valuable. Further studies exploring the utility of specific tests are needed for these patients.

648. Nanoclinic in the Brain. Nanoconjugates for MRI Virtual Biopsy and Treatment of Brain Metastatic Tumors

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Introduction: Differential diagnosis of brain magnetic resonance imaging (MRI) enhancement(s) remains difficult without invasive biopsies. Such MRI enhancement(s) can result from metastasis of primary tumors, radiation necrosis, infections, or a new primary brain tumor. Neurological symptoms are often the same on initial presentation. For precise noninvasive MRI diagnostics, a new class of nanoconjugates, nanoimaging agents (NIAs) and tumor-specific nanodrugs, based on a poly(β -L-malic acid) biodegradable polymer was developed.

Methods: We synthesized nanoconjugates carrying MRI contrast agent gadolinium-DOTA with novel 1-3-7 PEG-Star-Gd-DOTA⁺ molecules for enhanced MRI specific signal and antibodies recognizing tumor-specific markers and crossing blood brain barrier (BBB). Nanoconjugates were administered intravenously in a newly developed double brain tumor xenogeneic mouse models bearing human EGFR/EGFRvIII- and HER2-positive tumors. After treatment tumors were evaluated by immunohistochemistry and western blot analysis.

Results: HER2- and EGFR-expressing brain tumors were differentiated by nanoMRI-targeted agents. After nano-MRI diagnosis, breast and lung cancer brain metastases were successfully treated with tumor-targeted nanoconjugates carrying antisense molecular inhibitors of EGFR/EGFRvIII or HER2. These inhibitors were delivered to the tumor cell cytoplasm while sparing healthy brain tissue. The treatment resulted in significant increase in animal survival for 66% lung, 75% for HER2+ breast, and 107% for triple negative breast cancer brain metastases. Inhibition of important tumor markers associated with reduced expression of key proliferation and stem cell markers in treated tumors.

Conclusion: We achieved precise delivery of imaging agents and specific mRNA suppressors for efficient tumor treatment. They efficiently blocked the synthesis of new HER2 or EGFR/EGFRvIII, and suppressed the activation of downstream PI3K/Akt signaling. This technology for enhanced MRI specific signal shows promise for differential MRI diagnosis when brain biopsies are difficult to perform and demonstrate a novel treatment of brain metastases and other pathologies. Support: NIH grants U01 CA151815, R01 CA136841, R01 CA188743, R01 CA209921

649. Comparison of 1 vs. 2 year Oswestry Disability Index Outcomes in Lumbar Spine Surgery from a Prospective Registry

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Introduction: Prospective longitudinal patient reported outcomes (PROs) registries provide a means to accurately assess outcomes and determine the relative effectiveness of various spine treatments. Obtaining long-term PROs can be costly and challenging. To determine if 1-year PROs can accurately assess effective spine care for patients undergoing surgery for degenerative lumbar spine disease.

Methods: Patients enrolled into a prospective registry who underwent lumbar spine surgery were included for analysis. Baseline, 1-year, and 2-year Oswestry Disability Index (ODI) scores were captured. Previously reported minimum clinically important difference (MCID) for ODI (14.9) was used. Multivariable linear regression model was created to derive model estimated 2-year ODI scores. Absolute differences between 1-year and 2-year ODI were compared to absolute differences between 2-year and model-estimated 2-year ODI. Concordance rates in achieving MCID at 1-year and 2-year and predictive values were calculated.

Results: Total of 868 patients were analyzed. There was no difference in the mean absolute ODI scores at 1-year and 2-years. One-year ODI scores significantly differed from 2-year scores by an absolute difference of 9.7 ± 8.9 points and predictive modeling estimations of 2-year scores differed from actual 2-year scores by 8.8 ± 7.3 points ($p < 0.001$) for all procedures except for primary ($p = 0.932$) and revision microdiscectomy ($p = 0.978$) and primary laminectomy ($P = 0.267$). The discordance rates of achieving or not-achieving MCID for ODI were in the range of 8% to 27% for all procedures. Concordance rate was about 90% for primary and revision microdiscectomy. The positive and negative predictive value of 1-year ODI to predict 2-year ODI was 83% and 67% for all procedures and 92% and 67% for primary and 100% and 86% for revision microdiscectomy respectively.

Conclusion: One-year disability outcomes can potentially estimate 2-year outcomes for patient populations, but cannot reliably predict 2-year outcomes for individual patients, except for patients undergoing primary and revision microdiscectomy.

650. EVOLVE: A Prospective Multicenter Evaluation of Outcomes following Kyphoplasty for Vertebral Compression Fractures

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Introduction: Vertebral compression fractures (VCF) resulting from osteoporosis or cancer are common and painful. Kyphoplasty is a minimally invasive procedure to restore vertebral body height and stabilize the fracture. This study assesses its effects on quality of life, pain and disability.

Methods: 354 Medicare eligible subjects with painful, acute or subacute VCF were prospectively enrolled at 24 sites in the United States with 350 undergoing kyphoplasty. The study protocol identified four co-primary endpoints at 3 months. These included the short form 36 question physical component summary (SF-36v2 PCS) and Euroqol-5-domain (EQ-5D) quality of life assessments, the numeric rating scale (NRS) for back pain and the Oswestry disability index (ODI). Data was collected at baseline and at 1, 3, 6 and 12 months.

Results: At the 1, 3, 6 and 12-month time points, NRS back pain improved from 8.7 (scale 0-10) to 3.3, 2.7, 2.5 and 2.4, respectively. The ODI improved from 63.4 (scale 0-100) to 32.9, 28.1, 27.1, and 27.2. SF-36 PCS was 24.2 at baseline (scale 0-100) and improved to 34.9, 36.6, 36.6, 37.6, 38 at the same time points, while the EQ-5D improved from 0.383 points (scale 0-1) to 0.693, 0.731, 0.739, and 0.741. All measures were statistically significant with $p < 0.001$ at every time point. Five device or

procedure-related adverse events (AEs) were reported, each of which resolved with proper treatment.

Conclusion: This large, prospective, multicenter trial demonstrates that kyphoplasty is a safe, very effective and durable procedure for treating Medicare patients with VCF due to osteoporosis or cancer.

651. Predicting Thromboembolism after Pipeline Embolization: The Importance of Assay Selection in the Interpretation of Pre-Procedural Dual Antiplatelet Inhibition

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Introduction: Flow diverters such as the Pipeline Embolization Device (PED) are relatively thrombogenic with a greater than 50% incidence of peri-procedural ischemic lesions despite dual antiplatelet therapy. Platelet function testing (PFT) has been used to ensure adequate platelet inactivation peri-procedurally, however, it remains beset by substantial inter-assay variability and lack of validated target values.

Methods: Pre-procedural blood samples from PED patients pretreated for 7-10 days with dual anti-platelet therapy were simultaneously assayed with traditional light transmission aggregometry (LTA) (AA for aspirin and ADP for P2Y12 effect) and VerifyNow platelet function assays (aspirin reactivity (ARU) and P2Y12 reactivity (PRU)). Procedural ischemic lesions were detected by diffusion-weighted magnetic resonance imaging (DW-MRI) performed at 24 hours post-procedure. Correlations between assays were measured using Spearman's rho. Logistic regression and area under curve (AUC) characteristic were generated, with optimal PFT thresholds determined by maximizing Youden's J statistic.

Results: Twenty-seven of a total of 48 PED procedures (56%) showed post-procedural ischemic lesions with 2 of 27 (7.4%) transiently symptomatic and zero hemorrhage. Baseline clinical, procedural, and radiographic parameters were similar between groups. Aspirin reactivity was similarly suppressed in both groups, but P2Y12 reactivity was higher in ischemic patients (PRU 127.2 vs. 79.8, $p = 0.026$). Although there was significant correlation between LTA and PRU, only the latter was found to be a statistical predictor of ischemia (OR 1.10, CI 1.01-1.21 per 10 unit increase in PRU, $p = 0.03$) and AUC=0.68. The optimal threshold PRU was determined to be 42 (sensitivity 92.6%, specificity 42.9%), which is significantly lower than the generally accepted PRU threshold of 194.

Conclusion: These results confirm the important role of pre-procedural platelet function testing, lend support to preferential utility of the PRU assay over conventional LTA, and suggest the need for greater platelet inhibition to insure optimal reduction of PED-related peri-procedural ischemic events.

652. Factors Associated with Burnout Among Neurosurgical Residents: A National Survey Study

Young Neurosurgeons Abstract Award

Frank Joseph Attenello III, MD; Daniel Donoho; Timothy Wen, MD; Shirley McCartney; Alexander Khelessi, MD; Aaron Cohen-Gadol, MD; Joseph Cheng, MD; William Mack, MD; Clemens Schirmer, MD; Karin Swartz, MD; Adair Prall, MD; Ann Stroink, MD; Steven Giannotta, MD; Paul Klimo, MD (Los Angeles, CA)

Introduction: Excessive dissatisfaction and stress among residents may lead to inferior patient care, errors and physician burnout. Physician burnout has further attracted national attention as a focus of the new surgeon general. Burnout has not previously been formally evaluated among neurosurgical residents.

Methods: An 86-item questionnaire was distributed online to all residents within the AANS database completing the 2015 academic year. The survey project was promoted and funded through the Council of State Neurological Surgeons (CSNS). Questions evaluated personal and clinical

stressors, mentorship, satisfaction, and included the validated Malasch Burnout Inventory survey. Factors associated with burnout were determined using univariate logistic regression.

Results: The survey response rate was 37%(397 residents). The majority of residents were male(79%), 26-35 years old(92%), in a relationship (70%), and without children(75%). Respondents were equally distributed throughout all residency years. 81% reported being at least somewhat satisfied with their career and 74% felt their professional and personal life would improve following residency. 80% would choose neurosurgery again, though 65% would recommend neurosurgery to a medical student. The overall burnout rate was 43%. Notable factors associated with burnout included female gender (OR=1.67, $p=0.04$), second year of residency (OR=1.52, $p=0.03$), inaccurate perception of neurosurgery as a medical student (OR=2.88, $p<0.01$), lack of confidence in OR performance (OR=3.23, $p<0.01$), and personal stressors outside of work (OR=3.67, $p<0.01$). Both presence of mentorship and position as intern showed a trend towards decreased burnout ($p=0.06$). Of note, age, relationship status, and children were not associated with burnout. Of note, the 43% resident burnout rate was lower than that of practicing attending neurosurgeons (57%).

Conclusion: Rates of burnout and career satisfaction are high in neurosurgical residents. We identified several factors associated with burnout. Proven negative effects of burnout on patients, physicians and family members necessitate further study and potential interventions.

653. High Resolution Micro-ECOG Studies of Human Sensorimotor Cortex during Finger Movements

Chao-Hung Kuo, MD; Devapratim Sarma; Tim Blakely; James Wu; Jeremiah Wander; Jared Olson; Kelly Collins; David Caldwell; Jeneva Cronin; Kaitlyn Casimo; Rajesh Rao; Jeffery Ojemann (Seattle, WA)

Introduction: The activation of sensorimotor cortex as measured by electrocorticographic (ECOG) signals has been correlated with unilateral hand movements in humans, even to the level of individual digits. In the current study, we used micro-ECOG (μ ECOG) on sensorimotor cortex to examine the patterns of finger movements across several tasks.

Methods: The subjects who participated in this study were neurosurgical patients underwent epilepsy surgery over the eloquent cortex. During awake craniotomy, sensorimotor cortex of hand movement was localized by high-frequency responses measured by an $8 \times 8 \mu$ ECOG grid. Patients performed a flexion of thumb or index finger, or a pinch, based on visual cue. The activation of high-frequency band(70-230Hz) filtered ECOG was used to identify dominant electrodes associated with thumb and index movement. Hand movements were recorded by a dataglove simultaneous with ECOG recordings.

Results: In all 3 patients, the electrodes controlling thumb and index movements were clearly, and separately, identified by the high-frequency band filtered μ ECOG signal. Separate activations, approximately 3-6mm apart (1-2 electrodes), were seen for index finger and thumb movement. For pinch movement, the thumb or index signal was equal, or greater than, that observed during only thumb or index movement. However, during pinch movement, for the thumb, the cortical signal was increased or similar to isolated thumb movement despite a markedly decreased joint angle movement of the thumb during pinch. The index finger kinematics, and cortical signal, during pinch movement was similar with that during the index-only movement.

Conclusion: For pinch movement, the activation of high-frequency band filtered μ ECOG signal is combined with the activated thumb and index signal. However, there is not a fixed relationship between the cortical signal and the finger kinematics and appears to depend on the context of the movement. This may provide insight into the tuning of motor cortex toward specific types of motor behaviors.

654. Interhemispheric Subdural Hygromas Predict Shunt-Dependent Hydrocephalus after Decompressive Craniectomy for Traumatic Brain Injury

Aditya Vedantam, MD; Jose-Miguel Yamal, PhD; Hyunsoo Hwang; Claudia Robertson, MD; Shankar Gopinath, MD (Houston, TX)

Introduction: Post-traumatic hydrocephalus affects 11-36% of patients undergoing decompressive craniectomy and is an important cause of morbidity after traumatic brain injury (TBI). Early diagnosis and treatment of post-traumatic hydrocephalus can prevent further neurological compromise in patients recovering from TBI. There is limited data on predictors of shunting for post-traumatic hydrocephalus after decompressive craniectomy for TBI.

Methods: Prospective collected data from the Epo Severe TBI randomized controlled trial were studied. Demographic, clinical, and imaging data for enrolled patients who underwent a decompressive craniectomy were analyzed. All head CT scans were reviewed and assessed for post-traumatic hydrocephalus by the Gudeman criteria or the modified frontal horn index of 33%.

The presence of subdural hygromas was categorized as unilateral/bilateral hemispheric or interhemispheric. Using L1-regularized logistic regression to select variables, a multiple logistic regression model was created with ventriculoperitoneal shunting as the binary outcome. Statistical significance was set at $p<0.05$.

Results: A total of 60 patients who underwent decompressive craniectomy were studied. The majority of patients underwent unilateral decompressive hemicraniectomy ($n=46$, 78%). Post-traumatic hydrocephalus was diagnosed in 26 patients (43.3%), and 14 patients (23.3%) underwent ventriculoperitoneal shunting for post-traumatic hydrocephalus. Unilateral and bilateral hemispheric hygromas were seen 31 (82%) and 7 (18%) patients respectively. Interhemispheric hygromas were seen in 19 (32%) patients. The mean time from injury to first CT scan showing hemispheric subdural hygroma and interhemispheric hygroma was 7.9 ± 6.5 days and 14.9 ± 11.7 days respectively. The mean time from injury to shunting was 45.6 ± 15.3 days. Multivariate analysis showed that the presence of interhemispheric hygroma (OR 26.5, $p=0.001$) and younger age (OR 0.83, $p=0.01$) were significantly associated with need for shunt after decompressive craniectomy.

Conclusion: Presence of post-operative interhemispheric subdural hygroma was associated with shunt-dependent hydrocephalus after decompressive craniectomy in patients with TBI.

655. Desmoplastic infantile ganglioglioma/astrocytoma

American Brain Tumor Association Young Investigator Award

Anthony Chin-Hsiu Wang, MD; Isaac Abecassis, MD; Shelly Wang; Bonnie Cole; Sarah Leary; Christina Lockwood; James Olson; Eric Holland; David Capper; Richard Ellenbogen; David Jones; Jeffrey Ojemann (Los Angeles, CA)

Introduction: The WHO classification of CNS neoplasms categorizes desmoplastic infantile astrocytoma (DIA) and desmoplastic infantile ganglioglioma (DIG) together as one diagnosis, among Grade I entities under neuronal and mixed neuronal-glial tumors. High-grade characteristics have failed to correlate with worse clinical outcomes. Instead, these tumors have been reported to yield an excellent prognosis, particularly when completely resected.

Methods: We aimed to understand genetic underpinnings of DIG/DIA, and their natural histories. DNA sequencing was performed on specimens obtained from 30 patients diagnosed with DIG/DIA by histology. We also performed an individual patient data meta-analysis (IPDMA) of the existing literature.

Results: Among 30 native tumor samples, we found no genetic aberrations in 22 (73.3%). Within the other 8 native tumors, we discovered 4 (13.3%) BRAFV600E mutations, and 3 (10%) BRAFV600D mutations.

Three suffered malignant transformation. Each had a separate underlying oncogenic mutation, including TP53 mutation, ATRX mutation, and ALK-EML4 fusion. IPDMA included 75 articles with 137 patients. GTR was associated with HR 0.048 ($p = 0.003$) for mortality. Pathology, leptomeningeal spread, deep location, extent of resection, and malignant transformation were associated with tumor recurrence.

Conclusion: DIG/DIAs harbor either BRAFV600E and BRAFV600D mutations with a 23.3% frequency. No oncogenic mutation was consistently identified in wild-type BRAF DIG/DIAs. Malignant transformation was identified in 33.3% of the patients followed long-term at SCH, with two of these three patients developing a new oncogenic mutation when the malignant tumor was sequenced, which was not present on the native tumor. However, malignant transformation appears to remain uncommon among these tumors, as reported in the existing literature. IPDMA discovered that deep-seated tumors witness a worse prognosis, in terms of progression-free and overall survival. In addition, we identified incomplete resection, DIA pathology, multi-focal disease at presentation, and malignant transformation as independent predictors of poor outcome in DIG/DIA patients.

656. Lumbar Fusion for Symptomatic Mechanical Disc Collapse without Stenosis Improves Pain, Disability, and Quality of life: Rethinking the debate on degenerative disc disease (DDD)

Silky Chotai, MD; Matthew McGirt, MD; Clinton Devin, MD; Deborah Pfortmiller, PhD; Silky Chotai, MD; Mohamad Bydon, MD; Steven Glassman, MD; Anthony Asher, MD (Nashville, TN)

Introduction: The efficacy of lumbar fusion for degenerative disc disease (DDD) without stenosis remains unclear and highly debated by physicians, payers, and policy makers. Many patients with medically refractory mechanical axial back pain and significant lumbar disc height collapse are denied access to fusion procedures by their respective payer policies. Utilizing a standardized definition for DDD, we set out to determine if lumbar fusion was associated with improved patient-reported health benefits in a prospective nationwide registry.

Methods: N2QOD registry collects one-year patient-reported outcomes (PROs) after surgical care for six lumbar diagnosis groups. We queried all surgical cases that were enrolled under the DDD diagnosis group symptomatic mechanical disc collapse defined a priori as reproducible mechanical axial back pain with <50% disc height loss without stenosis or listhesis proven to be medically refractory <3 months. The relative prevalence, safety, and effectiveness of surgery for symptomatic mechanical disc collapse was assessed.

Results: 7618 patients from 74 hospitals in 26 U.S. states were enrolled and completed 12-month PROs. Symptomatic mechanical disc collapse represented the minority of these surgical cases at N2QOD hospitals [42(0.6%)]. All cases underwent single-level fusion and associated with mean EBL(327cc), length of stay(3.5days), discharge to inpatient rehabilitation(12%), 30-day morbidity(9%) and 90-day all-cause readmission(9%). Lumbar fusion resulted in 12-month improvement in back pain(BP-NRS: 8 vs 5.3, $p < 0.001$); leg pain(LP-NRS: 6.5 vs 4.3, $p < 0.001$); disability(ODI: 54 vs 42, $p < 0.001$); and quality of life(EQ5D: 0.49 vs 0.59, $p < 0.005$). Postoperative return to work reached 66% at 3mo and 100% by 12month.

Conclusion: Lumbar fusion for symptomatic mechanical disc collapse without stenosis or listhesis represented the minority of surgical practice at the 74 N2QOD centers between 2010 and 2015. However, those patients undergoing lumbar fusion for this narrowed definition of DDD experienced improvements in all measured domains of health, suggesting lumbar fusion is an effective treatment for back pain arising from mechanical disc collapse.

657. Validation of Frailty for Preoperative Risk Assessment in Neurosurgical Oncology Patients Using a National Registry

Brett Youngerman, MD; Alfred Neugut, MD, PhD; Jingyan Yang, MHS; Dawn Hershtman, MD, MS; Jason Wright, MD; Jeffrey Bruce, MD (New York, NY)

Introduction: Frailty is an emerging concept in preoperative risk assessment that takes into consideration aspects of both comorbidity and functional status. A modified frailty index (mFI), calculated from national registry data, has been validated in several surgical populations. Our objective was to determine if mFI correlates with morbidity and mortality in patients undergoing neurosurgery for intracranial neoplasms.

Methods: We identified patients in the National Surgical Quality Improvement Program (NSQIP) who underwent neurosurgical oncology procedures between 2008 and 2012. The mFI, ranging from 0 to 1, was calculated as the proportion of 11 possible risk factors present. We assessed the associations between mFI and adverse events in univariate and multivariable analysis.

Results: A total of 8,848 patients who underwent oncologic neurosurgery procedures were identified. Comparing those with mFI of 0 to those with an index ≥ 0.5 , the overall complication rate increased from 11.6% to 44.3% ($p < 0.001$), severe medical complications increased from 5.1% to 22.9% ($p < 0.001$), severe neurologic complications increased from 3.6% to 10.0% ($p < 0.001$), and mortality increased from 1.6% to 14.3% ($p < 0.001$). Frailty was independently associated with all adverse outcomes after adjusting for other risk factors including age, ASA score, and type of surgery. According to model fit statistics, mFI increased the ability to predict mortality by 34.2% and overall complications by 23.2%, compared to chance.

Conclusion: The mFI can be calculated from routine clinical data and is predictive of outcomes in patients undergoing surgery for intracranial neoplasms. Frailty may be useful in shared decision-making, perioperative planning, and risk-adjusted outcomes-based quality measurement using national registry data.

658. A Pilot Study on the Safety and Efficacy of Stenting Superior Sagittal Sinus Stenosis and a New Angiographic Naming System

Thomas Buell, MD; Daniel Raper; Jon Pomeranec; Dale Ding; Kenneth Liu (Charlottesville, VA)

Introduction: In some cases of refractory idiopathic intracranial hypertension, stenosis of the superior sagittal sinus with an associated pressure gradient has been observed. The safety and efficacy of stenting of the superior sagittal sinus (SSS) has not been well established.

Methods: We performed a retrospective review of a prospectively maintained database to identify patients undergoing stent placement in the SSS for intracranial venous stenosis. Patient and treatment factors, including pre- and post-procedural pressure gradients, were compared, and an angiographic naming system for segments of the SSS was created.

Results: Nineteen patients underwent placement of 32 stents, of which 42% had developed new SSS stenosis after prior stent placement for transverse sinus stenosis. The SSS may be split into 4 quadrants from the torcular to the frontal pole, termed S1-S4. SSS stenosis typically occurs in the S1 segment, and the anterior extent of SSS stents were placed at the S1-S2 junction in all but one case. Maximum pre-stent mean venous pressure (MVP) was 16.2 mmHg, and 13.1 mmHg post-stent ($p = 0.037$). Pre-stent pressure gradient across the stented area was 4.2 mmHg prior to, and 1.5 mmHg after stent placement ($p < 0.001$). There were no intra-procedural complications, and no cases of stent-adjacent stenosis at a mean follow-up of 4.2 months.

Conclusion: VSS in the SSS is safe and effective in reducing maximum MVP and pressure gradients for a subset of patients with evidence of SSS stenosis. The S1 segment of the SSS is most commonly affected by intracranial stenosis. Further prospective data and longer follow up will be necessary to better define the long-term efficacy of VSS in this patient population.

659. Perioperative Antibiotic Use In Vagus Nerve Stimulator Implantation – A Clinical Series

Jeffrey Steven Raskin, MD; Daniel Hansen; Arvind Mohan; Thomas Luerssen; Daniel Curry; Sandi Lam (Houston, TX)

Introduction: Preoperative antibiotics contributes up to one-third of total antibiotic use in major hospitals. Choice of antibiotic is not standardized, and polypharmacy regimens are used without knowing the effect on rates of surgical site infection, nonsurgical infections, or antibiotic resistance. Careful examination of trends in surgical prophylaxis must be evaluated. This study examines our institution's experience with vagus nerve stimulator (VNS) implantation, focusing on association between perioperative antibiotic practices and postoperative infectious outcomes.

Methods: We conducted a single center case control study using a retrospective chart review of fifty consecutively operated patients undergoing VNS implantation over twenty-four months by two experienced surgeons at our institution from July 2014 to March 2016. In each surgery, the technical procedure, operating room, and surgical team were the same while surgeon's preference in antibiotic prophylaxis differed. Group 1 received a single dose of intravenous (IV) cefazolin (n=26) and Group 2 received IV cefazolin paired with one or both of gentamicin/vancomycin, in addition to a 10 day outpatient oral course of clindamycin (n=24). Patient demographics, perioperative details, and 3 month follow-up for infection and healthcare utilization were recorded. Student t-tests were computed for significance.

Results: Group 1 patients on average were older than Group 2 patients [10.2, 7.1 years; p=0.01] and length of surgery was longer [115.5, 91.9 min; p=0.007]. There were no differences in number of surgeons gowned (p=0.11), presence of tracheostomy (p=0.43) or gastrostomy (p=0.20) tube, VNS infections (p=0.17), nonsurgical infections (p=0.32), number of postoperative emergency department visits (p=0.22) or readmissions (p=0.23).

Conclusion: Single preoperative dosing of one antibiotic appropriately chosen to cover typical skin flora conferred equal benefit to perioperative prophylactic polypharmacy in this study. There were no differences in postoperative infection events or ED visits/readmissions. Restraint with preoperative antibiotics shows equipoise in postoperative infection and overall resource utilization.

660. Intraoperative Provocation Delineates Nucleus Accumbens Subregions in DBS Surgery for OCD

Kai Joshua Miller, MD; Nolan Williams; Thomas Prieto; Casey Halpern (Stanford, CA)

Introduction: The role of intraoperative electrophysiology for targeting the ventral striatum in obsessive-compulsive disorder (OCD) has been of unclear benefit. Nucleus accumbens (NAcc) has been the most common target for deep brain stimulation (DBS) electrode lead placement, and most centers choose to perform this procedure with the patient asleep. We present a representative case in which the bilateral NAcc was implanted using frameless stereotaxy.

Methods: The patient had debilitating OCD, refractory to medical intervention, with specific compulsions associated with the bathroom, and toothbrushing in particular. A target lead position was determined at the base of the left ventral NAcc. Prior to placement of the DBS lead, a microelectrode was passed from 20mm above-target, pausing at approximately 1mm intervals for 30 seconds recordings while advancing to target. At 5/3/1mm above target, spiking cells were isolated, and confrontation/provocation was performed by bringing a toothbrush to the patient's face.

Results: On approach, distinct LFP oscillations were observed, with specific anatomic correlates: Alpha-oscillations in the Nacc, with focal gamma-oscillations in the ventral aspect; theta-oscillations dorsal to the commissure; and a focal high-beta-oscillation at the capsule-BNST interface. On toothbrush provocation, there was a robust increase in firing rate specifically in dorsal-Nacc 3mm above target, but neither at 1 nor 5mm above target.

Conclusion: Distinct anatomic subregions of Nacc can be measured electrophysiologically during DBS for OCD. Provocation with patient-specific compulsion-inducing stimuli selectively isolates responsive units in dorsal Nacc. These observations suggest we may need more closely spaced DBS electrodes that can discriminate sub-regions, as these regions may have conflicting roles, and this may explain why there has been variable response to Nacc DBS for OCD. If so, there may be a role for awake neurophysiology in DBS for OCD to isolate this dorsal sub-region, similar to current surgical strategies for STN in Parkinson's disease

661. Neurological Recovery in Patients with Favorable Outcomes after Severe Traumatic Brain Injury: Implications for Decisions on Withdrawal of Care in Patients with Severe TBI

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Introduction: Early withdrawal of life-sustaining treatment due to expected poor prognosis is responsible for the majority of in-house mortality in severe traumatic brain injury (TBI). With increased focus on the decision and timing of withdrawal of care in patients with severe TBI, data on early neurological recovery in patients with a favorable outcome is needed to guide physicians and families.

Methods: We reviewed prospectively collected data on 1241 patients with closed head injury from 1986-2012. We selected patients with severe TBI, motor GCS (mGCS) score <6 on admission, and those who had favorable outcomes (GOS= moderate disability or good recovery) at 6 months. Baseline demographic, clinical and imaging data was analyzed. The time from injury to first record of following commands (mGCS=6) after injury was recorded. The temporal profile of GOS scores at discharge through to 6 months after the injury was also assessed.

Results: We studied 218 patients (183 men, 35 women) with a mean age of 28.9±11.2 years. The majority of patients were able to follow commands (mGCS=6) within the first week after injury (71.4%), with most patients recovering on day 1 (28.6%). Recovery to following commands beyond 2 weeks from the injury was seen in 14.8% of patients, who endured significantly longer durations of ICP monitoring (p=0.001) and neuromuscular blockade (p<0.001). In comparison to patients with moderate disability, patients with good recovery had higher initial GCS score (p=0.01), lower incidence of anisocoria at admission (p=0.048), shorter ICU stay (p<0.001) and total hospital stay (p<0.001). There was considerable improvement in GOS scores from discharge to follow-up at 6 months.

Conclusion: Up to 15% of patients with a favorable outcome after severe TBI may begin to follow commands beyond 2 weeks from the injury. These data caution against early withdrawal of life-sustaining treatment in patients with severe TBI.

662. Multimodal Characterization of Supratentorial Gliomas: Relationship Among Morphological, Metabolic and Molecular features

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Introduction: The relationship between carbon-11-methionine PET (11C- METH PET) and molecular and conventional MRI biomarkers in patients affected by supratentorial gliomas who underwent surgery was evaluated.

Methods: A consecutive series of 109 patients with pathologically proven gliomas (M:F=64:45; median age 43 years), referred to our Institution from March 2012 to January 2015 for tumor resection and submitted to pre-operative 11C-METH PET, was analyzed. The trial was registered at www.clinicaltrials.gov (NCT02518061). Semi-quantitative evaluation for 11C-METH PET included SUVmax, SUVratio-to- normal brain and metabolic tumor volume (MTV). Imaging findings were correlated to disease

outcome in terms of progression-free survival (PFS), and compared with other clinical-biological data, including IDH1 mutation, 1p/19q co-deletion and MGMT promoter methylation. The cohort was monitored for a mean period of 16.7 months (median 13 months).

Results: We observed a statistically significant difference for SUVmax, SUVratio and MTV values based on tumor grade ($p < 0.001$). According to molecular analyses, IDH1 resulted mutated in 49 patients, 1p/19q co-deleted in 58 patients and MGMT promoter methylated in 74 patients. A significant inverse correlation was defined for SUVmax and SUVratio and IDH1 mutation ($p < 0.001$). Relapse or progression was documented in 48 cases (median PFS 8.7 months). SUVmax and SUVratio, tumor grade, IDH1 mutation, 1p/19q co-deletion and MGMT- promoter methylation proved to have a statistically significant association with PFS on Cox regression. Among them no independent prognostic factor could be defined on multivariate analysis.

Conclusion: 11C-METH PET parameters significantly correlate with histological grading and IDH1 mutation in gliomas. Grading, molecular biomarkers, SUVmax and SUVratio resulted prognostic factors with respect to PFS in this cohort of patients.

663. Early Apparent Diffusion Coefficient Changes in Normal-Appearing Brain in Pediatric Moyamoya Disease

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Introduction: Moyamoya disease often leads to ischemic strokes visible on diffusion-weighted imaging (DWI) and T2-weighted MRI, with subsequent cognitive impairment. In adults with moyamoya, apparent diffusion coefficient (ADC) is correlated with regions of steal phenomenon and executive dysfunction prior to any white matter changes. We propose that children with moyamoya exhibit global diffusion alterations prior to any signs of ischemic damage.

Methods: We performed a retrospective review of children with moyamoya disease and syndrome who underwent bypass surgery at our institution. We identified 29 children with pre-operative MRI without any radiographic signs of infarction. DWI datasets were used to calculate ADC maps for each subject as well as for 60 age-matched healthy controls. Using an atlas-based approach, the cerebral white matter, cerebral cortex, thalamus, caudate, putamen, pallidum, hippocampus, amygdala, and accumbens were segmented in each DWI dataset and used to calculate the volume and median ADC values for each region. A multivariate analysis of variance (MANOVA) was used for group comparison using the median ADC and volumetric values as dependent variables, age as a co-variate, and the class (moyamoya vs. controls) as the fixed factor modeled as an interaction with age.

Results: Children with moyamoya exhibited higher age-corrected ADC values in all brain structures compared to healthy controls while brain volumes are unchanged. MANOVA revealed a significant difference between children with moyamoya and healthy controls ($p < 0.0001$). Post-hoc analysis showed significant differences in median ADC values in all brain structures ($p < 0.024$) except for the hippocampus. No significant differences were found between the groups for the regional brain volume parameters.

Conclusion: Prior to having bypass surgery and in the absence of radiographic evidence of an ischemic stroke, children with moyamoya may have diffusion changes related to exhaustion of cerebrovascular reserve, which could contribute to delayed brain development and cognitive dysfunction.

664. Predictors of Hospital-Associated Complications Prolonging ICU Stay in Low-Grade aSAH Patients

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Introduction: Patients with aneurysmal subarachnoid hemorrhage (aSAH) are usually hospitalized for 14-21 days due to the high risk of

cerebral vasospasm. Lengthy hospital stays are however correlated with an increased risk of medical complications. This raises the concern that the high risk of medical complications may outweigh the benefit of close monitoring in patients with low-grade (Hunt-Hess 1-3) aSAH. We aim to determine the predictors of late hospital-associated medical complications in these patients.

Methods: We conducted a retrospective study of 424 patients with low-grade aSAH admitted to Thomas Jefferson University Hospital from 2008-2015. We collected data of patient comorbidities, Hunt-Hess grade, length of stay (LOS), and complications. We performed a logistic regression analysis to determine the predictors for hospital-associated complications (DVT/UTI/pneumonia).

Results: Out of 424 patients, 50 (11.8%) developed neurological complications after the first week that warranted prolonged ICU admission (mean 16.3 ± 6.5 days). Of the remaining 374 patients without neurological complications (88.2%), 83 (22.2%) developed late medical complications with mean LOS of 15.1 ± 7.6 days, while those without medical complications stayed 11.8 ± 6.2 days ($p = 0.001$). Of the 83 patients, 55 (66.3%) did not have any hospital-associated complications in the first week. Smoking ($p = 0.062$), history of cardiac disease ($p = 0.043$), H-H grade 3 ($p = 0.012$), IVH ($p = 0.012$), EVD placement ($p = 0.002$) and DVT/UTI/pneumonia in the first week ($p = 0.001$) were individually associated with late medical complications. Multinomial logistic regression showed early pneumonia/UTI/DVT ($p = 0.026$) and increasing H-H grade ($p = 0.057$) to be the most important risk factors for late medical complications.

Conclusion: While an extended ICU admission offers the benefit of closer monitoring, many patients develop hospital-associated complications despite being low risk for neurological complications. We report in detail the characteristics of low-grade aSAH patients who would benefit from early discharge in an effort to prevent hospital-associated complications.

665. Transition-to-Practice Curriculum in Graduate Medical Education

Byron Cone Pevehouse Young Neurosurgeons Award

Melanie Hayden Gephart, MD; Robyn Schaffer; Laurence Katznelson; Nancy Piro (Stanford, CA)

Introduction: Debt repayment, professional negotiation, and practice management skills are vital to a successful medical practice yet are undervalued in graduate medical education. Medical residents need additional training to confidently transition to independent practice, requiring the development of novel curricula.

Methods: We developed a trial practice management curriculum to educate senior Stanford residents and fellows through voluntary workshops. Topics discussed in the workshops included debt repayment, billing compliance, medical malpractice, contract negotiations, and lifestyle and financial management. Resident self-confidence was assessed and feedback was obtained through voluntary survey responses before and after attendance at a workshop and scored utilizing a Likert scale.

Results: 25 residents from 20 specialties attended a one-day session incorporating all lectures; 53 residents from 17 specialties attended a re-designed quarterly session with one or two topics per session. Survey evaluations completed pre- and post-workshop demonstrated an improvement in residents' self-assessment of confidence in contract negotiations ($p < 0.001$) and their first year in practice ($p < 0.001$); after the curriculum, 94% ($N = 42$) of respondents felt confident participating in contract negotiations and 93% ($N = 38$) of respondents felt confident about their first year in practice. 100% of respondents agreed that the presentation objectives were relevant to their needs as residents.

Conclusion: Participant response indicated a need for structured education in practice management for senior trainees. Senior residents and fellows will benefit most from curricula but have high familial and professional demands on their schedules.

666. Real-time MRI-guided delivery of AAV2-AADC gene therapy for Parkinson's Disease: Infusion strategies and their impact on coverage of the putamen

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Introduction: Gene therapy using adeno-associated virus (AAV2) carrying the amino acid decarboxylase (AADC) gene has the potential to improve the clinical response to levodopa when infused into the putamen of Parkinson's patients. Prior clinical trials have shown possible benefit, but may have been limited by inadequate anatomical vector delivery or off-target vector distribution. Intraoperative MRI-guided surgery and co-infusion of the vector with gadoteridol now allows real-time visualization of infusions.

Methods: Retrospective analysis of bilateral MRI-guided putaminal infusions for 10 subjects in an ongoing Phase Ib AAV2-AADC clinical trial. T1-weighted images were used to calculate coverage of the putamen.

Results: Reflux up the infusion cannula and spread along perivascular spaces were the two main causes of off-target distribution, with anterior and ventral infusion sites found to be most prone to perivascular spread. The infusion strategy evolved during the trial to maximize coverage of the putamen by modifying the cannula design, increasing the infusion volumes and altering the position of infusion sites along the cannula trajectories. Increasing the volume from 450 (cases 1-5) to 900 microliters per putamen and selecting cannula tip designs to match the individual putamen (cases 6-10) had the largest impact on coverage (mean 21% vs 34%); however, one higher volume case had only 25% coverage, indicating that higher volume alone was not sufficient to increase distribution within the target. Positioning of the cannula tip during infusion was changed from a single point infusion (cases 1-3, lower volume; 19-24% coverage), to two or more stacked infusions (cases 4-7, varying volumes; 17-36% coverage), to a progressive advancement strategy (cases 8-10, higher volume; 32-38% coverage). The post-commissural putamen was preferentially targeted in cases 6-10 with up to 51% coverage achieved.

Conclusion: Real-time MRI-guided delivery allows various infusion strategies to be employed to maximize target coverage.

667. Examination of the Current Role of Closed Reduction in the Management of Cervical Fracture-Dislocations

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Introduction: We sought to evaluate the utilization of closed reduction in the initial management of bilateral facet dislocations over the last 10 years at our institution.

Methods: We retrospectively reviewed the charts of patients who experienced subaxial cervical facet injury within the Penn Health System between 6/1/2006 and 6/1/2016 to identify patients with bilateral jumped/perched facets. The neurological injury was identified based on the ASIA spinal cord injury score. ANOVA and two-sample t-tests were used to compare continuous distributions, and chi square tests to compare categorical distributions. We considered a $p < 0.05$ to be statistically significant.

Results: We focused our analyses on patients that presented with bilateral jumped/perched facets with (ASIA A and B) or without (ASIA C, D, E) complete voluntary motor deficit, who underwent attempted closed reduction. We found that the rate of successful closed reduction was significantly higher in incomplete motor deficits (5/5, $p = 0.004$, chi-2 test) as compared to complete motor deficits ($n = 2/11$).

Conclusion: The rate of successful reduction for complete motor level injury is relatively low. At our institution there are several contributing factors including practice variability among the attendings and a trend towards attempting closed reduction but defaulting to surgery with difficult reduc-

tions. The more compelling result is the successful utilization in patients with incomplete injuries (100%). There were 2 patients in this group that underwent awake closed reduction followed immediately by surgical stabilization. In these cases there were no useful MEP signals, which would have precluded utilizing this modality to safely perform an open reduction. This would argue that the best utilization of awake closed reduction would be in incomplete patients who have the most to lose and in whom you cannot predictably rely on intra-operative monitoring.

668. MRI FLAIR Hyperintensity in Labyrinth is a Predictive Biomarker for Hearing Loss in Neurofibromatosis Type 2 Patients with Small Vestibular Schwannoma

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Introduction: Onset of inevitable hearing loss in neurofibromatosis type 2 (NF2) does not correspond to the size of the bilateral vestibular schwannomas (VS). Historically, invasive sampling revealed that elevated protein within inner ear perilymph is associated with VS and hearing loss. We have previously shown that pre-contrast fluid-attenuated inversion recovery magnetic resonance imaging (FLAIR) can non-invasively detect elevated intralabyrinthine protein in NF2, and that FLAIR hyper-intensity may be a specific marker for hearing loss. The purpose of this study was to investigate the natural history of FLAIR hyper-intensity and hearing loss in NF2 patients with naïve small VS ($<500\text{mm}^3$).

Methods: A prospective longitudinal study of NF2 enrolled 168 subjects between 2008 and 2016. Patients had 4.2 ± 1.2 year (y) follow-up with annual clinic visit, MR-imaging, and audiometry.

Results: Of the 68 ears (34 subjects, mean age 26.8y; range 4.6-67y) with small VS, 53 were eligible for the study. All 18/18 ears with baseline abnormal hearing had FLAIR hyper-intensity. Of the 35 ears with baseline normal hearing, 16/35 had baseline FLAIR hyper-intensity, 6/16 (37.5%) of which developed new hearing loss in 2.3 ± 1.5 y. New FLAIR hyper-intensity developed in 11/19 ears, 3 (27%) of which developed new hearing loss within 2.7 ± 1.2 y. No new hearing loss developed in 8 ears that remained FLAIR negative. New FLAIR hyper-intensity is significantly associated with development of new hearing loss (Chi-square; $p = 0.04$). FLAIR conversion has high sensitivity (1.00, 95%CI 0.39-1) and negative predictive value (1.00, 95%CI 0.63-1) for new hearing loss.

Conclusion: Findings from this study suggest that intralabyrinthine FLAIR hyper-intensity is a sensitive, non-invasive biomarker that precedes hearing loss (by 2y). Importantly, hearing loss did not develop in the absence of FLAIR conversion. The findings of the current study provide further insights for management strategies such as middle fossa decompression for NF2 hearing preservation.

669. Psychiatric Disorders in Children with Chiari Malformation Type I: Prevalence and Risk Factors

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Introduction: This cross-sectional study investigates prevalence and risks of psychiatric illnesses in a large cohort of children with Chiari malformation type 1 (CM1). To our knowledge, no study of this size has been previously undertaken.

Methods: Children with CM1 between the ages of 6 and 17 years were identified after receiving the diagnosis of CM1 during a neurosurgery clinic visit. Eighty-six participants were recruited between 2010-2016 [Age M = 11 years, 3 months (SD = 3 years, 5 months); 44 males, 42 females]. Parents of participants completed a pediatric medical history questionnaire and a semi-structured interview regarding the child's psychiatric, developmental, medical history, and family characteristics. A review of medical records was completed to complement interview data.

Results: Results revealed elevated rates of psychiatric conditions, including attention deficit hyperactivity disorder (22.1%), anxiety (12.8%) and depression (10.5%) when compared to the general population (attention deficit hyperactivity disorder, 3.4%; anxiety, 6.5%; depression, 2.6%). A two-step binary logistic regression analysis revealed that having problems during pregnancy (Wald = 6.98, $p = 0.01$) increased your risk of psychiatric disorder 9-fold. Being born premature (Wald = 6.90, $p = 0.01$) or having seizures (Wald = 3.72, $p = 0.05$) also significantly predicted psychiatric history among participants.

Conclusion: The current findings suggest a high prevalence of psychiatric illness in children with CM1. Pregnancy complications were associated with a high risk of a psychiatric diagnosis. CNS vulnerabilities during pregnancy may explain this relationship. Seizures and prematurity only slightly improved the prediction model.

670. Oberlin Neurotization Improves Early Supination Compared to Nerve Graft Repair in Neonatal Brachial Plexus Palsy

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Introduction: The use of nerve transfers vs nerve graft repair for Neonatal Brachial Plexus Palsy (NBPP) remains controversial. In adult brachial plexus injury, transfer of an ulnar fascicle to the biceps branch of the musculocutaneous nerve (Oberlin transfer) is reportedly superior to nerve graft repair for restoration of isolated elbow flexion. In pediatric patients with NBPP, limited evidence exists comparing outcomes for flexion and supination with nerve transfer and graft repair. Therefore, we compared outcomes for infants with NBPP who have undergone the Oberlin transfer vs nerve graft repair.

Methods: This retrospective cohort study reviewed 19 patients (mean age 7 months at operation) with Oberlin transfer and 31 patients (mean age 6 months at operation) with nerve graft repair at a single institution from 2005-2015. Active range of motion in elbow flexion and supination was evaluated by occupational therapists pre- and post-operatively at 1-year. Biceps muscle power was evaluated via Medical Research Council (MRC) grading scale.

Results: Comparing the mean change (pre- to post-operatively) in elbow flexion in adduction (54° vs 37° , $P=0.27$), elbow flexion in abduction (58° vs 62° , $P=0.74$), and MRC biceps strength (+1 grade vs +2 grades, $P=0.89$), no significant difference was observed between Oberlin transfer and nerve graft repair. The Oberlin transfer group gained significantly more supination compared to the nerve graft repair group (100° vs 19° , $P<0.0001$).

Conclusion: Our data demonstrate that the Oberlin transfer confers an advantageous early recovery of forearm supination over graft repair while equivalent in elbow flexion recovery. Given that both functions comprise quality of movement, these data support the use of Oberlin transfer over nerve graft repair for function in the WHO-ICF Activity and Participation modalities. Further studies that monitor real-world arm usage will provide more insight into the most appropriate surgical strategy for NBPP.

671. Transcranial Doppler Emboli Monitoring Prevents Stroke after Deployment of Flow Diverting Stents: Single Center Results from 108 Aneurysm Cases

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Introduction: Flow diverting stents (FDS) are increasingly used for treatment of intracranial aneurysms. While FDS can provide flow diversion of parent vessels, their high metal surface coverage can cause thromboembolism. Positive Transcranial Doppler (TCD) Emboli Monitoring has been shown to predict strokes both de novo and following neurointerventional procedures. Limited data exists regarding the use of TCDs for emboli monitoring in the periprocedural period after FDS placement. We evaluated

the rate of emboli and stroke after FDS deployment at our institution.

Methods: We retrospectively evaluated 108 patients who underwent FDS treatment between 2013 and 2016 using the Pipeline stent (Medtronic). All patients were pretreated with aspirin/clopidogrel and response tests were evaluated before PED deployment. All patients were therapeutic pre-operatively. TCD emboli monitoring was performed immediately after the procedure. Stroke rates were determined at discharge, 2-week and 6-month post-operatively.

Results: Average aneurysm size was 9.0 ± 6.7 mm with most in the anterior circulation ($n=96$) and the remainder in the posterior circulation ($n=12$). TCD emboli monitoring was positive in 12% ($n=13$) post-operatively and 'strongly positive' (>20 microembolic signatures per hour) in 3.7% ($n=4$). TCDs were repeated after treatment with heparin or another antiplatelet agent with normalization of TCD emboli monitoring in 92% of cases following additional treatment. Our overall stroke rates at discharge, 2-week and 6-months were: 2.8%, 4.6% and 5.6%, respectively.

Conclusion: TCD emboli monitoring provides early detection of thromboembolic events in patients treated with FDS. Impending stroke can therefore be avoided by modifying post-operative therapy.

672. Risk of Head and Neck Trauma in Patients with Parkinson's Disease: A Nationwide Population-Based Study

Wei-Lun Lo, MD; Chi-Yang Yeh, MS; Ming-Chin Lin, MD, PhD (New Taipei, Taiwan)

Introduction: Impaired balance function and sensory integration might facilitate trauma in patient with Parkinson's disease (PD). We proposed to evaluate the risk of head and neck trauma (HNT), cervical spine fracture (CSF), cervical spinal cord injury (CSCI), head injury (HI) and cervical spine degeneration (CSD) for the PD patients.

Methods: This is a case-control longitudinal study which data acquisition from National Health Insurance Research Database. From 2000 to 2009, 7762 patients diagnosed as PD were included. Age-gender matched subjects without PD (NPD, total 31615 subjects) were extracted randomly as control group with 4:1 case-control ratio. Cumulative risk and odds ratio were calculated independently for HNT, CSF, CSCI, HI, and CSD.

Results: Higher incidences of HNT, NS, CSF, CSCI in PD group than NPD group were observed (HNT: PD/NPD = 8%/5%, $p<0.001$; CSF: PD/NPD = 13%/9%, $p<0.001$; CSCI: PD/NPD = 0.45%/0.28%, $p=0.02$; HI: PD/NPD = 22%/13%, $p<0.001$). However, lower incidence of CSD was observed in patients with PD (PD/NPD = 5%/11%, $p<0.001$). However, Kaplan-Meier curve revealed that PD group are faster to develop CSD than NPD group (log-rank test, $p<0.001$).

Conclusion: High risk of head and neck trauma were observed in patients with Parkinson's disease. Probably postural instability is the leading cause. However, lower risk but faster development of cervical spine degeneration were revealed in our study. Inferior physical activity and postural deformity of neck in Parkinson's patients might be central to explanation.

673. Evaluation of brain tumor regrowth in relation to motor areas – a multimodal approach

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Introduction: Glioma cells are able to grow towards blood-supply-sufficient microenvironments and hypoxic conditions within the tumor increase the invasiveness and motility of cancer cells. Since neuronal activity induces a higher regional blood flow and oxygenation level in the respective area we examined if glioma recurrences show a bias to grow towards motor-eloquent areas.

Methods: 60 patients with motor-eloquent high-grade gliomas and tumor recurrences were enrolled. All patients underwent magnetic resonance imaging (MRI), navigated transcranial magnetic stimulation (nTMS)

for motor mapping, and nTMS-based tractography prior to surgery and suffered a relapse. To examine recurrence growth direction and speed in relation to motor-eloquent structures, all imaging data were fused. Measurements from the postoperative excision cavity edge to the farthest point reached by the recurrence were conducted and set into relation to the mapped motor areas. Measurements facing towards this region were defined as positive values, measurements facing away from it were included as negative values. According to postoperative MRI, patients were separated into three groups: patients without a residual tumor (group 1), patients with a residual tumor moving away from motor areas (group 2), and patients with a residual tumor moving towards motor areas (group 3).

Results: Average growth towards motor areas mapped by nTMS was 2.1 ± 4.5 mm/month in the FLAIR sequences and 2.2 ± 6.1 mm/month in the contrast-enhanced T1-weighted sequences. The rate of patients with the biggest extent of growth going towards motor areas differed significantly between the three groups with 81.3% in group 1, 28.6% in group 2, and 100% in group 3 regarding FLAIR sequences ($p=0.0108$).

Conclusion: This study suggests a new strategy to predict tumor regrowth patterns involving functional brain regions, which could improve the planning of both surgery and radiotherapy in the future.

674. Expression of PDL-1 on Pituitary Adenomas: A Role for Immunotherapy

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Introduction: Cushing's disease (CD) affects millions of people annually, causing hypertension, obesity, and even early death. First-line treatment for CD is surgical adenectomy, but 25% of these patients will recur within 5 years, many failing subsequent therapies. Our finding here of PDL-1 expression on pituitary adenomas provides a promising novel immunotherapeutic target for treatment.

Methods: For human studies, immunohistochemistry (IHC) was used to determine the expression of PDL-1 in 19 human pituitary adenoma samples, including 9 ACTH-secreting adenomas. For murine in vitro studies, the ACTH-secreting pituitary adenoma ATT20/D16v cell line was assayed by flow cytometry and RT-qPCR. For in vivo studies, ATT20/D16v cells were implanted into the flank of A/HeJ x C57L/J F1 mice. Tumor volume and mouse weight were assessed over time. PDL-1 levels were assessed by the same methods on harvested tumors as well as from control mouse pituitary glands.

Results: Our data reveal the upregulated expression of PDL-1 on pituitary adenomas of both patients and mice compared to normal pituitary. Human pituitary adenomas demonstrate significant (i.e. $\geq 1\%$ staining) PDL-1 expression in 32% of samples, including 22% of ACTH-secreting adenomas. Similar findings are observed in mice, where the ATT20/D16v cell line, when grown either in vitro or subcutaneously in vivo, demonstrates elevated PDL-1 expression. Furthermore, mice implanted with such tumors develop clinical signs of Cushing's disease.

Conclusion: PDL-1 is found significantly elevated on ACTH-secreting pituitary adenomas in patients and mice, and is anticipated to represent a viable immunotherapeutic target. A newly established model of murine Cushing's disease will permit pre-clinical evaluation of anti-PDL-1 monoclonal antibodies.

675. Effect of an immersive preoperative virtual reality experience on patient reported outcomes: a Randomized Controlled Trial

Kimon Bekelis, MD; Daniel Calnan; Nathan Simmons; Todd Mackenzie; George Kakoulides (Philadelphia, PA)

Introduction: There is a scarcity of well-developed quality improvement initiatives targeting patient satisfaction. We investigated the effect of exposure to a virtual reality (VR) environment preoperatively on patient-reported outcomes for surgical operations.

Methods: We performed a randomized controlled trial of patients undergoing cranial and spinal operations in a tertiary referral center. Patients underwent a 1:1 randomization to an immersive preoperative VR experience or standard preoperative experience stratified on type of operation. The primary outcome measures were the EVAN-G and the APAIS scores, as markers of the patient's experience during the surgical encounter.

Results: During the study period, a total of 127 patients (mean age 55.3 years old, 41.9% females) underwent randomization. The average EVAN-G score was 84.3 (SD 6.4) after VR, and 64.3 (SD 11.7) after standard preoperative experience (difference, 20.0; 95% CI, 16.6 to 23.3). Exposure to an immersive VR experience also led to higher APAIS score (difference, 29.9; 95% CI, 24.5 to 35.2). Additionally, VR led to lower preoperative VAS stress score (difference, -41.7; 95% CI, -33.1 to -50.2), and higher preoperative VAS preparedness (difference, 32.4; 95% CI, 24.9 to 39.8), and VAS satisfaction (difference, 33.2; 95% CI, 25.4 to 41.0) scores. No association was identified with VAS stress score (difference, -1.6; 95% CI, -13.4 to 10.2).

Conclusion: In a randomized controlled trial, we demonstrated that patients exposed to preoperative VR had increased satisfaction during the surgical encounter. Harnessing the power of this technology, hospitals can create an immersive environment that minimizes stress, and enhances the perioperative experience. Trial Registration. ClinicalTrials.gov ID NCT02619708.

676. Toll-like Receptor 9 Antagonism Inhibits Spinal Cord Astrocyte Proliferation and Migration

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Introduction: The glial scar is considered as an impediment to axonal regeneration, albeit studies also show that astrocytes are necessary for axonal re-growth following spinal cord injury (SCI). The principal cell type in the glial scar are proliferating and migrating reactive astrocytes, which secrete both helpful and harmful effectors. Modulation of astroglial proliferation and migration can alter the properties of the glial scar and influence the outcomes of SCI. Evidence indicates that Toll like receptors (TLRs), which are expressed by SC neurons, glia and infiltrating cells, play important roles in SCI. Our laboratory has previously shown that a TLR9 antagonist, CpG ODN 2088, administered intrathecally, improves the functional and histopathological outcomes of SCI, and attenuates the pro-inflammatory phenotype of SC astrocytes, in vitro, through direct actions. The current studies were undertaken to determine whether the TLR9 antagonist modulates astroglial functions pertinent to glial scar formation such as proliferation and migration.

Methods: Mixed glial cultures, derived from the SC of postnatal day 2-3 mouse pups were used to isolate astrocytes, which were passaged three times for 99% purification. Astrocyte cultures were incubated in Minimum Essential Medium containing 1% heat inactivated fetal bovine serum, in the presence or absence of CpG ODN 2088. EdU, a thymidine analogue was used to label proliferating cells whereas a scratch-wound assay and live cell imaging were utilized to assess the astroglial migration.

Results: CpG ODN 2088 significantly reduced by 40% the number of proliferating astrocytes ($p<0.001$; $n=4$). The antagonist also significantly decreased the astroglial migration into the gap formed by the scratch. These effects necessitated TLR9 since CpG ODN 2088 did not affect the proliferation or migration TLR9-/- astrocytes.

Conclusion: Astroglial TLR9 antagonism inhibits both proliferation and migration, in vitro. Thus, CpG ODN 2088 has the potential of targeting astrocyte functions pertinent to glial scar formation.

677. Anterior Cranio-Vertebral Junction Lesions: Can Endoscopy Expand the Indications for Surgery or Improve the Standard Technique?

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Introduction: Extended endoscopic endonasal approaches (EEA) are increasingly being used to address anterior craniovertebral junction (CVJ) pathologies. The variations of EEA and how these may expand the indications and change the standard technique in the surgical approaches to CVJ are discussed.

Methods: From 2009 to 2015 41 consecutive patients presenting anterior CVJ disorders underwent EEA alone or combined with open approaches at our institution. 22 tumors including: 5 ventral foramen magnum / clivus meningiomas, 8 chordomas and 9 metastases. Six patients underwent a combined anterior transcervical - endoscopic endonasal screw fixation approach for non union of odontoid fractures. The EEA was used in 12 patients with irreducible compression of the brainstem by the odontoid process. An endoscopic endonasal odontoidectomy was carried out with preservation of anterior C1 arch in all patients. We report a resection of a ventral pontine cavernous malformation via an EEA.

Results: Gross total removal was achieved in 4 meningiomas, in 6 chordomas and in 5 patients with metastases. Partial resections with adequate decompressions were achieved in all others patients. The most frequent complication was cerebrospinal fluid leakage in 2 patients with meningiomas. The radiological follow-up revealed a regular ossification in cases of C2 fractures and no evidence of spinal instability. Adequate bulbar-medullary decompressions were achieved in all patients with preservation of anterior C1 arch, in absence of instability and posterior fixation.

Conclusion: The transnasal endoscopic technique may represent an alternative approach to traditional open posterior and posterolateral approaches or the transoral approach for resection of ventral CVJ tumours. In contrast to the transoral approach, EEA also ensures adequate exposure of CVJ avoiding threatening complications. Moreover EEA allows the preservation of the anterior C1 arch, thus avoiding cranial settling, subaxial instability and the necessity for posterior fusion.

678. A novel tractography-based targeting method for focused ultrasound thalamotomy: Clinical outcomes

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Introduction: Focused ultrasound ablation (FUSA) of the ventral intermediate nucleus (VIM) was recently approved for the treatment of refractory essential tremor. Although transformative, this technology has reinvigorated the debate related to the safety and efficacy of lesioning procedures. Tractography-based VIM (T-VIM) targeting methods may address some of these concerns.

We prospectively targeted T-VIM with FUSA hypothesizing that it is safe and efficacious.

Methods: All patients underwent preoperative imaging (3-D T1 and DWI (60 directions, 2 mm isovoxel), Philips Ingenia CX). The lateral and posterior borders of VIM (pyramidal tract and medial lemniscus respectively) were visualized with streamline tractography (Stealth Viz, Medtronic Inc.). We placed a VIM seed 3 mm away from these borders and confirmed its structural connectivity with the motor cortex and dentate nucleus. The coordinates of T-VIM were noted for surgical targeting. We analyzed targeting coordinates (standard and T-VIM), clinical tremor scale (pre-, intraoperative, and post operative), and side effect profile. Continuous variables were compared with T-test and categorical variables with Chi-squared test and $p < 0.05$ was considered as statistically significant.

Results: T-VIM targeting was successful in 9 out of 10 patients. T-VIM

was more anterior than the standard coordinates (7.6 ± 1 versus 6.7 ± 0.3 mm anterior to posterior commissure). Therapeutic sonications ($>55^\circ\text{C}$ temperature for 10 seconds) of T-VIM improved intraoperative tremor ($>50\%$ improvement) without motor or sensory side-effects. Sustained significant improvement in tremor scores was observed at one month (preop CRST 59.3 ± 17.3 vs. 29.7 ± 11.6 , two tailed t-test $p=0.004$) and 3 months ($n=9$, CRST 26.9 ± 15.4 , two tailed t-test $p=0.0006$). No motor weakness and sensory deficits related to FUSA were observed during follow-up.

Conclusion: This is the first report of prospective T-VIM targeting for focused ultrasound thalamotomy. Our results suggest that T-VIM targeting is safe, reliable with satisfactory short-term clinical outcomes.

679. Flow, Liver, Flow: The Interplay of Liver Disease and Coagulopathy in Chronic Subdural Hematoma

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Introduction: Chronic subdural hematoma (cSDH) is a common neurosurgical ailment, with an increased incidence in the rapidly-expanding elderly population. While many factors influencing cSDH recurrence have been analyzed, a recent study uncovered a relationship between liver disease and recurrence. Here, we explore that relationship in an attempt to identify recurrence predictors in at-risk patients. We hypothesized that the association between liver disease and recurrence was due to coagulopathy secondary to liver disease.

Methods: We retrospectively reviewed all cSDH patients treated with burr-hole drainage by two surgeons between 2007-2015. Comorbidities and laboratory findings for each patient were examined by Pearson's chi-squared analysis or Mann-Whitney tests.

Results: There were 261 cSDH in 215 patients included. Patients had a mean age of 65.6 years and 72% were male. Sixteen cSDH required repeat surgery (6.1%). There were 123 coagulopathic patients (47.1%), and 14 had pre-existing liver disease (5.4%). All patients with liver disease were also coagulopathic ($p < 0.001$). Liver disease was associated with recurrence, with a relative risk of 4.07 ($p = 0.014$). Coagulopathic patients with liver disease were more likely to recur than patients with coagulopathy alone ($RR = 4.09$, $p = 0.019$), or non-coagulopathic patients ($RR = 4.89$, $p = 0.010$). Patients with liver disease had significantly elevated prothrombin time ($p = 0.013$) and reduced platelet counts ($p = 0.0001$). Thrombocytopenia remained significant in a multivariate analysis ($p = 0.0002$). Platelets were also reduced in coagulopathic patients with liver disease, as compared to those with coagulopathy alone ($p = 0.002$).

Conclusion: Liver disease is significantly associated with cSDH recurrence. While coagulopathy alone does not predict recurrence, patients with coagulopathy in the presence of liver disease are at higher risk for recurrence than those with coagulopathy alone. The effect of liver disease is reflected in certain hematologic lab values.

680. Optimizing Near-Infrared Optical Contrast Via "Second-Window ICG" for Glioma with both Intracranial Murine Model and Human Clinical Trial

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Introduction: Because of limitations of visible light spectrum dyes in fluorescent-guided surgery, our lab has focused on near-infrared (NIR) contrast agents. We utilized the enhanced permeability and retention effect for delivery of an FDA-approved NIR fluorescent dye to tumors. Previous pre-clinical studies using subcutaneous tumor models concluded that the optimum signal to background ratio (SBR) occurs 24 hours following dye administration. We extended this work to the intracranial environment in an effort to optimize the Second Window ICG technique for fluorescent guided brain surgery.

Methods: Intracranial tumors were established and confirmed via bio-

luminescence in 10 mice using U251-Luc-GFP. Rodents were visualized with PerkinElmer IVIS and VisionSense IridiumTM systems at multiple time points up to 72 hours later. Fifteen human patients with glioma were enrolled in a clinical study and infused with 5mg/kg ICG the day prior to surgery. The main tumors and surgical margins were visualized intraoperatively. Signals were analyzed posthoc using VisionSensePlayer, ImageJ and LivingImage softwares. Pathology was used as the gold standard to determine the accuracy of NIR fluorescence in identifying tumor.

Results: In the mice, intracranial tumors could be visualized as early as three hours post-injection (SBR=3.6), with peak contrast emerging twelve hours post-injection (SBR=9.5). In human gliomas, NIR-imaging was performed 24±4 hours after injection. 12/15 tumors displayed positive fluorescence (mean SBR=9.5). The average SBR for tumors visualized prior to 23 hours post-infusion was higher than those imaged after. NIR visualization of the main tumor and margins demonstrated 98% sensitivity (n=71).

Conclusion: The "Second-Window ICG" technique can be used to identify glioma and residual disease intraoperatively, with sensitivity better than visible light alone. Contrasting previous findings, and based on the data from our murine model and human clinical trial, we hypothesize that optimal imaging may be achieved earlier than 24 hours.

681. Effects of Employment Status on Surgical Effectiveness, 30-Day Readmission and Patient Reported Outcomes

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Introduction: Growing scrutiny has placed hospitals at the center of readmission prevention, as 30-day readmission rates are increasingly being used as a proxy for quality of care delivered. The relationship between pre-operative employment status, length of hospital stays and 30-day readmission rates after elective spine surgery remains unclear.

Methods: The medical records of 360 patients (Employed:n=174, Unemployed:n=70, Retired:n=40, Disabled:n=76) undergoing elective spine surgery at a major academic medical center were reviewed. Patient demographics, comorbidities, and post-operative complication rates were recorded. All patients had comprehensive 1-year patient reported outcomes measures. We hypothesized that employment status is associated with decreased length of hospital stay and decreased risk of 30-day readmission after elective spine surgery. All-cause readmissions within 30 days of discharge was the primary outcome variable.

Results: Baseline characteristics were similar in all cohorts. There was no difference in operative time, estimated blood loss, or number of fusion levels between all patient cohorts. There were no significant differences in peri-operative complication rates between patient cohorts. On average, the length of hospital stay was shorter for the employed compared to non-employed patients (4.89 days vs. 5.26 days). The rate of 30-day readmission was 2-fold greater unemployed compared to employed patients (5.17% vs. 10%). At 1-year after surgery, employed patients were more likely to express functional improvement (change in ODI score) compared to unemployed patients (ODI: employed: 33.80 vs. unemployed: 41.93).

Conclusion: Our study suggests that employment status may be associated with shorter duration of hospital stay, lower 30-day readmission rates and greater functional improvement.

682. Frail Patients Achieve Greater Health Related Quality of Life Improvement Following Adult Spinal Deformity Surgery

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Introduction: The ASD-FI is a risk stratification tool which predicts major complications and prolonged hospital length of stay. The impact of frailty on postoperative improvement in HRQOL is unknown.

Methods: ASD patients who underwent ≥ 4 level instrumented fusion and had minimum 2-year follow-up were stratified by ASD-FI score into categories: not frail 0-3 (NF); frail 3-5 (F); and severely frail >5 (SF). We compared baseline demographic, HRQOL, and radiographic parameters. The primary outcome measure was reaching substantial clinical benefit SCB (SCB) in ODI, SF-36 PCS, back and leg pain. Secondary outcomes included: absolute and change in ODI, PCS, MCS, back and leg pain. SCB thresholds for outcome following lumbar fusion were utilized.

Results: 332 patients were identified with 2-year follow-up: 135 NF, 175 F, and 22 SF. F and SF patients were significantly older, had more comorbidities, worse baseline HRQOL and pain scores (e.g. ODI 69.5, 52.5, 27.6 for SF, F, and NF; $p<0.0001$), and worse radiographic deformity (e.g. SVA 130.5, 85.9, and 28.4mm for SF, F, and NF; $p<0.0001$). At 2-years, ODI, PCS, MCS, back and leg pain were all worse in F/SF than NF patients. More NF than F patients reached SCB for back pain (63.4 vs. 57.5%; $p=0.045$) whereas more F than NF reached SCB for ODI (43.7 vs. 29.3%; $p=0.025$), PCS (56.9 vs. 51.2%; $p=0.03$), and leg pain (45.8 vs. 23.0%; $p=0.003$). SF patients were least likely to achieve SCB for ODI (28.6%), PCS (18.2%), and back pain (28.6%).

Conclusion: Despite higher preoperative risk stratification scores, worse baseline HRQOL scores, and greater complication rates, frail patients experience greater improvement in HRQOL and likelihood of reaching substantial clinical benefit compared to non-frail patients.

683. Hold that thought: Human subthalamic nucleus beta oscillations are coherent with lateral cortex during working memory inhibition

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Introduction: There is growing evidence that the subthalamic nucleus, together with cortical areas, plays a role in preventing or delaying motor responses. The roles the STN may play in non-motor cognition, however, remain relatively unexplored. Here we examine whether the coordinated activity between the cortex and STN modulates the inhibition of memory.

Methods: We simultaneously captured STN single-unit spiking, STN local field potentials, and cortical electrocorticography during DBS surgery as patients performed a novel working memory task. Subjects were sequentially shown 8 numbers and asked to either encode or ignore each number based on a simultaneously presented shape.

Results: During all correct trials, we observed a decrease in beta band (15-30 Hz) activity in the STN, the frontal cortex, and the lateral cortex. Crucially, this decrease was reversed to an increase in both the lateral cortex and the STN during the ignore trials. These two areas also showed increased beta band coherence during the ignore trials. Furthermore, the spiking of the STN neurons was also modulated during the task. In the neurons that demonstrated a decrease in firing rate, we observed decreased beta band oscillatory spiking activity during the task, which notably was also reversed during the ignore trials.

Conclusion: In line with previously held notions that the STN acts as a gate that influences whether or not an action occurs, our results suggest that the same beta band gating mechanisms that inhibit movement in both motor control and pathological states such as Parkinson's disease may also play a role in inhibiting memory encoding.

684. Carbamylated Erythropoietin (CEPO) Promotes Neuroplasticity after Traumatic Brain Injury in Rats

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Introduction: Carbamylated erythropoietin (CEPO) is a carbamylated derivative of erythropoietin which shares the neuroprotective properties of erythropoietin but lacks any hematopoietic effects. This study was designed to investigate the neurorestorative effects of CEPO after traumatic brain injury (TBI) in rats.

Methods: Adult male Wistar rats (n=16) were injured with controlled cortical impact (CCI) and treated either with CEPO (50 mg/kg) or saline (control). Treatment was administered intraperitoneally 6, 24 and 48 hours after injury. A sham group (n=8) underwent sham surgery without injury and received no treatment. Neuromotor function and spatial learning were assessed using modified Neurological Severity Score (mNSS) and Morris Water Maze (MWM) tests, respectively. All animals were sacrificed 35 days after surgery, and sections were stained for immunohistological analysis. To examine whether CEPO activates the Sonic hedgehog signaling pathway (Shh/Gli1) and proneuronal basic helix-loop-helix (bHLH) gene Mash1, real-time polymerase chain reaction (RT-PCR) and Western blot analyses were performed on extracts from rat neural progenitor cells treated with CEPO (10 ng/ml), *in vitro*.

Results: There was statistically significant improvement in neuromotor function (mNSS) and spatial learning (MWM) in animals treated with CEPO compared to control ($p < 0.05$). CEPO treatment also significantly reduced lesion volume ($p < 0.05$) and enhanced neurogenesis ($p < 0.05$) as well as angiogenesis ($p < 0.05$). *In vitro* RT-PCR and Western blot analysis showed that CEPO activates Shh/Gli1 pathway and bHLH gene Mash1 in rat neural progenitor cells.

Conclusion: CEPO enhances functional recovery after TBI in rats. It facilitates brain remodeling by enhancing neurogenesis and angiogenesis, possibly through upregulating Shh/Gli1 signaling pathway.

685. Improvement of Frontline Therapy for GBM by Targeting the DNA Damage Response

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Introduction: The DNA Damage Response (DDR) induced by temozolomide (TMZ) or ionizing irradiation provides opportunities to therapeutically target activated signaling networks of the DDR. Our laboratory has identified a novel combination therapy that targets the Akt-Mdm2 signaling network in the context of TMZ. Inhibitors of Akt and Mdm2 were selected based on structural properties related to blood-brain barrier permeability, and pharmacokinetic profiles of plasma, normal brain, and intracranial GBM tumors.

Methods: Molecularly characterized GBM cell lines (GBM10, GBM43, and GBM26) were used to determine the effect of frontline therapy in combination with Akt (GDC0068) and Mdm2 (RG7112) inhibitors. Effect on cell growth was determined *in vitro* by methylene blue staining and *in vivo* by intracranial xenografts in NOD/SCID gamma null mice. Inhibitor levels in tissues were determined by HPLC/mass spectrometry.

Results: TMZ and ionizing irradiation activate the DDR which leads to activation of Akt and increased Mdm2. Isobolograms and combination indices indicated that Akt (GDC0068) and Mdm2 (RG7112) inhibitors either together or in combination with TMZ, resulted in synergistic inhibition of cell growth in both mtp53 and wt53 GBM cell lines. When RG7112 and GDC0068 (at a ratio of 0.5:1) were combined with TMZ, strong synergism was evident at multiple dose-ratios. For *in vivo* studies, an intermittent dosing regimen of TMZ+RG7112+GDC0068 was developed to avoid normal tissue toxicity. Mice with GBM43 intracranial tumors were treated 3 × weekly for 2 weeks. Combination of TMZ+RG7112+GDC0068 significantly delayed tumor progression. In mice with GBM43 intracranial tumors, survival was significantly increased by GDC0068+RG7112 (13 days), and further increased by TMZ+RG7112+GDC0068 (24 days) compared to TMZ alone (n=8-9 per group, $p < 0.05$).

Conclusion: These data suggest that blocking the Mdm2-Akt signaling network in the context of TMZ-mediated DNA damage holds therapeutic promise. Studies to identify mechanism and appropriate biomarkers of response are in progress.

686. Efficacy of Intraoperative Epidural Triamcinolone Application in Lumbar Microdiscectomy: a Matched-control Study

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Introduction: The aim of this study is to investigate whether the intraoperative application of epidural steroids (ES) on the decompressed nerve root improves subjective and objective clinical outcomes after lumbar microdiscectomy.

Methods: Retrospective analysis of a prospective, two-center database, including consecutive patients undergoing lumbar microdiscectomy. All patients who had received ES (40mg triamcinolone; intervention group) were matched to patients who had not received ES (control group). Back and leg pain (visual analog scale), functional impairment (Oswestry (ODI) and Roland-Morris disability index (RMDI), and health-related quality of life (hrQoL; SF-12 physical component score (PCS) and Euro-Qol index) were measured at baseline, postoperative day three (D3) and week six (W6). Objective functional impairment (OFI) was determined using age- and sex-adjusted T-scores.

Results: 53 patients with ES were matched with 101 control subjects and there were no baseline group differences. On D3, the intervention group had less disability on the RMDI (7.4 vs. 10.3, $p = 0.003$) and higher hrQoL on the SF-12 PCS (36.5 vs. 32.7, $p = 0.004$). At W6, the intervention group had less disability on the RMDI (3.6 vs. 5.7, $p = 0.050$) and on the ODI by trend (17.0 vs. 24.4, $p = 0.056$), better hrQoL, determined by the SF-12 PCS (44.3 vs. 39.9, $p = 0.018$), and lower OFI (T-score 100.5 vs. 110.2, $p = 0.005$). While complications were similar, there was a tendency for shorter hospitalization in the intervention group (5.0 vs. 5.8 days, $p = 0.066$).

Conclusion: Intraoperative application of ES on the decompressed nerve root is an effective adjunct treatment to lower functional disability and increase hrQoL after lumbar microdiscectomy.

687. Postoperative Emergency Department Utilization After 7,294 Cranial Neurosurgery Procedures at a Tertiary Neuroscience Center

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Introduction: Hospital re-admission and the reduction thereof has become a major quality improvement initiative in neurosurgery. However, little research has been performed on why neurosurgical patients utilize hospital emergency departments (ER) with or without subsequent admission in the post-operative setting.

Methods: Retrospective, single-center review of all surgical cranial procedures performed from 6/2013–6/2016 in patients who survived to discharge. The study was approved by our institutional review board.

Results: We identified 7,294 cranial procedures performed during 6,596 hospital encounters. The rate of post-operative emergency department use within 30 days after surgical hospitalization across all procedure types was 13.6%. The most common presenting complaints were pain control (33%), medical complication (19.5%), and altered mental status (11.2%). We constructed a multivariable backward-elimination logistic regression model utilizing surgical procedure type, length of hospitalization, patient age, gender, ASA classification, Severity of Illness (SOI) score, and Risk of Mortality (ROM) score. In this model, increased age (OR 0.988, $P < 0.0001$) and deep brain stimulation electrode placement (OR 0.506, $P = 0.0009$) were associated with less ER utilization. Ommaya placement (OR 2.72, $P = 0.0009$), cranial shunt placement (OR 1.37, $P = 0.0002$), and SOI score (OR 1.15, $P = 0.022$) were associated with increased ER utilization.

Conclusion: We report the rates of and reasons for ER utilization in post-operative cranial neurosurgical patients. We identified risk factors and protective factors associated with return to the ER after cranial surgery. Most established patient risk metrics did not predict ER utilization. These findings will direct future quality improvement via prospective implementation of care pathways for high-risk procedures.

688. The effect of smoking status on instrumentation success after rhBMP-2 supplemented lumbar fusion constructs

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Introduction: The primary objective of this study is to examine the effects smoking status on rhBMP-2 supplementation in spinal fusion constructs.

Methods: Patient records were retrospectively reviewed for a consecutive set of patients who underwent first-time posterolateral, instrumented fusion of the lumbar spine for degenerative spinal disease. All operations included arthrodesis supplementation with rhBMP-2. All patients were followed for at least two years. The primary endpoint of this study was reoperation for pseudarthrosis, instrumentation failure, and/or adjacent segment disease. Following rigorous sensitivity analysis, measure of association was calculated with a multivariable logistic regression controlling for smoking, age, and number of spinal levels fused.

Results: Of the 110 patients in the study population, 82 (74.6%) were non-smokers and 28 (25.5%) were smokers. Among perioperative predictors, smokers were younger in age (53.9 ± 9.6 vs 61.1 ± 13.1 , $p=0.008$) and had shorter length on inpatient hospital stay (4.1 ± 1.8 vs 5.3 ± 3.0 , $p=0.039$). After a mean follow up of 59 months, the 32% incidence of reoperation for pseudarthrosis, instrumentation failure, and/or adjacent segment among smokers was statistically significantly higher than the 13.4% incidence in non-smokers ($p=0.027$). Following multivariable logistic regression, the odds of reoperation among smokers was 4.75 times higher than non-smoker ($p=0.009$, 95% Confidence Interval [1.48–15.24])

Conclusion: While rhBMP-2 supplements arthrodesis of instrumented lumbar fusion constructs, smoking status ascertains the strongest predictor of reoperation for pseudarthrosis, instrumentation failure, and/or adjacent segment.

689. Noninvasive neuromodulation and thalamic mapping with low intensity focused ultrasound

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Introduction: Ultrasound has long been known to influence the activity of electrically excitable tissues. Advances in ultrasound technology have renewed an interest in focused ultrasound applications in the brain. Acoustic energy can inhibit and stimulate neural tissues by non-thermal mechanisms. Thus transcranial focused ultrasound could potentially be safely used to noninvasively map the brain. The objective of this study was to demonstrate the effects of low intensity focused ultrasound (LIFU) for neuromodulation.

Methods: Eight Yorkshire swine were used in two cohorts of experiments. In the first cohort, the ventrolateral sensory thalamus was stereotactically targeted with LIFU, and somatosensory evoked potentials (SSEPs) were recorded from an epidural grid electrode. In the second cohort, the ventromedial (trigeminal) and ventrolateral (tibial) sensory thalamic nuclei were alternately targeted, while recording SSEPs. Upon completion electrophysiological experiments, the contralateral thalamus was imaged using magnetic resonance thermography during LIFU and HIFU sonications to assess tissue heating at the acoustic focus. Tissues were assessed histologically for damage.

Results: In the first cohort, LIFU targeting the ventrolateral thalamic nucleus inhibited SSEPs to $71.6 \pm 11.4\%$ compared to baseline recordings. In the second cohort, we found that the ventromedial thalamic nucleus could be inhibited without effecting the ventrolateral nucleus, and vice versa. Trigeminal SSEPs were inhibited to $76.9 \pm 7.5\%$ of baseline recordings while tibial SSEPs were unchanged. Similarly, when the ventrolateral thalamic nucleus was targeted, trigeminal SSEPs were unchanged, how-

ever tibial SSEPs were reduced to $83.9 \pm 4.3\%$ baseline. During magnetic resonance thermography imaging, there was no observed tissue heating during LIFU sonications.

Conclusion: These results suggest that low intensity focused ultrasound can be safely used to modulate neuronal circuits in the central nervous system and that noninvasive brain mapping with focused ultrasound is feasible for use in humans.

690. Electrical Modulation of the Trigeminal Nerve as a Novel Resuscitation Strategy for Acute Blood Loss

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Introduction: Hemorrhagic shock (HS) remains the major cause of preventable death after trauma. Despite significant progress in trauma resuscitation there are limited options for the treatment of HS in the critical early hours after injury. Trigeminal nerve has previously been linked to body's innate oxygen conserving reflex and pressor response via its projection to rostral ventrolateral medulla (RVLM). Neuromodulation via this pathway as a novel resuscitation strategy has never been studied before. In this study, we explore trigeminal nerve stimulation (TNS) as a resuscitative approach in a hemorrhagic shock model.

Methods: A volume controlled HS model (50% of the total blood volume removal over 20 minutes) was developed using male Sprague-Dawley rats. Animals were divided into three groups: (1) sham, (2) HS, and (3) HS with TNS. TNS was performed by introducing two needles (26G) subcutaneously bilaterally along the V1 distribution. Electrical pulses (0.5ms) were delivered at 25Hz, 4V continuously. The 3-hour survival rate, plasma nor-epinephrine (NE), lactate dehydrogenase (LDH), aminotransferase (AST) and creatinine were quantified 2 hours post-hemorrhage.

Results: Acute hemorrhage produced mean arterial pressure (MAP) decrease from 115.0 ± 18.7 to 38.3 ± 10.4 mmHg ($n=21$). Fifteen minutes of TNS after HS increased MAP from 38.3 ± 10.4 to 68.3 ± 14.2 mmHg ($p=0.014$; $n=17$). TNS improved the survival rate significantly (HS vs. HS+TNS: 15.4% vs. 64.7%; $n=30$, $p<0.05$). TNS was associated with significant decreases in organ damage markers (LDH: 155.5 ± 31.0 vs. 42.3 ± 14.6 U/L; AST: 90.9 ± 18.1 vs. 44.3 ± 5.2 U/L; Creatinine: 0.945 ± 0.007 vs. 0.89 ± 0.06 mg/dl; $n=5$, $p<0.05$). Plasma NE level was decreased in TNS group (14.4 ± 3.3 vs. 5.9 ± 2.5 ng/ml; $n=4$, $p<0.05$).

Conclusion: This study demonstrates that electrical TNS may be beneficial in attenuating end-organ damage and improving survival after severe HS.

691. NF2 Disruption by Genomic Rearrangements Drives a Subset of Radiation-Induced Meningiomas

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Introduction: Majority of pediatric cancers require the irradiation of the central nervous system (CNS), and as more patients survive into adulthood from improved oncological therapy there is an increasing prevalence of the sequelae of radiation therapy. Radiation-induced meningiomas (RIMs), one such secondary effect, demonstrate a clinically more aggressive behaviour than sporadic meningiomas (SMs). We aimed to describe the genomic mutational landscape of RIMs.

Methods: We analyzed a principal cohort of 18 RIMs, with 31 RIMs overall, from patients who received childhood radiation therapy and 30 SMs, as a comparator population. We performed a multiplatform integrative genomic analysis; including methylation, whole exome and RNA sequencing.

Results: RIMs exhibited a five-fold increase in copy number alterations, the loss of chromosome 1p (17/18 RIMs) and 22q (17/18 RIMs), which was

significantly more than observed in sporadic meningiomas. Furthermore, RNA sequencing data revealed an NF2 gene fusion event in 35.3% of RIMs. In all 6 cases, there was a complete NF2 exon spliced into a complete exon of a reciprocal gene, suggesting that the breakpoints of genomic rearrangement are intronic. All tumours with the NF2 fusion also possessed monosomy of chromosome 22q, rendering the cells with homozygous disruption of NF2. Clinically, RIMs with the NF2 fusion exhibited ill-defined borders and a tendency to develop in anatomic frontal location. Also, targeted sequencing panel confirmed that RIMs had fewer nonsynonymous NF2 mutations (6.5% vs. 30% in SM) and absence of mutations in TRAF7, SMO, KLF4, PIK3CA and AKT1, genes traditionally involved in SMs.

Conclusion: Our study demonstrates that RIMs have distinct genomic drivers of oncogenesis as compared to SMs, specifically NF2 inactivation through fusion event. Radiation therapy possibly triggers genomic structural rearrangements through error-prone repair of double-stranded DNA breaks.

692. Impact of Gender Disparities on Short- and Long-Term Patient Reported Satisfaction and Outcome Measures After Elective Spine Surgery: A Single Institutional Study of 384 Patients

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Introduction: Identifying patient factors and disparities that may influence postoperative outcomes and patient reported outcomes (PROs) is important. The aim of this study was to determine whether there is a difference between men and women in three-month and on-year PROs and satisfaction after elective spine surgery.

Methods: This was a retrospectively analyzed study from a maintained prospective database. The medical records of 384 patients who underwent elective spine surgery at a major academic institution were included in this study. Patients were categorized by gender, with 199 (51.8%) males and 185 (48.2%) females. Patient demographics, comorbidities, post-operative complication rates, and discharge were collected. PRO instruments (ODI, VAS-BP/LP, EQ-5 VAS, and EQ-5D) were completed before surgery, then at 3- and 12-months after surgery along with patient satisfaction measures.

Results: Baseline patient demographics and comorbidities, and intra-operative variables and complications were similar between both cohorts. Baseline PRO measures were different between both cohorts, with Female-cohort having greater ODI ($p < 0.0001$) and VAS-BP ($p = 0.0004$), and a lower EQ-5D ($p = 0.0001$). The mean change of baseline and three-month PROs were similar between both cohorts for all measures. At one-year follow up, the Male-cohort had a significantly greater mean change in VAS-LP ($p = 0.04$), along with greater VAS-BP ($p = 0.06$) and EQ-5 VAS ($p = 0.054$) scores. At one-year a significantly higher portion in the Male-cohort found that surgery met their expectations, compared to the Female-cohort (65.0% vs. 49.5%, $p = 0.02$).

Conclusion: Our study suggests that there may be a difference in perception of health, pain and disability between males and females at baseline, short- and long-term follow up which may influence overall patient satisfaction.

693. Motorcycle Helmets and Cervical Spine Injuries: A Five Year Experience at a Level One Trauma Center

Paul Page, MD; Zhikui Wei, MD; Nathaniel Brooks, MD (Madison, WI)

Introduction: Motorcycle helmets have been shown to decrease the incidence and severity of brain injury after crashes. However, some data and speculation still exists suggesting that their use is associated with a higher likelihood of cervical spine injury. This information is frequently utilized to argue against universal helmet laws in states without them. Herein, we examine cervical spine injuries over a five year period at a level one trauma center to shed further light on if a correlation between helmet use and cervical spine injuries exist.

Methods: We performed a retrospective review of all patients with motorcycle crashes evaluated at one level 1 trauma center from January 1st 2010 to January 1st 2015. Biometric, clinical, and imaging data were

collected. Patients were divided into two distinct groups, helmeted and unhelmeted. Baseline and functional characteristics were compared between the two groups. Student t test was used for continuous variables and the X2 test was used for categorical variables to statistical analysis.

Results: In total 1064 patients were examined with 735 being unhelmeted (69.1%) and 329 being helmeted (30.9%). On average helmeted riders had a much lower injury severity score (ISS) 9.63 $\pm$ 8.52 vs 13.8 $\pm$ 11.5 ($p < 0.0001$). Among these two groups, cervical spine fractures occurred in 4.3% of helmeted riders compared with 10.8% of unhelmeted riders ($p < 0.001$).

(Relative Risk Ratio [RRR] = 2.67; 95% confidence interval [CI]: 1.5 - 4.6). Additionally, the incidence of fractures of C5 and C6 was significantly lower ($p < 0.05$). There was no statistical difference regarding the incidence of thoracic or lumbar fractures ($p < 0.05$).

Conclusion: Helmeted motorcyclists demonstrated a statistically significantly lower ISS and incidence of cervical spine fractures. This information provides further evidence that helmet use is not associated with a higher incidence of cervical spine fractures.

694. Insights from Sham Surgery: Observer Bias and Placebo Response in Essential Tremor and Parkinson's Disease

Aaron E Bond, MD, PhD; Mor Dayan, BSc; W Elias, MD (Charlottesville, VA)

Introduction: Placebo response has previously been observed in essential tremor and Parkinson's disease. We investigated the observer bias and placebo response from two randomized sham-controlled trials of focused ultrasound for ET and PD.

Methods: Observer bias was determined by comparing the tremor scores in the ET trial between the blinded video and blinded site reviewers. Placebo response was determined by comparing the 3 month changes in tremor scores, UPDRS scores, disability scores and quality of life scores in the sham surgery cohorts.

Results: A significant observer bias was measured even with blinded site reviewers. The baseline mean tremor scores between the site and video raters were 20.0 (SD 4.7) and 17.5 (SD 4.8), difference 2.5 (SD 2.6), $p < 0.001$. Only site reviewers were used for inclusion, if video reviewers were used then 9% of patients would have been excluded. The between group difference in tremor scores at 3 months decreased from -9.8 to -8.3 using video reviewers, difference -1.5 [95% CI -3.0 to 0.0], $p = 0.053$ (15% decrease). The placebo effect in the ET patients was negligible across all parameters. PD patients had significant placebo responses in disability scores (-2.3pts, $p = 0.052$) and PDQ-39 scores (-5.7pts, $p = 0.053$), and notable non-significant placebo responses in tremor scores (-17%, $p = 0.183$) and UPDRS motor scores (-1.7pts, $p = 0.150$).

Conclusion: In the ET trial observer bias occurred, validating the need for independent video review. Placebo response was observed in the PD trial, not the ET trial, highlighting the importance of sham surgery in PD.

695. Moyamoya Disease and Pregnancy: A Single Institutional Experience in the USA

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Introduction: Moyamoya disease is a progressive bilateral stenocclusive disease of the terminal internal carotid arteries accompanied by development of collateral moyamoya vessels. It affects a younger population and thus, women in the reproductive years.

We aim to define the practices, comorbidities and outcomes of pregnancies in women with moyamoya disease.

Methods: We conducted a retrospective review of 39 patients and 46 pregnancies at Stanford Health Care/Lucile Packard Children's Hospital from our institutional database by surveys and chart review.

Results: Thirty-nine women with moyamoya disease had a total of 46 successful pregnancies. There were 31 single pregnancies, of which 10 had single normal vaginal deliveries (NVDs), 4 women had 2 each NVDs and 1 woman had 4 NVDs; 1 woman had a cesarean section. Twenty-one had unknown mode of deliveries and 2 were waiting to deliver. Their ages at diagnosis ranged 13 to 42 years. Twenty-four patients presented with stroke at the time of their moyamoya diagnosis, 22 with transient ischemic attacks, 21 with headaches, 6 with seizures and 2 with hemorrhage. Two pregnancies were complicated by hypertension and pre-eclampsia each. Pre-treatment mRS scores were 1 in 17, 2 in 7, 3 in 4, and 4 in 1 at the time of presentation with moyamoya disease, and post-treatment scores were 0 in 17, 1 in 9, and 3 in 1, which did not change after childbirth.

Conclusion: Our study shows that the trend in the USA is toward vaginal delivery in patients with moyamoya disease, as opposed to the studies based in Korea and Japan. We also show that both the patients and babies do well. The complication rate is minimal, including no strokes in the peripartum period, and we would advocate vaginal deliveries in the absence of any other contraindications.

696. A Novel Tool for Deformity Surgery Planning: Determining the Magnitude of Lordotic Correction Required to Achieve a Desired Sagittal Vertical Axis

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Introduction: The relationship between pelvic incidence and lumbar lordosis – the parameter most readily modifiable during deformity surgery – is a key determinant of global sagittal alignment. We sought to create a model capable of predicting the magnitude of pelvic incidence-lumbar lordosis (PI-LL) correction necessary to achieve a desired sagittal vertical axis (SVA).

Methods: We performed a retrospective review of a prospectively maintained multicenter adult spinal deformity database collected by the International Spine Study Group (ISSG) between 2009 and 2014. The independent variable of interest was the degree of correction achieved in the PI-LL mismatch at 6 weeks post-surgery. The primary outcome was change in global sagittal alignment (in mm) at 6 weeks and 1 year after surgery. We used a linear mixed-effects model to determine the extent to which corrections in the PI-LL relationship affected post-operative changes in SVA.

Results: A total of 1053 adult patients were identified. Of these, 590 were managed surgically. 87 surgically managed patients were excluded due to incomplete PI-LL measurements; the remaining 503 of these patients were selected for inclusion. For each degree of improvement in the PI-LL mismatch at 6 weeks, the SVA decreased by 2.18 mm (95% CI: -2.56, -1.79, $p < 0.01$) and 1.67 mm (95% CI: -2.07, -1.27, $p < 0.01$) at 6 weeks and 12 months, respectively. A high SVA measurement (< 50 mm) at 1 year post-surgery was negatively associated with health-related quality of life as measured by the SRS-12 outcomes assessment.

Conclusions: We describe a novel model that illustrates how surgical correction of the PI-LL relationship affects post-operative changes in SVA. This model will enable surgeons to determine pre-operatively the amount of lumbar lordosis necessary to achieve a desired SVA. Further validation of our results in the form of a prospective trial remains warranted.

697. Individual variation in the ventral and dorsal language pathways: implications for insular tumor resection

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Introduction: Understanding the functional architecture of language is important for surgical management of temporo-insular lesions. Given the variability of individual language circuitry, appreciation of structural

variations is critical. We therefore investigated inter-individual white matter connectivity variations using a large MRI dataset.

Methods: Using a diffusion atlas averaged over 842 control subjects from the Human Connectome Project (842-HCP), we generated deterministic connectivity between left inferior frontal gyrus (IFG) and posterior superior temporal gyrus (pSTG). This conserved connectivity as determined through the atlas was compared to individualized probabilistic connectivity for 50 subjects using identical parameters. For the probabilistic analysis, we quantified the number of tracts traversing the arcuate fasciculus (dorsal language pathway), and the extreme capsule (ventral language pathway).

Results: Deterministic connectivity analysis using the 842-HCP dataset only found arcuate fasciculus connecting IFG and pSTG, and no other conserved significant connections. Using the subject-specific probabilistic analysis, however, both dorsal and ventral pathways were seen in all. Connectivity ratios comparing dorsal and ventral pathways varied greatly, with only 16/50 subjects demonstrating more than 1% of connecting tracts traversing the extreme capsule. The median connectivity was 0.53%, and 8/50 subjects demonstrated ventral connectivity greater than 10%.

Conclusion: While all subjects individually demonstrated dorsal and ventral pathways connecting IFG and pSTG, the degree of connectivity through the two pathways varied greatly. Individuals with significant extreme capsule connectivity, for example, would be at increased risk of language disruption during insular surgery. Preoperative identification of these language pathways would be useful for surgical planning and patient counseling.

698. Beta Oscillations and Bicoherence of Local Field Potentials in the Human Parkinson's Disease OFF State Recorded During Deep Brain Stimulation

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Introduction: Local field potential (LFP) recordings from the subthalamic nucleus (STN) of the human Parkinson's disease (PD) state have revealed characteristic beta frequency oscillations and harmonic bicoherence. We recorded LFP activity and performed subsequent data analysis on PD patients undergoing DBS surgery in the OFF state both at rest and during movement in order to identify any reproducible pathophysiological signatures of the disease.

Methods: LFPs were recorded in 5 patients with PD during bilateral DBS lead placement within the STN. Following DBS lead insertion, recordings were performed for 2 minutes at rest and another 2 minutes with contralateral repetitive hand grasp movements. All recordings were performed in the OFF state. Recordings were transformed into the frequency domain via the fast Fourier transform (FFT). The power spectra, bispectra and bicoherence were analyzed, specifically in the alpha and beta bands using Matlab. While the power spectra represents the independent energies associated with oscillations at a specific frequency, it does not describe interactions between those frequencies. Bispectral analysis is a first order, non-linear descriptor of the strength of correlations between two frequencies and a third frequency which is the sum of the two analyzed frequencies. A significant bicoherence represents phase locking of the two frequencies. Beta oscillation power and bicoherence at each DBS contact were subsequently correlated with the contact independently chosen for stimulation during programming.

Results: Predominance of low and high beta band frequencies (13-20 and 20-35 Hz respectively) was observed both at rest and during continuous active movement. Paradoxically, stronger beta-beta coupling occurred during active movement as opposed to rest in the PD OFF state, which contrasts previous observations. There appears to be positive correlation between bicoherence of beta oscillations and the most efficacious DBS contact for programming.

Conclusions: In patients with PD, beta band coupling that paradoxically synchronizes with movement may be a unique feature of the OFF state. This beta band activity appears to also correlate with the most active DBS lead contact.

699. Managing Concurrent Surgery: An Analysis of 1018 Neurosurgical and Spine Cases

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Introduction: The practice of concurrent surgery has recently come under intense scrutiny, although data on the effects of concurrent procedures on patient outcomes are lacking. We examined the impact of concurrent surgery on complication rates in neurosurgical patients.

Methods: We conducted a retrospective review of neurosurgical procedures performed from May 12, 2014, to May 12, 2015, by any of the five senior neurosurgeons at our institution authorized to schedule concurrent cases. Concurrent surgery was defined as any case where two patients were under anesthesia at the same time under the care of a single lead surgeon for any duration. Primary outcome was the occurrence of any complication from the beginning of surgery to 30 days after discharge. Secondary outcome was the occurrence of a serious complication—defined as a life-threatening or life-ending event—during this period.

Results: One thousand eighteen patients met inclusion criteria for the study. Of these, four hundred seventy-five patients underwent concurrent surgery (46.7%). Two hundred seventy-one patients (26.6%) experienced one or more complications, with one hundred thirty-four (13.2%) suffering a serious complication. The overall complication rate was not significantly higher for concurrent cases compared with non-concurrent cases (26.3% vs. 26.9%, $p=0.837$) nor was the rate of serious complications (14.7% vs. 11.8%, $p=0.168$). On multivariable analysis, concurrent surgery remained unassociated with overall complications (odds ratio 0.810; 95% confidence interval 0.592-1.109, $p=0.189$) or serious complications (odds ratio 0.979; 95% confidence interval 0.661-1.449, $p=0.915$).

Conclusion: In this cohort, patients undergoing concurrent surgery were not at increased risk for overall complications or serious complications.

700. Outpatient versus inpatient ACDF: a population-level analysis of outcomes and cost

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Introduction: Outpatient anterior cervical discectomy and fusion (ACDF) is a promising candidate for US healthcare cost reduction as several studies have demonstrated that overall complications are relatively low and early discharge can preserve high patient satisfaction, low morbidity and minimal readmission. We sought to compare clinical outcomes and cost associated between inpatient and ambulatory setting in 50,000 patients at a state-wide database level.

Methods: Demographics, comorbidities, emergency department (ED) visits, readmissions, reoperation rates, and 90-day charges were analyzed for patients undergoing elective ACDF in CA, FL, and NY from 2009-2011 in State Inpatient and Ambulatory Databases.

Results: 3,135 ambulatory and 46,996 inpatient ACDFs were performed. Mean Charlson comorbidity index (CCI), LOS, and mortality were 0.2, 0.4 days, and 0% in the ambulatory cohort and 0.4, 1.8 days, and 0.04% for inpatients ($P<0.0001$). Ambulatory patients were younger (48.0 versus 53.1) and more likely to be Caucasian. 168 ambulatory patients (5.4%) presented to the ED within 30 days (mean 11.3 days), 51 (1.6%) were readmitted, and five (0.2%) underwent reoperation. Among inpatient surgeries, 2,607 patients (5.5%) presented to the ED within 30 days (mean 9.7 days), 1,778 (3.8%) were readmitted (mean 6.3 days), and 200 (0.4%) underwent reoperation. Higher CCI increased rate of ED visits (ambulatory OR 1.285, $P<0.05$; inpatient OR 1.289, $P<0.0001$) and readmission (ambulatory OR 1.746, $P<0.0001$; inpatient OR 1.685, $P<0.0001$). Overall charges were significantly lower for ambulatory ACDFs (\$33,362.51 versus \$74,667.04; $P<0.0001$).

Conclusion: ACDF can be performed in an ambulatory setting with

comparable morbidity and readmission rates, and lower costs, to those performed in an inpatient setting.

701. Mammillary Body Changes After Laser Interstitial Thermal Therapy of the Mesial Temporal Lobe

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Introduction: The mammillary bodies have long been known as the primary relay center for the hippocampus. The fornix is the primary efferent pathway of the hippocampus, with its postcommissural fibers terminating in the mammillary bodies. In this study, we describe the change in mammillary body volume after laser interstitial thermal therapy (LiTT) for mesial temporal lobe epilepsy and correlate volumetric changes to seizure outcomes.

Methods: Pre- and post LiTT ablation magnetic resonance imaging was reviewed in axial and coronal planes to determine mammillary body volume as calculated by the ellipsoid method. Patient demographics, clinical semiology, and seizure localization were analyzed. The primary end-point was seizure freedom at 1 year after LiTT. The changes in the size of the mammillary body were correlated with the postoperative seizure freedom at 1 year using the Wilcoxon/Kruskal-Wallis test for statistical significance.

Results: Between December 1, 2012 and June 1, 2015, 22 patients underwent LiTT for mesial temporal lobe epilepsy. Two patients were excluded due to lack of follow up. Of the remaining 20 patients, 13 were seizure free at 1 year. In the seizure free group, there was an average 34.6% ($\pm 13\%$) decline in ipsilateral mammillary body volume, as opposed to an average decline of 8.4% ($\pm 10.9\%$) in patients with continued seizures ($P=0.0026$).

Conclusion: Our findings show a statistically significant correlation between postoperative volume reduction in ipsilateral mammillary body and seizure outcomes after LiTT. With further validation, this finding could be a useful surrogate of adequacy of ablation, regardless of ablation volumes, and determinant of potential benefit of additional surgical intervention in patients with poor outcomes after LiTT.

702. Small Aneurysms Account for Majority and Increasing Percentage of Aneurysmal Subarachnoid Hemorrhage: a 25-Year Study

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Introduction: Prospective studies of unruptured aneurysms (e.g. ISUIA) have shown low rates of rupture for small ($<10\text{mm}$) aneurysms and suggested the risk outweighs benefit of treatment. However, common clinical practice shows that patients with aneurysmal subarachnoid hemorrhage (aSAH) frequently have small aneurysms. We sought to investigate the proportion of ruptured small and very small ($<5\text{mm}$) aneurysms in patients presenting with aSAH over a 25-year period.

Methods: A prospective, IRB-approved database of all patients presenting to our institution with aSAH from 1991-2016 was analyzed. Cerebral angiography was performed to identify the source of hemorrhage and aneurysm characteristics. Patients with traumatic SAH, angiogram-negative SAH, or other non-aneurysmal etiologies were excluded. In patients with multiple aneurysms, the ruptured aneurysm was identified from the blood pattern on head CT, aneurysm morphology, and intra-operative records.

Results: Data was available for 1306/1562 patients (83.6%) with aSAH from 1991-2016. The average age was 52.8 years and 72% of patients were female. 55% were Caucasian, 40% were African American, and 5% were other ethnicities. The average size of a ruptured aneurysm over the 25 year period was 8.0mm ($\pm 5.7\text{mm}$). The average size of ruptured aneurysms decreased steadily with each successive five-year interval: 10.1mm(1991-1996), 9.1mm(1996-2001), 8.2mm(2001-2006), 6.8mm(2006-2011), 6.6mm(2011-2016). Overall, aneurysms $<5\text{mm}$ in size were responsible for aSAH in 41.3% of the patients. The percentage

of very small ruptured aneurysms rose from 28.8% during the initial five-year period (1991-1996) to 49.6% in the most recent period. Likewise, the percentage of ruptured aneurysms that were 5-9mm rose from 26.3% to 33.8%. In the most recent 5-year period, 83.5% of ruptured aneurysms were <10mm in size.

Conclusion: Ruptured small (<10mm) and very small (<5mm) aneurysms represent a majority and increasing share of aSAH. Identification and prophylactic treatment of these aneurysms remains an important clinical role for cerebrovascular neurosurgery.

703. Limbic Leucotomy for Severe Self-injurious Behavior: Long Term Follow-up of 2 Cases

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Introduction: Self-injurious behavior (SIB) is amongst the most severe and treatment-refractory psychiatric conditions. Limbic leucotomy combines the lesions of the anterior cingulotomy and subcaudate tractotomy and has demonstrated efficacy in the treatment of severe, intractable SIB. However, there have been no long-term follow-up reports. Here, we describe the 18+ year outcomes of limbic leucotomy in two adults with severe SIB unresponsive to an exhaustive treatment regimen.

Methods: Two female patients (age 23 and 31) were treated at the Massachusetts General Hospital with limbic leucotomy. Bilateral radio-frequency thermocoagulation lesions were stereotactically placed in the anterior cingulate and posterior medial orbitofrontal regions. Outcomes were assessed using the Clinical Global Improvement (CGI), Current Global Psychiatric-Social Status (CGPS), and DSM-IV Global Assessment of Functioning (GAF) scales.

Results: Throughout more than 18 years of follow-up, the patients continue to improve without significant effects on cognition or neurologic function. Their CGI scores remain stable at 2 and 2/3, respectively and CGPS scores remain stable at 3 and 2, respectively. GAF scores in both patients improved from 5 preoperatively to 70 at the last follow-up time point. Both patients experienced cessation of SIB and are working and living independently.

Conclusion: The results of these two cases provide evidence of the long term benefit of limbic leucotomy for severe SIB in patients that have exhausted conventional treatment modalities. Though new technologies such as deep brain stimulation have provided a non-permanent alternative to lesioning, the enduring safety and efficacy of ablative surgery for severe intractable psychiatric disease ought to be emphasized.

704. Combination Immunotherapy With Whole Tumor Cell Vaccination and OX40 Stimulation Overcomes Tumor-Associated Immunosuppression and Prolongs Survival in Mice with Intracranial Glioma

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Introduction: While immune checkpoint inhibition via blockade of the PD-1/PD-L1 axis is being explored in patients with glioblastoma, direct activation of antigen specific T-lymphocytes via OX40 ligation is relatively unexplored. We examine the hypothesis that irradiated whole tumor cell vaccination and OX40 stimulation are complementary and synergistically effective against murine intracranial glioma.

Methods: GL261 tumor cells were injected into the frontal lobes of syngeneic C57/Bl6 mice. Both subcutaneous injection of irradiated GM-CSF expressing GL261 cells and intraperitoneal delivery of anti OX-40 antibody occurred on days 3,6, and 9 after implantation of tumor. Animals were analyzed for survival by the Kaplan-Meier method. Animals were sacrificed on day 21 after tumor implantation for analyses of systemic immunity (ELISPOT) and tumor-infiltrating lymphocyte status (flow cytometry).

Results: Combination immunotherapy with irradiated GM-CSF express-

ing glioma cells and intraperitoneal delivery of agonist monoclonal antibody against OX40 was more effective than either therapy alone and prolonged survival in mice with established intracranial GL261 tumors. Elispot analyses of peripheral lymphocytes revealed that combination immunotherapy reverses the Th2 cytokine skew that is induced by the presence of intracranial glioma. OX40 stimulation alone and in combination with vaccination drove high levels of interferon gamma expression by splenocytes harvested from glioma-bearing animals, while IL-10 expression was little changed. Flow cytometric analyses of tumor infiltrating lymphocytes demonstrated that vaccination alone improved the CD8+ T-lymphocyte / CD4+FoxP3+ lymphocyte ratio, while treatment with OX40 ligation significantly reduced expression of lymphocyte exhaustion markers, including PD-1 and LAG3.

Conclusion: Combining whole tumor cell vaccination with OX40 stimulation effectively controls the growth of intracranial glioma. Mechanistic explanations include improving the CD8+/CD4+FoxP3+ T lymphocyte ratio intratumorally, driving a systemic Th1 antitumor immune response, and reversing T-lymphocyte exhaustion in tumor infiltrating lymphocytes.

705. Does Myelopathy or Alignment Improvement Drive Acute Post-Operative Outcomes in Cervical Deformity Patients?

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Introduction: Surgical correction for adult cervical deformity (ACD) typically involves both radiographic malalignment correction and nerve decompression for pain and motor skill improvement. It is unclear whether acute patient outcomes are more driven by myelopathy or alignment improvements.

Methods: 69 ACD patients ≥18yrs with pre/post-op radiographs and outcome scores included. Cervical alignment improvement was determined by ranking patients' pre- and post-operative cSVA and T1S-CL according to the following ranges: $0 \leq \text{cSVA} \leq 40\text{mm}$, $0 \leq \text{T1S-CL} \leq 20^\circ$. Patients were divided into 4 groups based on BL-3M differences in myelopathy scores and cervical alignment: M:mJOA improvement only; A:Alignment improvement only; B:improvement in both categories; N:improvement in neither category. At baseline, mJOA scores were ranked on severity (Mild [15-17]/Moderate [12-14]/Severe [1-11]). Bivariate correlations, independent t-tests, and ANOVA compared BL and 3M EQ-5D scores between groups.

Results: The distribution of patients in improvement groups based on BL-3M changes was as follows: 'M'(n=7), 'A'(n=15), 'B'(n=4), 'N'(n=28). The pre-operative EQ-5D scores among the improvement groups were all statistically similar ($p > 0.05$ all cases). At 3M, the EQ-5D score was significantly better only in the 'B' patient group ($p=0.033$): 'M': 43.57 ± 27.50 ; 'A': 71.13 ± 22.27 ; 'B': 36.25 ± 37.72 ; 'N': 62.15 ± 24.75 . At 3M, 13 patients (18.8%) reached MCID for mJOA. 22 patients (31.9%) that improved in post-operative cervical alignment categories. At 3M, mJOA was correlated ($r=-0.281, p=0.021$) with EQ-5D. Among pre-operative cSVA and T1S-CL, only cSVA was moderately correlated with baseline EQ-5D ($r=0.256, p=0.05$), and neither dichotomous alignment group was correlated with 3M EQ-5D. The change in mJOA from BL-3M was also significantly correlated with 3M EQ-5D score ($r=0.295, p=0.021$).

Conclusion: Patients that reach post-operative alignment and myelopathy improvement goals displayed better overall outcomes compared to those that only improved in selective categories. Pre-operative planning to take such factors into account is important for optimizing outcomes following ACD correction.

706. Stereotactic Radiosurgery for Spetzler-Martin Grade IV and V Arteriovenous Malformations: An International Multicenter Study

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Introduction: The aims of this international eight center, retrospective cohort study are to evaluate the outcomes after single-session stereotactic radiosurgery (SRS) for SM grade IV-V AVMs and determine predictive factors.

Methods: We retrospectively pooled data from 233 patients (mean age 33 years) with SM grade IV (94.4%) or V AVMs (5.6%) treated with single-session SRS data in the International Gamma Knife Research Foundation. Pre-SRS embolization was performed in 71 AVMs (30.5%). The mean nidus volume, SRS margin dose, and follow-up duration were 9.7 cm³, 17.3 Gy, and 84.5 months, respectively. Statistical analyses were performed to identify factors associated with post-SRS outcomes.

Results: The actuarial obliteration rates at 3, 7, 10, and 12 years were 15%, 34%, 37% and 42%, respectively. The annual post-SRS hemorrhage rate was 3.0%. Symptomatic and permanent RIC occurred in 10.7% and 4% of the patients, respectively. Only larger AVM diameter ($p=0.04$) found to be an independent predictor of unfavorable outcome in the multivariate logistic regression analysis. The rate of favorable outcome was significantly lower for unruptured SM grade IV-V AVMs compared to ruptured ones ($p=0.042$). Prior embolization was a negative predictor of AVM obliteration ($P=0.024$) and RIC ($P=0.05$).

Conclusion: In this multi-institutional study, single session SRS had limited efficacy in the management of SM grade IV-V AVMs. Favorable outcome was only achieved in a minority of unruptured SM grade IV-V AVMs, which supports less frequent utilization of SRS for the management of these lesions. A volume staged SRS approach for large AVMs represents an alternative approach for high grade AVMs, but it requires further investigation.

707. Tracking Career Paths of Women in Neurosurgery

Louise Eisenhardt Travel Scholarship

Jaclyn Janine Renfrow, MD; Analiz Rodriguez, MD, PhD; Taylor Wilson, MD; Isabelle Germano, MD; Aviva Abosch, MD, PhD; Stacey Wolfe, MD (Winston Salem, NC)

Introduction: Women represent a growing cohort of US neurosurgeons. Following residency training, the sub-specialization, practice environment, and updated academic rank among the cohort of female neurosurgeons has yet to be described.

Methods: Databases from the AANS/ABNS capturing data from 1964 to 2013 were reviewed for female neurosurgery residency graduates. Data on post-residency fellowship training, practice environment (private vs. academic), academic rank, ABNS board certification, and AANS/CNS Joint Section on Women in Neurosurgery membership status were collected in 2016. Academic rank was verified using faculty listings from the program website and electronic correspondence with identified individuals. Faculty members were asked to self-report directorship positions and tenure. WINS membership status was verified by datasets from the AANS/CNS Joint Section on Women in Neurosurgery.

Results: A total of 379 female neurosurgery residency graduates were identified in this 50 year span. Of these, 70% became ABNS certified, and 2.1% chose to pursue other careers after completing neurosurgery residency. Following residency, 27% of female graduates ($n=103$) pursued fellowship training, with pediatric neurosurgery (33%) the most common fellowship selected. After training, 26% entered academic medicine ($N=91$), with 46% ($N=42$) at the rank of assistant professor, 36% ($N=33$) attaining the rank of associate professor, and only 18% ($N=16$) reaching the rank of full professor.

Conclusion: The proportion of female neurosurgery residents in the

US is slowly increasing. After training, the distribution of women in private vs. academic environments is roughly equal in proportion to male neurosurgeons. The number of female neurosurgeons in academic leadership positions remains exceedingly low, with only a single female neurosurgery department chair, and under-representation of women in higher academic ranks. Tracking the percentage of women graduating from neurosurgery residency programs, and their career paths is a necessary first step to identifying and overcoming obstacles.

708. Laminoplasty vs. Laminectomy-fusion For the Treatment of Cervical Myelopathy: Preliminary Data from the CSM-Study Comparing Cervical Sagittal Alignment and Clinical Outcomes

Vijay Mysore Ravindra, MD; Jill Curran, MS; Praveen Mummaneni, MD; Adam Kanter, MD; Erica Bisson, MD, MPH; Robert Heary, MD; Todd Albert, MD; K Daniel Riew, MD; Subu Magge, MD; Robert Whitmore, MD; Zoher Ghogawala, MD (Salt Lake City, UT)

Introduction: Both laminoplasty and laminectomy-fusion effectively treat cervical spondylotic myelopathy (CSM). A direct comparison of cervical sagittal alignment and overall health related quality of life outcomes was performed.

Methods: A multi-center prospective, randomized study of CSM is underway. Patients who underwent laminoplasty or laminectomy-fusion were included. Pre-operative and post-operative C2-7 sagittal vertical axis (SVA) and Cobb angle were measured on lateral radiographs. Outcomes were assessed with the mJOA scale, NDI, SF-36 PCS and SF-36 MCS, and Euro-QOL-5D pre-operatively, at 6 months, and 12 months postoperatively.

Results: A total of 55 patients were available for analysis. There was significantly greater improvement in the SF-36 PCS (8.3 vs. 3.5, $p=0.03$) in the laminoplasty group at 6 months, which did not persist at one year ($n=35$). All patients had improved mJOA scores and most patients achieved a minimal clinically important difference for each outcome. Twenty-two patients had one-year radiographic follow-up: laminectomy-fusion ($n=11$) and laminoplasty ($n=11$). There were no differences in pre-op Cobb angle, C2-7 SVA, or outcome measures. The mean post-operative Cobb angle (12.7 vs. 2.5, $p=0.14$) and SVA (23.1 vs. 27.6, $p=0.42$) was similar, with no significant change from baseline; SVA did not predict improvement. Laminoplasty patients developed worse sagittal balance (+2.8 mm) post-operatively, while laminectomy-fusion patients showed improved sagittal balance (-3.3 mm), both non-significant.

Conclusion: Both laminoplasty and laminectomy-fusion are effective in treating CSM. At 6 months there was a significantly greater improvement in SF-36 PCS with laminoplasty, but at 1 year both groups were comparable. Further studies will define health resource utilization after surgery.

709. Acute clinical effects of stimulation in a patient with Nucleus Accumbens DBS – Insights from a structural connectivity study

Vibhor Krishna, MD; Andrew Bigler; Francesco Sammartino, MD; Emily Weichart; Ammar Shaikhouni, MD, PhD; Punit Agrawal; John Corrigan, PhD; Jennifer Bogner; Per Sederberg; Ali Rezai, MD (Columbus, OH)

Introduction: Acute clinical effects (ACE) are occasionally observed during deep brain stimulation (DBS) adjustments. Studying the changes in the structural connectivity associated with ACE may inform the network integration of the stimulation target and guide programming. We had the unique opportunity of studying ACE in a refractory obesity patient who underwent Nucleus Accumbens DBS under a research protocol.

Methods: Postoperative, unilateral, acute stimulation adjustments were performed and self-reported scores in three clinical domains (anxiety, mood and energy levels) were recorded using a 10-points scale. Meaningful ACE was defined as a change of $\geq \pm 1.5$ from baseline. The volumes of tissue activation (VTA) for stimulation parameters were used as seeds for probabilistic tractography (FSL, 3 fibers/voxel model) using

preoperative imaging (DWI with 60 diffusion directions, 2 mm iso-voxel). We calculated the connectivity to a validated ICA-based resting state network atlas (Gordon et al. Cerebral Cortex 2014). The voxels in each cortical mask connecting with the VTA were converted into T-scores to determine structural connectivity. Significant changes ($\geq 2SD$) in structural connectivity associated with ACE were reported.

Results: From 94 observations, 15 were considered meaningful ACE (decreased anxiety $n=7$, improved mood and energy $n=4$ each). Changes in structural connectivity to default mode (#1, #6, #259), visual (#5, #15, #298), cingulo-opercular (#21, #223), somatomotor (#53), and attention (#62) networks were common to ACE in all three domains. However a few connectivity changes were unique to specific ACE e.g. dorsal attention networks (#74, #100, #106) were only associated with mood changes. Stimulation changes between 4-6 volts at Contact 1 were associated with ACE in all three domains. Incidentally this contact was also used for long-term stimulation.

Conclusion: This is the first study reporting structural connectivity changes associated with ACE. Studying the tractography correlates of ACE may have implications for future DBS targeting and programming.

710. Neurodegenerative CSF-biomarkers Tau and Amyloid Beta Predict Neurological, Neuropsychological, and Quality of Life Outcomes after Aneurysmal Subarachnoid Hemorrhage

Holger Joswig, MD; Wolfgang Korte, MD; Severin Fröh; Lorenz Epprecht, MD; Gerhard Hildebrandt, MD; Jean-Yves Fournier, MD; Martin Stienen, MD (Sankt Gallen, Switzerland)

Introduction: Cerebrospinal fluid (CSF) biomarkers might be useful for predicting outcome after aneurysmal subarachnoid hemorrhage (aSAH).

Methods: Ventricular CSF was obtained from 24 aSAH patients at admission (D0), day 2 (D2) and day 6 (D6). CSF total (t)Tau, phosphorylated (p)Tau(181P), Amyloid beta 40 and 42 (A β 40/A β 42) levels were compared between patients with favorable and unfavorable neurological (modified Rankin Scale (mRS)), neuropsychological (Montreal Cognitive Assessment and detailed neuropsychological assessment), as well as health-related quality of life outcome (Euro-Qol (EQ-5D)) at three months (M3) and one year (Y1).

Results: Patients with unfavorable neurological outcome (mRS 4-6) at M3 and Y1 had higher CSF tTau/pTau and lower A β 40/A β 42 at D0, D2 and D6 with varying degrees of statistical significance. In terms of predicting neuropsychological outcome, CSF pTau showed a strong correlation with the z-scores of executive function ($r=-0.7486$, $p=0.0080$), verbal memory ($r=-0.8101$, $p=0.0025$), attention ($r=-0.6498$, $p=0.0304$), and visuospatial functioning ($r=-0.6944$, $p=0.0177$) at M3. At Y1, CSF pTau had moderate to strong correlations with the z-scores of executive function ($r=-0.5356$, $p=0.0895$), verbal memory ($r=-0.7473$, $p=0.0082$), attention ($r=-0.4941$, $p=0.1224$), and visuospatial functioning ($r=-0.6678$, $p=0.0247$). Patients with unfavorable hrQoL outcome (EQ-5D z-score ≤ -1.0) at the M3 and Y1 follow-up had higher CSF tTau/pTau and lower A β 40/A β 42 at D0, D2 and D6.

Conclusion: Higher tTau/pTau as well as lower A β 40/A β 42 CSF-levels in the acute phase of aSAH predict unfavorable long-term functional, neuropsychological and hrQoL outcomes. Neuropsychological deficits at M3 and Y1 follow-up correlate well with increased CSF tTau and pTau concentrations. Further validation is needed before clinical implementation of these biomarkers.

711. Multisector Whole-exome Sequencing of Glioblastoma Reveals Profound Intratumoral Diversity: Implications for Precision Medicine

Ronald L. Bittner Award on Brain Tumor Research

Ananth Kesav Vellimana, MD; Tatenda Mahlokozeru; Tiandao Li, PhD; Daniel Marcus, PhD; Sarah Fouke, MD; Jian Campian, MD; Christopher Miller, PhD; Albert Kim, MD, PhD (St Louis, MO)

Introduction: The current diagnostic paradigm following biopsy or resection of glioblastoma involves molecular sequencing-based analysis of a limited,

single site in the tumor. We hypothesized that multisector next-generation sequencing of tumors would provide an improved representation of clonal architecture and potentially therapeutically relevant molecular information.

Methods: DNA was harvested from two ($n=9$) or four ($n=1$) spatially distinct regions of ten newly diagnosed, IDH1 wildtype glioblastoma tumors. Tumor DNA and matched blood DNA underwent whole-exome next-generation sequencing with an average of 80-100X coverage. The clonal architecture of each tumor was inferred from the variant allele frequencies of single nucleotide variants in copy-number neutral regions using SciClone. Each SNV and indel was assigned clonal or subclonal status, and exploratory analysis of therapeutically relevant gene mutations was performed using the Drug Gene Interaction database (DGIdb) in a sector-specific manner. Each patient was also HLA-typed and the pVAC-Seq pipeline was used to predict clonal and subclonal MHC Class I and II neoantigens in each tumor sector.

Results: In all samples, only 11% of mutations were clonal and 6% subclonal and shared between sectors. Remarkably, 83% of all observed mutations were subclonal, private mutations. In one hypermutated tumor, the majority of mutations were found in only one sector of the tumor. Analysis of clonal architecture demonstrated substantial differences between different sectors of one tumor, suggesting regionally divergent evolution. Predicted therapeutically relevant mutations differed substantially in presence and frequency in spatially distinct regions. Similarly, different sites exhibited extreme divergence in the predicted neoantigen landscape: only a minor fraction of neoantigens were clonal in most tumors.

Conclusions: Whole-exome sequencing of different sites in glioblastoma revealed a considerable degree of regional heterogeneity. These results have potential clinical implications for our interpretation of current single-site diagnostics and suggest that multi-site analyses may be necessary for accurate molecular characterization of glioblastoma.

712. Brief Electrical Stimulation to the Human Amygdala Enhances Recognition Memory for Neutral Images

Cory Inman; Joseph Manns, PhD; Kelly Bijanki, PhD; David Bass, MD, PhD; Robert Gross, MD, PhD; Stephan Hamann, PhD; Jon Willie, MD, PhD (Decatur, GA)

Introduction: Emotional events are often better remembered than neutral events, and this benefit depends on the amygdala. We have previously demonstrated that brief basolateral amygdala electrical stimulation enhances memory in rodents. This study examined whether human amygdala stimulation immediately following the presentation of neutral object photographs enhanced later recognition memory.

Methods: We recruited 14 epilepsy patients undergoing intracranial EEG (iEEG) with depth electrode contacts placed in basolateral amygdala and sub-regions of the hippocampus. During continuous iEEG, each participant was presented a series of photographs of neutral objects, half of which were followed immediately by a unilateral stimulation to the amygdala (8 trains of 50-Hz pulses for 1-second at 0.5 mA after image offset). No epileptiform activity was elicited by the stimulation. Participants reported no awareness of the stimulation.

Results: Recognition memory and subjective confidence for half the photographs was tested immediately after the study session and for the other half of the photographs the following day. On the recognition memory test administered the following day, participants recognized neutral objects initially followed by amygdala stimulation more accurately than control objects. The result was similar when only high-confidence judgments were included. On the immediate recognition memory test, participants performed similarly for both object conditions. We are also currently investigating the effects of amygdala stimulation on network oscillatory activity, autonomic physiology, and emotional processing.

Conclusion: Similar to the prior rodent studies, the current results indicate that brief electrical stimulation to the human amygdala can enhance item-specific memory for neutral stimuli even in the absence of awareness of the stimulation, reflecting a key role of the amygdala in prioritizing experiences for long-term storage in declarative memory. Amygdala stimulation

likely engages amygdala-hippocampus connections that normally serve to prioritize memory for emotional events and may provide a therapeutic route for patients with memory deficits.

713. Genetic Predisposition to Lumbar Disk Herniation in Pediatric Patients

Courtney Rory Goodwin, MD; Travis Fulton, MS; A. Karim Ahmed, BS; Daniel Sciubba, MD; Nicholas Theodore, MD (Baltimore, MD)

Introduction: As disks become mechanically incompetent, the spine may become unstable and lose the ability to properly distribute weight. IVDD has traditionally thought to be attributed to natural 'wear and tear' and mechanical insult. Studies in the past two decades, however, have demonstrated the role for genetic influence instead of solely environmental factors. The objective of this study was to assess the genetic influences that predispose lumbar intervertebral disk disease (IVDD). This was accomplished in a pediatric and young adult population, where disk herniation due to environmental exposure could be mitigated.

Methods: A cohort of patients with definitively diagnosed lumbar intervertebral disk disease was compiled. The cohort was younger than the average age of presentation and excluded based on environmental risk factors for IVDD. A genome-wide association study (GWAS) was performed to characterize the genetic influences that may predispose IVDD.

Results: Missense mutations in collagen encoding genes were observed in 13 out of 15 patients in the cohort with intervertebral disk disease. Moreover, the odds ratios of key variants in Collagen 9A2 (COL9A2) and Collagen 11A1 (COL11A1) were greater than 1. The IVDD cohort also demonstrated statistical significance for 2 variants in the gene encoding for aggrecan—which facilitates load-bearing properties in the cartilaginous end plate.

Conclusion: These results support the previously published work for collagen variants as a genetic risk factor for intervertebral disk disease. However, the present study sheds new light on the role for variants in aggrecan, which sustains the cartilaginous end plate. Genetic predisposition to IVDD, therefore, may be a multimodal combination of mutations in the nucleus pulposus, annulus fibrosus, as well as cartilaginous end plates.

714. Hippocampal RNA Expression Varies According to Seizure Outcome and Seizure Frequency following Anterior Temporal Lobectomy with Amygdalohippocampectomy

Robert Wagner Bina, MD; Ryan Sprissler, MS; Christina Walter, MS; David Labiner, MD; Michael Hammer, PhD; Martin Weinand, MD (Tucson, AZ)

Introduction: Previous studies have demonstrated meaningful differences in the expression of temporal cortical genes in patients with temporal lobe epilepsy (TLE) that are seizure-free after anterior temporal lobectomy with amygdalohippocampectomy (ATL/AH) compared to those with continued seizures after surgery. The current study was conducted to test the hypothesis that RNA expression varies between patients who are seizure-free and those who continue to have seizures after ATL/AH. Additionally, the hypothesis that RNA expression differs between patients with differing preoperative seizure frequency was tested.

Methods: Hippocampal tissue from 12 selected patients all of whom underwent ATL/AH for medically intractable TLE was collected. RNA isolates were analyzed and patient seizure outcome and frequency were compared. RNA expression from patients who were seizure-free were compared to those who were not. Also, RNA expression from patients with high baseline seizure frequency were compared to patients with low seizure frequency.

Results: 50% of patients were seizure free post-operatively at last follow-up (12-53 months, average 31). 117 hippocampal genes had upregulated expression and 190 had downregulated expression when seizure outcomes following ATL/AH were compared. 58% of patients had high seizure frequency. RNA expression of 37 genes was upregulated and expression of 2126 genes was down regulated when the genomes of high and low seizure frequency patients were compared.

Conclusion: Presented here is evidence that post-operative seizure freedom can be predicted by the expression of genes in hippocampal RNA isolates. Also presented are possible hippocampal genetic markers of seizure frequency. Genes with changes in RNA expression in both of the investigated groups include GnRH, Transferrin, catenin 3, CCK, Cannabinoid Receptor 1, wnt, and others. Though the contribution of each gene to the overall outcome is yet to be determined, these genes and these data present targets for future research and potential therapeutic targets.

800. A Pilot Study of Deep Brain Stimulation in Treatment Resistant Schizophrenia

Best International Abstract Award

Laura Salgado; Alexandra Roldán, MD; Rodrigo Rodriguez, MD; Beatriz Gomez, MD, PhD; Iluminada Corripio, MD, PhD; Enric Alvarez, MD, PhD; Joan Molet, MD, PhD (Barcelona, Spain)

Introduction: Deep brain stimulation (DBS) has proven its effectiveness in different types of psychiatric disorders, neuropathic pain and neurodegenerative diseases. Schizophrenia remains one of the leading causes of disability worldwide, with 30% of the patients refractory to the treatment. We hypothesize that DBS may be an effective treatment in patients with refractory schizophrenia. Our purpose is to describe our protocol and the preliminary results of the first 5 cases of schizophrenia treated with DBS.

Methods: This is a prospective randomized double-blind clinical trial in patients with treatment-resistant chronic paranoid schizophrenia. Patients were randomized to DBS of the nucleus accumbens or the subgenual area (based on two different physiological hypothesis). After clinical stabilization, we also performed a cross-type sequence randomization (generator on/off) every 6 months. The primary outcome was the changes from baseline score to 1-12 months scores in the Positive and Negative Syndrome Scale for Schizophrenia (PANSS). We define diagnostic, inclusion and exclusion criteria. Demographic and clinical characteristics of each patient, neuropsychological scales and complementary test are also described.

Results: From December 2014, 5 patients (60% men) underwent surgery (the target was in 3 cases the nucleus accumbens and in 2 the subgenual area). The mean age was 42.4 years (± 6.4 SD). Mean follow-up was 14.6 months (IQR 13). The most remarkable changes included progressive improvement in all patients of the social isolation type symptoms and auditory hallucinations. The average improve in the PANSS score was 37.5%. One patient presented complications related to the surgery. The study is currently under analysis and collection of patient outcomes and will be finished in 2017 (4 more cases will be recruited).

Conclusion: Preliminary results support the hypothesis that DBS can be an effective therapy to treat refractory schizophrenia. Complete the ongoing study, a comprehensive analysis of the data and larger multicenter trials are needed to obtain definitive answers.

801. Southwestern Aneurysm Severity Index (SASI) for Predicting Outcomes in Unruptured Intracranial Aneurysms treated with Microsurgery

Vin Shen Ban, MA, MB, BChir, MRCS; Salah Aoun, MD; Jeffrey Beecher, DO; Tarek El Ahmadi, MD; Awais Vance, MD; Om Neeley, MD; Cameron McDougall, MD; Joan Reisch, PhD; Babu Welch, MD; H. Hunt Batjer, MD; Duke Samson, MD; Jonathan White, MD (Dallas, TX)

Introduction: The Southwestern Aneurysm Severity Index (SASI) has recently been studied as an outcome prediction tool for ruptured aneurysms treated microsurgically. We now assess its relevant components with the aim of building a tailored prediction model for unruptured intracranial aneurysms treated microsurgically.

Methods: Patients presenting to our institution with unruptured aneurysms from 1996-2015 treated with microsurgery were included. Outcome was defined as GOS at discharge (GOSd) dichotomized to 1-3 vs 4-5.

The SASI was composed of multiple prospectively recorded patient demographic, clinical, radiographic and aneurysm specific variables. Univariate and multivariate analyses were used to construct the best predictive models for patient outcome. In constructing a modified SASI scoring system, the cohort was randomly split, with one half acting as the derivation sample and the other as the validation sample.

Results: We identified 1,708 eligible patients. The GOSd was 1-3 in 294 patients (17.2%) and 4-5 in 1414 patients (82.8%). Univariate chi-square analyses revealed age ($p<0.001$), sex ($p<0.001$), Non-Neurological ASA score (NNASA, $p<0.001$), aneurysm location ($p<0.001$), multiple aneurysms with the intent to treat ($p<0.001$), calcification/thrombosis ($p<0.001$), size <20 mm ($p<0.001$), and intraoperative rupture ($p=0.01$) to be associated with unfavorable GOS.

In a multivariate stepwise logistic regression, the best predictive model for poor outcome included size <20 mm ($p<0.001$), aneurysm location ($p<0.001$), age ($p<0.001$), NNASA ($p=0.001$), intraoperative rupture ($p=0.01$), and calcification/thrombosis ($p=0.01$).

Conclusion: Patient clinical, radiographical, and aneurysmal characteristics were identified as being predictive of GOS at discharge. A modified version of the SASI scoring system for unruptured aneurysms treated microsurgically will be presented at the meeting.

802. Internal Jugular Vein Compression: A Novel approach to mitigate blast induced hearing injury

ThinkFirst Injury Prevention Award

Brian D. Sindelar, MD; Michael Shinnars, MD; Julian Bailes, MD; Sydney Sherman, BS; Kevin Novak, PhD; Kristine Erickson; Vimal Patel, PhD (Gainesville, FL)

Introduction: Internal jugular vein (IJVC) has been demonstrated in studies to reduce axonal and vascular injury associated with TBI when used as a prophylactic measure (Turner '12, Smith '12, Myer '16, Sindelar '16). IJVC's effect on not only intracranial, but also intracochlear pressure may potentiate blast induced hearing injury (BIHI) therefore precluding its use as a prophylactic therapy for TBI. We hypothesized that the use of IJVC compression prior to blast injury will increase the risk of BIHI.

Methods: Twenty Sprague-Dawley rats were exposed to a 17.9 ± 0.4 PSI (195.8 dB SPL) right-sided shock wave in which ten had application of a custom IJVC collar prior to injury. All rodents received baseline and post blast injury otoacoustic emission (OAE) and auditory brainstem response (ABR) testing followed by cochlear histology.

Results: IJVC was shown to significantly reduce ABR and OAE threshold shifts in comparison to the non-intervention group by:

14.9 $\pm$ 4.8 dB (right ear ABR 0.5 kHz day 1 post blast, $p=0.01$), 13.1 $\pm$ 4.9 dB (right ear ABR 4 kHz Day 1 post blast, $p=0.04$), 16.5 $\pm$ 4.5 dB (right ear ABR click Day 1 post blast, $p=0.003$), 12.1 $\pm$ 4.6 dB (right ear ABR click Day 6 post blast, $p=0.04$), and 14.0 $\pm$ 3.2 dB (both ears OAE 3.2-10kHz, $p<0.0001$). Also, those animals with collar application had a greater number of total hair cells per mm from 70-100% distance from the cochlear apex following blast injury in comparison to those without intervention (Blast: 211.8 $\pm$ 27.5 vs. Blast+collar: 355.5 $\pm$ 39.5 ($p=0.0002$)).

Conclusion: IJVC prior to BIHI was shown to reduce both functional and structural inner ear pathology in a rodent model. This fascinating study proposes a new prophylactic mechanism that not only provides benefits for TBI mitigation, but also may revolutionize our approach to traumatic hearing injury in both the military and civilian population.

803. Brachial Plexus Injury and the Road to World War I

Zachary S. Hubbard; Alexander Busko, BS; Sarah Jernigan (Miami, FL)

Introduction: Friedrich Wilhelm Victor Albert, or Wilhelm II, was born on January 27, 1859 to Prince Wilhelm of Prussia and Princess Victoria of Great Britain. Wilhelm II suffered from Erb-Duchenne palsy due to a brachial plexus

injury during his birth. Princess Victoria became obsessed with her son's disability and consulted numerous physicians who initiated a succession of therapies that likely did more harm than good. These therapies included electrotherapy, employment of a stretching machine, tying his functioning right hand to his side, and placing his arm in freshly slaughtered hares. One can only assume that Wilhelm's traumatic youth, fraught as it was with painful therapies and failed attempts to please his mother, left the Prince with deep feelings of resentment and inadequacy. This bellicose personality led to tension between Wilhelm, his government, and the eventual fallout with Otto von Bismarck, the Prussian statesman who negotiated extensive European relations throughout the late 1800s. However in 1890, the Kaiser removed the 85-year-old Bismarck from his position, and named Leon von Caprivi his successor. The dismissal of Bismarck was the key event to diplomatic fallout, and within two decades Wilhelm II would inevitably lead the German country into World War I and eventual collapse.

Conclusion: This is an extraordinary case of an obstetric injury that burdened the man at the helm of the Central Powers. Interestingly, effective treatments for peripheral nerve injuries were refined during World War I. This evolution would eventually give rise to the successful surgical management of brachial plexus injury that exists today.

804. From Hippocrates to Shunts and Neuroendoscopy: the History of Hydrocephalus and its Treatment

A. Nimer Amr, MD; Andreas Kramer, MD; Darius Kalasauskas, MD; Eleftherios Archavlis, MD (Mainz, Germany)

Introduction: Although hydrocephalus has been described since ancient times, it is only in the last century that effective long term treatments have been developed. We explore the history of our understanding of the pathophysiology of hydrocephalus and its treatment, from Hippocrates and Galen, Albucasis, Avicenna, and explore the pre-contemporary treatments of Quincke, Mikulicz, and Anton, and discuss current trends of hydrocephalus therapy.

Methods: We performed an exhaustive search of the Ovid MEDLINE and Pubmed databases, as well as the historical literature in the German and English languages on the subject of hydrocephalus treatment with particular reference to the history of our understanding of its pathophysiology and the therapy options available through the ages. We furthermore researched the current state of cutting edge hydrocephalus treatment and possible future directions in its therapy.

Results: The history of hydrocephalus therapy is intertwined with our understanding of the pathophysiology and anatomy of the central nervous system. Even in the early era of medicine, humankind identified hydrocephalus, even if "treatment" was confined to mere observation of its symptoms. With a deeper understanding of the circulation of the cerebrospinal fluid, treatment options such as ventricular punctures, serial lumbar punctures, permanent shunts and ventriculostomies became available. We identify three eras of hydrocephalus therapy: the observation era that stretches to the 18th century, the "crude therapy" era, till the modern era of hydrocephalus therapy with sophisticated shunting devices and neuroendoscopy.

Conclusion: Parallels can be made between the progress of medicine as a whole and hydrocephalus therapy. Although the treatment of hydrocephalus still poses a challenge today, we have come far from the crude treatment stage of serial lumbar punctures, and indeed from the observation era. Intra-uterine surgery, robotics, and image-guided surgery raise hopes for even better outcomes in hydrocephalus therapy of the future.

805. Niccolò Massa (1485–1569), a Renowned Anatomist of Medical Renaissance in Sixteenth Century and Discovery of Cerebrospinal Fluid in Brain

Shyamal C. Bir, MD, PhD, FAHA; Shyamal Bir, MD, PhD; Tanmoy Maiti; Devi Patra, MD, MCh; Papireddy Bollam, MD; Anil Nanda, MD, MPH (Shreveport, LA)

Introduction: Niccolò Massa (1485–1569), is one of the pioneer and

famous Italian anatomists, physicians and historians of the 16th century who had various innovations in anatomy. His works had some important contribution to the pre-Vesalian anatomical study of the human. Here, we describe Dr. Massa's life and his pioneering work on describing cerebrospinal fluid (CSF).

Work on cerebrospinal fluid: One of his pioneer works in anatomy is clear and detailed description of CSF in 1536. In his original work *De modo seccandi cerebri substantia ut ventriculos omnes videre possis et alias pres*, he described CSF in following quote; *Vide in cavitatibus supfluitate aquea expurgate forame. Semp has cavitates inveni plenas, aut semiplenas dictae aquose substantiae in English, observe watery superfluity in ventricles escaping through foramina and ventricles are always full or semifull of watery substance aforementioned.*

Other highly recognized works: He has also described the olfactory nerve, muscles of anterior abdominal wall, the prostate and the peritoneum. In addition, he reported about syphilis and its treatment with mercury, and on the plague.

Honors and Publications: His notable publications are "Liber introductorius anathema" on anatomy, "Liber morbo gallico" on syphilis and *Liber de febre pestilentiali* on fever.

Conclusion: He was also regular dissector of human body to study anatomy as well as to understand the etiopathogenesis of disease. In the field of neurosurgery, Dr. Massa should be highly recognized and credited for his pioneer works particularly on neuroanatomy and detail description of cerebrospinal fluid.

806. Charles E. Locke Jr. (1895-1929): Ohio's First Neurosurgeon

Pranay Soni, MD; Ghaith Habboub, MD; Varun Kshettry, MD; Fred Lautzenheiser; Donald Dohn, MD; Edward Benzel, MD (Cleveland, OH)

Introduction: The Cleveland Clinic was established in 1921 under the direction of four experienced physicians. When asked to assist in the search for a neurosurgeon to lead the department of neurosurgery, Harvey Cushing recommended Dr. Charles Edward Locke, a former student. Locke's life and career were both tragically ended prematurely, but not before he would leave a lasting legacy, both at the Cleveland Clinic, and in the field of neurosurgery.

Methods: A historical review was conducted at the Cleveland Clinic medical archives, Cleveland Clinic library, and via online searches.

Results: Despite a tragically shortened career, Locke's academic achievements were no less profound than his mentors'. His works include early castings of the lateral ventricles, reports of subtemporal decompression for neurosyphilis, one of the largest case series of carotid-cavernous fistulas, and several other works that were unfortunately lost in the Cleveland Clinic fire. Charles Locke's life was tragically taken in 1929, when an exposed light bulb ignited a roll of nitrocellulose x-ray film in the radiology department. The ensuing explosions took the lives of 80 visitors and 43 employees. Among them was Charles Locke, the father of neurosurgery at the Cleveland Clinic.

Conclusion: Charles Locke left a legacy that has already lasted nearly a century. He fathered a department of neurosurgery at an institute where the neurosurgery program continues to be one of the best in the country. Charles Locke was buried in Forest Lawn Memorial Park, Glendale, California, and while his body lays there in rest, his legacy lives on in commemoration.

807. Seizure outcome after surgical resection of insular glioma

Journal of Neuro-Oncology Award

Doris Du Wang, MD; Shawn Hervey-Jumper, MD; Edward Chang, MD; Mitchel Berger, MD (San Francisco, CA)

Introduction: A majority of patients with insular tumors present with seizures. Although a number of studies have shown that greater extent of

resection improves overall patient survival, few studies have documented post-operative seizure control after insular tumor resection. The aim of this study was to 1) characterize seizure control rates in patients undergoing insular tumor resection, 2) identify predictors of seizure control, and 3) evaluate the association between seizure recurrence and tumor progression.

Methods: The study population included adults who had undergone resection of WHO Grade II, III, or IV insular gliomas between 1997 and 2015 at the University of California San Francisco. Preoperative seizure characteristics, tumor characteristics, surgical factors, and postoperative seizure outcomes were reviewed.

Results: Of 287 patients who underwent insular glioma resection, 183 (64%) presented with seizures and 92 patients with sufficient clinical data were included. At one year after surgery, 62 patients (67%) were completely seizure free (Engel IA) and 80 patients (87%) were free from disabling seizures (Engel IA or IB). At final follow-up, 35 patients (38%) were seizure free and 69 patients (75%) had Engel IA or IB outcome. Multivariate proportional hazard analysis revealed that later seizure onset age (Hazard Ratio [HR]=0.0905, 95% CI [0.0129, 0.5854], p=0.0112), greater extent of resection (HR=0.1276 [0.0303, 0.5510], p=0.0063), and longer time to tumor progression were significant predictors of seizure freedom (HR=0.0076 [0.0004, 0.0890], p<0.0001). Seizure recurrence was significantly associated with tumor progression. Repeat resection offered additional seizure control as nine of the 21 patients (43%) with recurrent seizures became seizure free after re-operation.

Conclusion: Maximizing the extent of resection in insular gliomas not only offers survival benefit, but also portends greater seizure freedom after surgery. Seizure recurrence is predictive of tumor progression, and repeat operation can lead to additional seizure control.

808. Long-term follow-up data from 123 patients with recurrent high grade glioma from three Phase 1 trials of Toca 511 and Toca FC: Update and justification for a Phase 2/3 trial

Tiffany T Huang; Manish Aghi, MD; Michael Vogelbaum, MD; Steven Kalkanis, MD; Daniela Bota, MD; Bob Carter, MD; Clark Chen, MD; Bradley Elder, MD; George Kaptain, MD; Santosh Kesari, MD, PhD; Timothy Cloughesy, MD; Tobias Walbert, MD (San Diego, CA)

Introduction: Toca 511 (vocimagene amiretrorepvec) is an investigational, conditionally lytic, retroviral replicating vector. The vector infects human cells with selectivity for cancer cells because genome integration is dependent on cell division and viral replication is inhibited by innate and adaptive immune responses, defective in malignant tissues. Toca 511 spreads through cancer cells and stably delivers the gene for an optimized yeast cytosine deaminase that converts the prodrug Toca FC (an investigational, extended-release version of 5-fluorocytosine) into 5-fluorouracil (5-FU). The combined treatment is designed to generate 5-FU in the tumor micro-environment, directly killing cancer cells leading to activation of antigen presenting cells. 5-FU can also kill nearby immunosuppressive myeloid cell, leading to further immune system activation against the tumor.

Methods: The safety, viral kinetics, immune response, and preliminary efficacy of this combined treatment have been investigated clinically since 2010 in three Phase 1 studies of 123 of 126 treated patients with recurrent high grade glioma (rHGG), each evaluating different methods of Toca 511 administration. Repeated courses of oral Toca FC follow Toca 511 administration.

Results: Results to date include good tolerability; no persistent viremia; successful gene transduction within resected tumors: no evidence for clonality; and increased median overall survival compared to historical controls with all three methods of vector administration. Partial responses and complete responses with a median duration of initial response of < 20 months, occur in patients starting 6-19 months after Toca 511 administration, and are associated with a long term survival. Examination of IDH1 mutation status shows patients with a response are either wildtype or mutant.

Conclusion: Preliminary data from these studies supported initiation of a randomized, Phase 2/3 study in patients with rHGG (NCT02414165) in 2015. Updated data for the Phase 1 studies will be presented.

809. Winston Churchill: The Effect of his Health on his Leadership and of his Leadership on his Health

Gail L. Rosseau, MD, FAANS (Glen Ellyn, IL)

Introduction: Winston Churchill was, arguably, one of the greatest leaders of the 20th century. He survived, and even thrived, during two global wars, despite multiple significant threats to his health. These included pneumonias, motor car and airplane accidents, myocardial infarctions and stroke. His ability to rise above physical challenges permitted, and even enhanced, his extraordinary powers of leadership.

Methods: A Google search was performed to conduct a thorough literature review of all publications related to Churchill's health. This search led to a reading of over 200 books which covered the topic of Winston Churchill and his health. The project included participation in 3 international conferences of the National Winston Churchill Center. Interviews with recognized authorities on Churchill were conducted, including Dr. Jon Mather, MD, leading historian on the life and writings of Lord Moran, Churchill's personal physician, and Richard Langworth, publisher of *Finest Hour*, the Journal of Winston Churchill and his Times.

Results: A complete list of all of Churchill's known health problems, and his own writings about them was created. The effect of these maladies on Churchill's leadership was analyzed, and compared with his contemporaries, as well as other historical world leaders.

Conclusion: The many serious health challenges faced by Winston Churchill, particularly during and after WWII, affected his quality, style and duration of leadership. These effects will be thoroughly discussed in the presentation, which is illustrated by Churchill's own paintings. The study of Churchill's response to his health challenges and its incorporation into his leadership style is instructive for neurosurgeons.

810. Plasticity of motor representations in patients with brain lesions: a navigated TMS study

Brainlab Neurosurgery Award

Sandro Krieg, MD; Lucia Bulubas, MD; Nico Sollmann, MD; Noriko Tanigawa; Bernhard Meyer, MD (Munich, Germany)

Introduction: The present study investigates the spatial distributions of motor representations in terms of tumor-induced brain plasticity by analyzing navigated transcranial magnetic stimulation (nTMS) motor maps derived from 100 patients with motor eloquently located brain tumors in or adjacent to the precentral gyrus (PrG).

Methods: 8,774 motor evoked potentials (MEPs) were elicited in 6 muscles of the upper and lower extremity by stimulating four gyri (superior frontal gyrus=SFG, middle frontal gyrus=MFG, PrG, and postcentral gyrus=PoG) in patients with five possible tumor locations (frontal tumor: n=24, Rolandic tumor: n=35, postcentral tumor: n=17, temporal tumor: n=5, and parietal tumor: n=19). Regarding the MEP frequency of each muscle-gyrus subdivision per patient, the expected frequency was 3.53 (8,774 divided by 100 patients, further divided by 6 muscles and 4 gyri). Accordingly, the patient ratio for each subdivision was calculated by defining the per-patient minimum data points as 3.

Results: 60.71% of the MEPs were elicited in the PrG. The overall and tumor-location specific patient ratios were rather high (APB-in-PrG: 93.00%) and balanced, indicating robust motor representations in the PrG. Regarding the motor representations in SFG and MFG, the overall patient ratios were much lower (APB-in-SFG: 16.00%, APB-in-MFG: 36.00%). The tumor-location specific patient ratios were higher for frontal tumors in both gyri (ADM-in-SFG 29.17%, ADM-in-MFG 50.00%) than for other tumor locations. This suggests that the finger representation reorganization in these frontal gyri, which corresponds to location of dorsal premotor areas, might be due to within-premotor reorganization rather than relocation of motor function from PrG into premotor areas one might expect from the Rolandic tumors.

Conclusions: Reorganization of the finger motor representations might

be limited along the middle-to-dorsal dimension of the dorsal premotor areas (posterior MFG and SFG) and might not cross rostrally from the primary motor cortex (PrG) to the dorsal premotor cortex.

811. The First Successful Primary Brain Tumor Removal: "An Idea Whose Time Has Come"

Tanmoy Kumar Maiti; Shyamal Bir; Deviprasad Patra; Piyush Kalakoti, MD; Anil Nanda (Shreveport, LA)

Introduction: 25th November 1884 marks an auspicious day in the journey of Neurosurgery. Sir Rickman Godlee (1849-1925), a 35 year-old-surgeon performed first successful excision of an intrinsic brain tumor. The scientific developments paving the way for this surgery is often under-recognized.

The build-up and the surgery: The localization of intrinsic brain tumors in a normal appearing skull, on the basis of neurological symptoms and signs was a new concept. Paul Broca and Hughlings Jackson hypothesized the presence of organized anatomical and physiological localization of brain function, based on their clinical experience. David Ferrier published the results on localized electrical stimulation of the motor cortex in dogs. This method of functional neurological mapping is still used today. On November 3, 1884, a 25 year-old Scottish farmer was admitted in 'The Hospital for Epilepsy and Paralysis', London, with paralysis of left arm. Dr. Hughes Bennett, the concerned neurologist, extensively studied the case, possibly discussed with Dr. Jackson and Dr. Ferrier, and finally came to conclusion that the lesion lay somewhere around the right precentral gyrus. Dr. Godlee, [nephew of Sir Joseph Lister, pioneer of antiseptic surgery] was called in to perform the surgery. This event attracted significant interest among medical community. Dr. Bennett, Dr. Jackson, Dr. Ferrier, and Dr. Horsley were physically present during the surgery. The description of tumor, and the steps of surgery had been documented meticulously, and later presented in scientific meeting. Unfortunately, the patient died of meningitis and infarction on 28th post-operative day. But sections of the brain revealed no residual tumor.

Legacy: Like many discoveries, this novel surgery met wide criticisms at first, especially from the Anti-vivisectionist group.

Finally, the surgery marks the beginning of a new chapter, emphasizing the importance of functional brain-mapping, and the successful collaboration of neurologist and neurosurgeons; basic science and clinical medicine.

812. Comparing Resting State Functional Magnetic Resonance Imaging to Invasive Electrocortical Stimulation Mapping in Pediatric Patients

Jarod Roland, MD; Carl Hacker; David Limbrick, MD, PhD; Matthew Smyth, MD; Eric Leuthardt, MD (St Louis, MO)

Introduction: Localizing neurologic function remains a significant challenge in neurosurgery. When precise mapping is necessary, electrocortical stimulation remains the clinical gold standard. Several adjunctive procedures have been proposed and are utilized to varying degrees. Functional magnetic resonance imaging (fMRI) is one such adjunct that allows non-invasive whole brain analysis. Task based fMRI (t-fMRI) paradigms are the traditional methodology. Resting state fMRI (rs-fMRI) affords similar advantages while avoiding the need for a cooperative subject. This uniquely meets the needs of pediatric neurosurgeons whose patients are often difficult to effectively map.

Methods: We previously trained a multilayer perceptron (MLP) machine learning algorithm to identify seven canonical resting state networks (RSN). Here we evaluate its performance in pediatric patients prior to invasive electrocorticography monitoring. We compare the sensorimotor RSN to bedside stimulation mapping. Descriptive statistics and receiver-operator curve (ROC) analysis are used to determine parameters for RSN mapping.

Results: We identified 20 subjects for inclusion in this study (11 male). Mean age was 11.6 years (range 3.1 to 18.6 years). Sedation was used in 35% (N=7) for MRI acquisition. Sensitivity and specificity was calculated for varying thresholds of MLP scores and in a winner-take-all method across all subjects with motor or sensory positive stimulation sites (N=17). ROC of

the mean across subjects yields an area under the curve of 0.70. A threshold of 0.822 yields specificity of 90% and sensitivity of 29%. Winner-take-all analysis yields a specificity of 88% and sensitivity of 33%.

Conclusion: Resting state fMRI is a valuable tool to screen for sensorimotor cortex. We demonstrate good performance across a wide age range in a cohort of pediatric patients by comparing to the clinical gold standard of bedside stimulation mapping. The ability to acquire rs-fMRI alongside routine anatomic imaging and under sedation make this technique particularly advantageous to the pediatric neurosurgeon.

813. Misdiagnosis is a Prevalent Cause of Inappropriate Lumbar Spine Surgery

William H. Sweet Young Investigator Award

Vijay Yanamadala, MD; Jean-Christophe Leveque, MD; Alicia Edwards, MBA; Quinlan Buchlak; Anna Wright, PhD; Farokh Farrokhi, MD; Robert Mecklenburg, MD; Rajiv Sethi, MD (Seattle, WA)

Introduction: Lumbar spine surgery in the United States has increased eight-fold over three decades. While effective in a randomized controlled trial settings, some nationwide analyses show overall outcomes no better than non-operative care.

Methods: After institutional review board approval, we retrospectively reviewed 19,218 vascular surgery, orthopaedic joint surgery, and neurology consultations. 3,114 consecutive patients presented for lower extremity pain. We identified patients who had prior lumbar spine surgery. Records were reviewed for (1)symptoms leading to spine surgery; (2)post-surgical symptoms; and (3)vascular or orthopaedic procedures. Statistical significance was $p < 0.05$ using a Chi-squared-test.

Results: 111 (23.9%) of 464 patients presenting to vascular surgery with claudication symptoms underwent prior lumbar spine surgery at outside institutions in seven states compared to seven (0.7%) of 1,000 non-claudication patients (Chi-squared=230.6; $p < 0.01$). 89 patients (80.2%) had modest/minimal benefit from spine surgery, all of whom had an abnormal lower extremity pulses with mean ankle-brachial-index of 0.72. 17 patients (20.2%) underwent vascular procedures with improvement (mean follow-up: 15 months). Mean delay-in-diagnosis was 18 months (range:5–32). 82 (7.6%) of 1,089 patients presenting to orthopaedics with hip or knee pain underwent prior lumbar spine surgery at outside institutions compared to eleven (1.1%) of 1,000 upper extremity patients (Chi-squared=50.7; $p < 0.01$). 47 patients (57.3%) had modest/minimal benefit. 28 patients underwent total joint arthroplasty with 27 patients reporting improvement (mean follow-up 22 months). Mean delay-in-diagnosis was 19 months (range:4–36). 13 (0.8%) of 1,561 patients presenting to neurology underwent prior spine surgery at outside institutions without improvement. Eight patients had evidence of peripheral neuropathy on electromyography.

Conclusion: With the limitations of a single-institution retrospective study, our analysis reveals that misdiagnosis is a significant event in lumbar spine surgery. Vascular claudication and osteoarthritis were frequently misdiagnosed as lumbar spondylosis leading to numerous futile surgeries. Importantly, many patients had substantial delays in diagnosis, in some cases years.

814. Intra-tumoral Infusion of DNAtrix's Oncolytic Adenovirus DNX-2401 Using Alcyone's Micro-fabricated Cannula

Deep Singh; Loredana Guseila; Bradley Elder, MD; Nam Tran, MD, PhD; Martin Brady, PhD; Frank Tufaro, PhD; PJ Anand; Frederick Lang, MD (Lowell, MA)

Introduction: Limitations with intra-tumoral infusions include backflow of infusate and inability to verify drug delivery. The FDA-approved Alcyone MEMS Cannula (AMC) has a micron-scale tip, features to prevent backflow, and two independent channels. We tested the ability of the AMC to intra-tumorally deliver DNX-2401, an active oncolytic adenovirus manu-

factured by DNAtrix in a Phase 2 clinical trial for recurrent glioblastoma (NCT02197169). Drug delivery was assessed using the aura-method, in which a small Gadolinium infusion was followed by DNX-2401, where the Gadolinium would distribute around the periphery of the DNX-2401 distribution forming a ring/arc (aura) which could be MR-imaged to assess backflow and distribution.

Methods: The AMC was stereotactically placed into enhancing tumor in nine patients. Seven infusions were done using the aura-method. Magnevist was infused through one channel (150 μ L, 0.5mM, 15 μ L/min), followed by DNX-2401 through the second channel (1mL of 3x10¹⁰ vp, 15 μ L/min). MRI was performed immediately after infusion (<30min, N=7) and at delayed times (<2hrs, N=3). Two infusions were done with just DNX-2401.

Results: Semi-quantitative analyses indicated successful DNX-2401 infusions in all cases without evidence of backflow. A Gadolinium aura (ring or arc) was seen radially away from the tip without backflow in all aura-method infusions, indicating drug distribution within the arc. The average volume inside the arc (assuming spherical infusion) was 1.9mL (N=4 measured). Delayed scans revealed washout of Gadolinium after 2-hours.

Conclusion: The AMC was able to reproducibly infuse DNX-2401 intra-tumorally at high flowrates without backflow, and the aura-method could successfully assess distribution of DNX-2401 in the tumor with MRI within 2 hours.

815. Neurosurgery-ENT hand shake in the 20th century: Catalyst for the Modern Day Skull Base Evolution

Jai Deep Thakur, MD; Brian Manzi; Lauren Lange; Gale Gardner; Bharat Guthikonda; Anil Nanda (Shreveport, LA)

Introduction: Basis of skull base techniques used in neurosurgery has been inspired from the intellectual crossover and the prism of knowledge expressed by Otorhinolaryngologist in their era of modern surgical renaissance. This historical perspective highlights the critical overlap between the two rapidly evolving surgical specialties of the 20th century.

Methods: PubMed, historical archives and google scholar search engines were used to extract pertinent literature.

Results: Early 20th century saw the overlap of two specialties to introduce the trans-sphenoidal approach. The endoscopic avenue was tested for the first time for the paranasal sinuses in 1901 by Hirschmann. Gerald Guio, a French neurosurgeon took close lessons from growing ENT technological advances and introduced a possibility of endoscopic exposure of the sella and set the stone for using a multidisciplinary approach with Otorhinolaryngologist and craniofacial surgeons. Apuzzo et al built on the growing bond to define the use of endoscopy for sellar tumors. In 1990's team of French Otorhinolaryngologist published their surgical experience of pure endoscopic sellar surgery and few years later the otorhinolaryngological-neurosurgeon team including Sethi and Pillay from the Singapore General Hospital and Jho and Carrau from Pittsburgh revolutionized the skull base surgery. This vignette further highlights the overlap between the two fields in the evolution of microscopic neurosurgery by Kurze, Donaghy and Yasargil and the evolution of fat graft/flaps in sellar and otorhinological surgeries.

Conclusion: The Neurosurgery-ENT growing collaboration fueled the evolution of modern day skull base surgery and only emphasizes a global practice of this doctrine for better patient care.

816. Percutaneous Doxycycline Treatment: A Novel Approach to Aneurysmal Bone Cysts of the Spine

David Lee Dombos III, MD; Jeffrey Leonard, MD; Lacey Lubeley; William Shiels II, DO; James Murakami, MD (Columbus, OH)

Introduction: Aneurysmal bone cysts (ABCs) of the spine are benign bony neoplasms that are often locally aggressive and difficult to treat, with a high recurrence rate (10-44%) following surgical resection. In addition to its antimicrobial properties, doxycycline inhibits angiogenesis, is cytotoxic to osteoclasts and enhances osteogenic bone production. Percutaneous

injection of doxycycline has been proven effective in treating ABCs of the appendicular skeleton, but this technique has not yet been evaluated in the spine.

Methods: We retrospectively reviewed 24 patients who underwent staged percutaneous injection of biopsy-proven ABCs with doxycycline from 2006 through 2016. The mean age was 14.0 years (range, 6 to 24 y), with pathology distributed between the cervical (9), thoracic (3), lumbar (2) and sacral (10) spine. Treatment response was evaluated by radiographic measurement of lytic volume and symptomatic improvement. New areas of lytic destruction following completion of treatment indicated recurrence. Minimum follow-up was 12 months (mean, 31.2 months). Statistical analysis was performed using a two-tailed paired t-test and intention-to-treat analysis.

Results: All patients demonstrated reduction in lytic destruction with a mean decrease of $91.1 \pm 2.2\%$ ($p < 0.0001$) in the total lytic volume, being replaced by new bone formation. One patient demonstrated recurrence (4.2%) at 54 months and successfully underwent single-session retreatment. Prior to treatment, moderate to severe pain was noted in 95.8% (23/24) and radiculopathy in 29.2% (7/24). Following treatment, mild pain was noted in 25.0% ($p < 0.0001$) and radiculopathy was only experienced by one patient ($p < 0.001$). No symptomatic complications occurred.

Conclusion: Treatment with percutaneous doxycycline injection of spine ABCs yields a significant regression in lesional lytic volume with concurrent bony replacement. This coincides with a significant reduction in associated pain and radiculopathies. Given its safety and rate of recurrence lower than that in the established literature, this provides a novel approach to treating these difficult lesions.

817. Prospective comparison of long-term pain relief rates after first-time microvascular decompression and stereotactic radiosurgery for trigeminal neuralgia

Doris Du Wang, MD; Kunal Raygor, MD; Tene Cage, MD; Mariann Ward, MS; Nicholas Barbaro, MD; Edward Chang, MD (San Francisco, CA)

Introduction: Common surgical treatments for trigeminal neuralgia (TN) include microvascular decompression (MVD), stereotactic radiosurgery (SRS), and radiofrequency ablation (RFA). Although the efficacy of each procedure has been described, few studies have directly compared these treatment modalities on pain control for TN. Using a large prospective longitudinal database, we aimed to 1) directly compare long-term pain control rates for first-time surgical treatments for idiopathic TN and 2) identify predictors of pain control.

Methods: We reviewed a prospectively collected database for all patients with TN who underwent treatment for TN between 1997 and 2014 at the University of California San Francisco. Standardized data collection of preoperative clinical data, surgical procedure and postoperative outcomes were performed. Data analyses were limited to those patients who received a first-time procedure for treatment of their idiopathic TN with >1 year follow-up.

Results: Out of 764 surgical procedures performed, 340 patients underwent first-time treatment for idiopathic TN (164 MVD, 168 SRS, and 8 RFA) with >1 year follow-up. Immediate postoperative pain-free rates (BNI I) were 96% for MVD and 75% for SRS. Percent of patients with BNI I score at one, five, and ten years following MVD were 83%, 61%, and 44%, and those for SRS were 71%, 47%, and 27%, respectively. Median time to pain recurrence was 94 months (IQR 57-131 months) for MVD and 53 months (IQR 37-69 months) for SRS ($p = 0.006$). Multivariate regression demonstrated that shorter preoperative symptom duration (HR 1.005 [1.001-1.008], $p = 0.006$) was associated with favorable outcome for MVD and that post-SRS sensory changes (HR 0.392 [0.213, 0.723], $p = 0.003$) were associated with favorable outcome for SRS.

Conclusion: In this prospective longitudinal study, patients who received MVD had longer pain-free interval compared to those of SRS. For those receiving SRS, postoperative sensory change was predictive of favorable outcome.

818. Language lateralization with resting state and task-based functional MRI in pediatric epilepsy

Virendra R. Desai, MD; Aditya Vedantam, MD; Varina Boerwinkle, MD; Sandi Lam, MD (Houston, TX)

Introduction: Determining language laterality in pediatric epilepsy cases is important in operative planning. The gold standard for language lateralization is WADA testing, though its invasiveness and requirement for patient cooperation limits its use in pediatrics. Task-based functional MRI (tb-fMRI) is an alternative. Recently, resting state fMRI (rs-fMRI) has been employed to lateralize language in patients with medically intractable focal epilepsy (1). In this study, we determine the correlation between rs-fMRI and tb-fMRI in language lateralization in a general pediatric population with intractable epilepsy.

Methods: Pediatric epilepsy cases seen at Texas Children's Hospital (TCH) between January 1, 2015 and June 30, 2016 were retrospectively analyzed. Initial exclusion criteria involved age less than 10 years old and sedation during fMRI. Cases in which both rs-fMRI and tb-fMRI were performed were included. Standard tasks included verb generation, word generation and sentence completion. A board-certified pediatric neuroradiologist analyzed each tb-fMRI, while a board-certified pediatric neurologist, who has evaluated over 1,500 individual rs-fMRIs for language lateralization, analyzed each rs-fMRI.

Results: 16 cases had both rs-fMRI and tb-fMRI performed during the study time period. tb-fMRI suggested left dominance in 12 cases (75%), right in 2 (12.5%), and non-diagnostic in 2 (12.5%). None had bilateral dominance on tb-fMRI. rs-fMRI correlated with tb-fMRI in 13 cases (81.3%) overall. When tb-fMRI noted left-sided dominance, rs-fMRI lateralized to left in 11 cases (91.7%) and equal in 1 (8.3%). When tb-fMRI noted right-sided dominance, rs-fMRI lateralized to right in both (100%). When tb-fMRI was non-diagnostic, rs-fMRI had no correlation, lateralizing to left in one and bilateral in the other.

Conclusion: rs-fMRI had significant correlation with tb-fMRI in lateralizing language in our general pediatric epilepsy population. This suggests a role for identifying hemispheric dominance via rs-fMRI in cases in which tb-fMRI cannot be performed. Further study is warranted, and validation is needed.

819. Targeted Nanoparticle-based Vehicle for Delivery of Small Molecule Inhibitors to Primary and Metastatic Brain Tumors

Rupa Juthani, MD; Barney Yoo, PhD; Kai Ma; Li Zhang, MD; Sean Carlin, PhD; Jason Huse, MD, PhD; Michael McDevitt, PhD; Michael Overholtzer, PhD; Ulrich Weisner, PhD; Michelle Bradbury, MD, PhD; Cameron Brennan, MD (Cleveland, OH)

Introduction: While cancer treatment has been revolutionized by small molecule inhibitors, treatment of brain tumors remains elusive owing to poor blood brain barrier (BBB) penetration and diffusion, with doses limited by systemic toxicity. This study investigates the use of a nanoparticle-based vehicle to enhance drug delivery to malignant brain tumors.

Methods: Ultra-small silica nanoparticles containing Cy5 (Cdots) were conjugated with analogs of the EGFR inhibitor gefitinib (Gef-NDC) or the Src kinase inhibitor Dasatinib (Das-NDC). Cdots for intracranial study were additionally modified with targeting peptides (cRGDY-C) or a scrambled peptide (cRAD-C), as well as a radiolabel (124I-RGDY-C, 124I-cRAD-C). The RCAS-tv-a mouse glioma model was used to investigate intracranial distribution. Transgenic TVA-expressing mice were stereotactically injected with RCAS-PDGFB. Following tumor confirmation by MRI, mice were injected with 124I-cRGDY -C, 124I-cRAD-C, Das-NDC, or Das-cRGDY-NDC with fluorescent BBB tracers and sacrificed at 3 and 96 hours. To study Gef-NDC, mice bearing NSCLC derived ECLC26 flank xenografts were treated with vehicle alone, gefitinib (150mg/kg PO.) or Gef-NDC and sacrificed at 6 and 18 hours. Cd dot distribution was assessed by autoradiography, fluorescence microscopy, and in-vitro analysis. Target inhibition was assessed by western blot and immunohistochemistry(IHC).

Results: Mice bearing RCAS/tv-a gliomas demonstrated strong tumor specific accumulation and retention of Cdots. Das-NDC treated tumors demonstrated a time-dependent target inhibition as measured by suppression of pPRAS-40 on IHC. RGD targeting resulted in higher tumor to brain ratios of labeled particle, with increased diffusion through the tumor compared to non-targeted particles. In mice bearing ECLC26 xenografts, Gef-NDC treated tumors demonstrated potent pEGFR target inhibition at 18 hours post-treatment.

Conclusion: These initial results provide a strong basis for development of a nanoparticle-based vehicle for enhancing drug delivery to malignant brain tumors. Further evaluation of alternative drugs, dosing intervals, and comparisons of therapeutic index will further guide application of these particles.

820. Extraordinary Measures: Harvey Cushing's Early Struggle with Patient Mortality and End-of-Life Care

Courtney Pendleton, MD; Alfredo Quinones-Hinojosa, MD (Philadelphia, PA)

Introduction: In contemporary neurosurgery, and medicine as a whole, the discussion of medical futility, extraordinary measures, and end-of-life care remains a controversial topic. A review of the records of Harvey Cushing demonstrates these concerns arose while the foundations of modern American neurosurgery were being built.

Methods: The Johns Hopkins Hospital surgical records from 1896-1912 were reviewed. Twenty-two cases in which extraordinary measures for preservation of patient life – defined as artificial respiration, placement of tracheostomy/gastrostomy, or use of transfusions/pharmacologic stimulants explicitly documented for patient resuscitation – were selected for further analysis. Information regarding age, gender, and race/ethnicity of these patients was acquired from the front page of each chart. Given the difference in societal perception of, and medical care available to, patients perceived to be non-caucasian during the era reviewed, the following sub-categories were established for analysis: Caucasian, Immigrants (including all patients with a foreign nationality documented, other than Canadian and English), and African American.

Results: Of the twenty-two patients in which extraordinary life-preserving measures were documented, the majority were Caucasian (63.6%), non-Caucasian immigrants and African Americans made up 14.6% and 9.1% respectively. Two patients had no nationality/ethnicity documented in the chart demographic page (9.1%). Ten patients (45.5%) were female. The mean age was 25.8 years (range: 0.92 – 55). Overall, 18 patients (81.8%) died during their admission.

Conclusion: This review of Cushing's early use of extraordinary measures to sustain patient lives in the peri- and intra-operative period highlights the ubiquity of end-of-life care challenges, and offers a historical context for the contemporary neurosurgeons' goal of considering the role of medical futility and palliative treatment while providing exhaustive and compassionate patient care.

821. Correlation of fetal MRI findings with need for postnatal VP shunt placement in children born with myelomeningocele

Suresh N. Magge, MD, FAANS; Wahab Syed, BS; Eva Rubio, MD; Robert Keating, MD; Chima Oluigbo, MD; John Myseros, MD; Dorothy Bulas, MD (Washington, DC)

Introduction: Fetal MRI is increasingly being used after the in-utero diagnosis of myelomeningocele (MMC), but the prognostic value is not well understood. We examined features of the fetal brain on prenatal MRI (including ventricular size, hindbrain herniation, and presence/absence of cisterna magna) and correlated those findings with the possible need for postnatal VP shunt.

Methods: This was an IRB-approved, retrospective study. We examined MRI imaging (n=24) of fetuses (mean age 24 weeks gestation when imaged) diagnosed with MMC. Lateral ventricle size was measured at the

frontal horns. Additional features included 3rd and 4th ventricular dilatation, hindbrain herniation, and presence/absence of cisterna magna. Patients were evaluated for whether they had a VP shunt placed by one year of age.

Results: Mean prenatal ventricle size was greater in fetuses who later received a VP shunt postnatally compared to those who did not receive a VP shunt (11.4 mm vs 9.5mm; $p < 0.05$). For fetuses with ventricle sizes < 15 mm, 100% (4/4) went on to receive a VP shunt postnatally. For fetuses with ventricle sizes 10-15mm, 37.5% (n=3/8) went on to receive a VP shunt, and for fetuses with ventricle sizes 5-10 mm, 50% (n=6/12) went on to receive a VP shunt. No significant correlation was found between 3rd and 4th ventricular dilatation and postnatal VP shunt placement. Absence of cisterna magna on fetal MRI was found to be a statistically significant predictor ($p < 0.05$) of postnatal VP shunt placement.

Conclusion: This study correlated prenatal ventricular size and other fetal MRI findings (of fetuses with MMC) with potential need for a VP shunt after birth. All fetuses with prenatal ventricle size greater than 15 mm required a VP shunt. This study can be used by the clinician as a tool to aid in the evaluation of prenatal MRIs and in discussions with parents.

822. Prediction of Clinical Outcomes after Transforaminal Lumbar Interbody Fusions Based on Preoperative Opioid Use

Alan T. Villavicencio, MD, FAANS; E Nelson, MD; Vinod Kantha, BA; Sharad Rajpal, MD; Colson Tomberlin; Sigita Burneikiene, MD (Boulder, CO)

Introduction: Opioid analgesics have become one of the most prescribed drugs in the world, despite the lack of long-term studies evaluating benefits vs. risks for chronic conditions and the fact that long-term use may be associated with worse long-term clinical outcomes. The primary objective of this study was to identify if preoperative opioid use predicted inferior clinical outcomes in patients undergoing transforaminal lumbar interbody fusion.

Methods: A prospective observational study was performed. A total of 93 patients were enrolled undergoing one- to two-level transforaminal interbody fusions and divided into two groups based on preoperative opioid use. The preoperative and clinical outcomes scores at 12-month follow-up were compared.

Results: A total of 60 (64.5%) patients preoperatively used prescribed opioid medications. The patients who preoperatively used opioid medications had significantly higher low back ($p = 0.016$) VAS scores, more disability ($p = 0.013$), and lower health-related quality of life PCS scores ($p = 0.03$) at the 12 months follow-up. The SF-36 MCS scores remained significantly lower ($p = 0.035$) in the opioid user group, but this was due to the significantly lower baseline scores.

Conclusion: The use of opioid medications to control pain symptoms prior to undergoing lumbar fusion for degenerative lumbar conditions was associated with less favorable clinical outcomes postoperatively. This is the first study that has demonstrated this association in a homogeneous population of patients, which should be studied further to confirm these conclusions.

823. Quality of Life after Single Level Selective Dorsal Rhizotomy in Ambulant Children with Cerebral Palsy.

Salima Wahab; Lucinda Carr; Neil Wimalasundera; Stephanie Cawker; Deepti Chugh; Kristian Aquilina (London, England)

Introduction: The use of single-level selective dorsal rhizotomy (SDR) at the conus continues to increase. The effects of SDR on the quality of life of the child and family have largely only been investigated for the traditional multi-level laminectomy or laminoplasty technique.

Methods: 27 ambulant children, aged 3 to 10, underwent single-level SDR between October 2014 and December 2015. To minimise bias in this self-reporting methodology, only children who were funded by the National Health Service were included. On the Gross Motor Function Classification System (GMFCS), 10 children were level II and 17 were

level III. Changes in motor function were evaluated using the Gross Motor Function Measurement (GMFM) – 88 scale. The PediQOL self-reporting questionnaire was used to evaluate changes in quality of life after surgery.

Results: There were no surgical complications. Mean GMFM-88 scores increased from 85 to 89 (GMFCS II) and from 60.9 to 70.4 (GMFCS III) ($p < 0.01$) at 1 year. Maximal changes, up to a mean of 120%, occurred in the E (walking, running, jumping), D (standing) and C (crawling, kneeling) domains. Maximal changes on quality of life scores at 1 year occurred for pain, emotional well-being and family health. Changes in these parameters were already statistically significant at 6 months, $p < 0.02$.

Conclusion: Single-level SDR is not only associated with improvements in motor function but also with significant and clinically relevant increases in quality of life parameters as early as 6 months post-operatively. This occurs despite reduction in functional ability that ambulant children demonstrate in the early postoperative phase. It confirms that recovery from single-level SDR is rapid and only leads to brief minimal interruption of a child's ongoing therapeutic gains.

824. Surgical Outcome of Adult Hemispheric Glioblastoma is Determined by the Molecular-Subset: An Analysis of 142 Patients.

Koray Ozduman, MD, PhD; Cemaliye Akyerli, PhD; Ozlem Yapicier, MD; Erdal Cosgun, PhD; M Cengiz Yakicier, MD, PhD; Sirin Yuksel, BSc; Alp Dincer, MD; Ozge Can, PhD; M Necmettin Pamir, MD (Istanbul, Turkey)

Introduction: Glioblastoma is commonly perceived as a single entity with uniformly fatal outcome. However molecular genetic studies have shown distinct molecular-subsets among glioblastomas, which differed tumor biology. We hypothesized that molecular subsets based on 3 molecular markers would have clinical correlation in adult hemispheric glioblastomas.

Methods: 142 adult hemispheric diffuse-gliomas (Median age 56.5, range 20-85), which were WHO grade IV at initial presentation were retrospectively tested for IDH-mutations, TERT-mutations and H3.3 mutations. 4 molecular subsets were identified: IDH-mutant (9.9%), TERT-mutant only (64.1%), H3.3-mutant (1.4%) and triple-negative (24.7%). These 4 subsets were compared for age, anatomical localization, Ki67 index, nuclear TP53 immunopositivity, overall-survival and progression-free survival.

Results: Age at presentation for IDH-mutant, TERT-mutant only, H3.3-mutant and triple negative were 44, 58, 31.5 and 50 years respectively and these were significantly different (ANOVA, $p = 0.000139$). Ki-67 index was comparable in all molecular subsets (ANOVA, $P = 0.71$). There were no differences in anatomical localizations. Mean overall-survival was 60.7 ± 8.2 , 24.1 ± 2.2 , 13.5 ± 2.5 , 35.1 ± 3.4 months for IDH-mutant, TERT-mutant only, H3.3-mutant and triple negative subsets respectively. Mean time to recurrence was 23.9 ± 4.7 , 13.2 ± 2 , 13.5 ± 2.5 , 19.9 ± 2.5 months for IDH-mutant, TERT-mutant only, H3.3-mutant and triple negative subsets respectively. Differences in overall-survival (Log rank, $p < 0.0001$) and progression-free survival (Log rank, $p = 0.004$) were highly significant among different molecular subsets.

Conclusion: Four molecular-subsets based on IDH, TERT and H3.3 mutations are strongly correlated with clinical behavior in adult hemispheric glioma.

825. Origins of "HHH" Therapy for SAH Vasospasm: Thoralf M. Sundt, Jr., MD

Kelly Gassie, MD; Nnenna Mbabuike, MD; Benjamin Brown, MD; Robert Wharen, MD; William Freeman, MD (Jacksonville, FL)

Introduction: Dr. Thoralf M. Sundt Jr. was a vascular neurosurgeon at Mayo Clinic who contributed to our knowledge and understanding of the pathophysiology of subarachnoid hemorrhage (SAH), vasospasm (VSP) and treatment, particularly "Triple H" (hemodynamic, hemodilution and hypertension) therapy. Although early studies of VSP were ongoing before and during his career, the origins of who first described this medical treatment remain historically elusive. Herein we describe Dr. Sundt's

first description and contributions to our current understanding of clinical vasospasm after SAH and its modern day ICU treatment.

Methods: We searched Pubmed using key words triple H, subarachnoid hemorrhage and vasospasm and later with adding author Thoralf M. Sundt Jr. Individual articles were recalled and refined with regard to their precision to HHH physiology and significance in the management of subarachnoid hemorrhage and vasospasm.

Results: After selecting using SAH and triple H search criteria, we discovered 92 publications, with the first using the term triple H specifically in 1990 by Oritano et al. Using other search combinations and the author, we found 39 specific publications on the subject. Two articles were eliminated due to discussions not on SAH. In 1973, Dr Sundt described using pressors and fluids to increase cerebral blood flow and augment cardiac output in VSP SAH patients in an original article in *Mayo Clinic Proceedings* and *Journal of Neurosurgery*. We believe this represents the first physiological and early description of so-called triple H therapy for VSP.

Conclusions: The term triple H therapy for SAH VSP was originally coined in the 1990 as the concept caught on, but the original description of this physiologic intervention appears described by Dr. Sundt in the *Mayo Clinic Proceedings* and *Journal of Neurosurgery*. His contributions to our understanding of clinical vasospasm are unparalleled in the field of neurosurgery.

826. Long-term Outcome Analysis of Children Presenting with Traumatic Brain Injury Secondary to Nonaccidental Trauma (NAT)

Stephen J. Lehnert; Daniel Fulkerson, MD (Indianapolis, IN)

Introduction: Treatment of pediatric traumatic brain injury (TBI) is complicated by a number of factors. TBI secondary to nonaccidental trauma presents clinical as well as social complexity. There are very few studies addressing long-term outcomes in patients with TBI secondary to NAT. The purpose of our study is to determine the indicators and long-term outcomes of patients with TBI secondary to NAT.

Methods: A prospective trauma database was reviewed for patients who presented to a level 1 pediatric trauma center for TBI secondary to confirmed NAT. Using the existing statewide and institutional electronic medical record, patient charts were retrospectively reviewed to determine last known functional status including schooling, occupational status, functional status, and medical status. Statistical analyses and classification trees were formed for patient outcomes based on modeled predictor variables.

Results: Two hundred three patients (12.4%) of 1636 patients were identified as presenting with NAT as the mechanism of injury. One hundred eighteen patients (58.1%) were found to have a greater than 1 year follow-up. The cohort had an average 12.7 year follow up time. Patients were found have improved outcomes with a mean follow-up peds GOS 4.4 ± 0.83 compare to a discharge peds GOS score 3.7 ± 0.72 ($p = .000$). 67 patients (56.8%) had improved GOS scores compared to 6 patients (5.1%) whose functional status declined since discharge. Positive long-term outcomes were most strongly associated with the eye opening on initial neurological examination.

Conclusion: This study describes a cohort of 118 patients who were studied over a decade after NAT TBI. The findings suggest significant improvements to overall functional outcome. Hospital factors that favored greater outcomes were presenting GCS score, eye opening response, multiple injuries, and ethnicity.

827. Atypical Pituitary Adenoma: a Clinicopathologic Case Series

Martin John Rutkowski, MD; Ryan Alward, BS; Rebecca Chen, BA; Jeffrey Wagner, BA; Arman Jahangiri, BS; Derek Southwell, MD, PhD; Sandeep Kunwar, MD; Lewis Blevins, MD; Han Lee, MD; Manish Aghi, MD, PhD (San Francisco, CA)

Introduction: In 2004 the World Health Organization (WHO) classified atypical pituitary adenoma as a distinct adenoma subtype. However, the clinical significance of this distinction remains undetermined.

Methods: We reviewed records of patients undergoing resection of pituitary adenoma at our institution from 2007-2014. Statistical analyses were performed using chi-square, Fisher's exact test, T test, log rank, and logistic regression.

Results: From 2007-2014, 701 patients underwent resection for pituitary adenoma with 36 tumors (5%) proving to be atypical. The mean age of atypical patients was 37 years, significantly lower than the mean of 49 years seen for non-atypical patients ($p < 0.001$). Atypical adenomas were more likely to be functional than non-atypical adenomas ($p < 0.001$). Functional atypical adenomas were significantly larger than functional non-atypical adenomas ($p = 0.008$), as were nonfunctional atypical adenomas and nonfunctional non-atypical adenomas ($p = 0.01$). Among the entire adenoma cohort, larger presenting tumor size was associated with cavernous sinus invasion ($p < 0.001$), while subtotal resection was associated with cavernous sinus invasion ($p < 0.001$) and larger size ($p < 0.001$) on binomial multivariate regression. The median time until recurrence was 56 months for atypical adenomas, 129 months for functional non-atypical adenomas, and 104 months for nonfunctional non-atypical adenomas ($p < 0.001$). Functional atypical adenomas recurred more frequently and significantly earlier than functional non-atypical adenomas ($p < 0.001$). When accounting for extent of resection, cavernous sinus invasion, size, age, gender, and functional subtype, atypicality remained a significant predictor of earlier recurrence among functional adenomas ($p = 0.002$).

Conclusion: When compared to non-atypical pituitary adenoma, atypical adenomas are more likely to present in younger patients at a larger size, are more often functional, and are more recurrent. These features lend credence to atypical pituitary adenoma being a distinct clinical entity in addition to a discrete pathological diagnosis.

828. Spinal Cord Stimulation (SCS) Infection Rate and Incremental Annual Expenditures: Results from a US Payer Database

Alissa H Doth; Steven Falowski, MD; David Provenzano, MD; Ying Xia, MS; Alissa Doth (Minneapolis, MN)

Introduction: Surgical Site Infections (SSIs) result in significant negative clinical and economic outcomes. The objective of this study is to estimate the infection rate and the annual health expenditures associated with SCS-related infection.

Methods: Patients with SCS neurostimulator generator implant during calendar years 2009 – 2014 were identified from Truven MarketScan® Commercial Claims and Medicare Supplemental databases. Patients were continuously enrolled for at least 12 months before and after implant. The patients were further divided into initial group or replacement group. Annual expenditures were estimated for patients who experienced a device-related infection versus those without infection. A generalized linear model was used to estimate annual expenditures, utilizing a gamma distribution and log link function. All models were controlled for presence of all-cause infection before generator implant, Charlson comorbidity index score, as well as patient demographics (including age, gender, region, insurance type). Costs were adjusted to 2014 USD.

Results: The study included 6,615 patients: 5,563 (84.1%) initial group, and 1,052 (15.9%) replacement group. The overall SCS-related infection rate within 12-months post-implant was 3.11%. Multivariable expenditure models revealed that patients with infection have higher annual expenditures than patients without infection in initial and replacement groups. Estimated incremental annual healthcare expenditures for patients with an infection were \$59,716 (95% CI: \$48,965-\$69,480) for initial group and \$64,833 (95% CI: \$37,377 - 86,519) for replacement group. 27% of patients who were explanted for infection received a subsequent re-implant.

Conclusion: The approximate 3% device-related infection rate within 12-months after SCS implant determined from a large administrative database emphasizes the need for improvement in SCS infection control practices. The expenditure burden associated with SCS-related infection is substantial, and management of SCS-related infections is important from both clinical and economic standpoints. Additional education, research

and mitigation strategies are needed to minimize infection caused by SCS implant.

829. Expanding the Applications of Responsive Neurostimulation: Early Experience in Pediatric Patients

Saadi Ghatan, MD; Malgosia Kokoszka, PhD; Fedor Panov, MD (New York, NY)

Introduction: The responsive neurostimulation system (RNS) is a cranial device for chronic recording of brain activity and programmed delivery of electrical stimuli that interrupt epileptic events. It is an approved adjunctive treatment in adults, but not in children, with pharmacoresistant focal epilepsy. We present the first pediatric application of RNS.

Methods: Eight pediatric patients (5M, 3F, ages 9-17 years) were deemed candidates for RNS implantation at a multidisciplinary epilepsy surgery case conference. Results: Indications included: 3 cases of bilateral focal epilepsy with bilateral MRI lesions, one previously treated with hemispherotomy; 3 non-lesional cases of failed focal resections/disconnections and/or VNS; and 2 cases of seizure foci in eloquent areas, one in a boy with Rasmussen's encephalitis who was not a candidate for hemispherotomy. In addition to 2 active cortical and/or depth electrodes at the putative seizure foci in all 8 cases, a decision was made to also implant one or two leads at suspected seizure foci in 2 of the 8 patients, and bilateral anterior thalamic depth electrodes in 2 more cases – based on evidence from deep brain stimulation trials. So far, 3 children have had the RNS parameters adjusted to a therapeutic level, with 50 to 90% seizure reduction after 5 to 12-months with no side effects.

Conclusion: RNS may provide a palliative benefit in selected pediatric patients. Unlike in adults, where RNS can be applied based preference for non-resective treatment, desire to reduce medication dose, or for diagnostic purposes, the pediatric application of RNS should be limited to cases such as unresectable seizure foci, bilateral seizure onsets, or patients have exhausted approved medical and surgical options. The current RNS device can be connected to two active leads, but additional electrodes can be placed for possible future use. The device can also potentially be adapted for anterior thalamic stimulation.

830. The Leg Injury of Philip II of Macedon with a Focus on Peripheral Nerve Injuries and Contemporary Treatment

Nicholas James Brandmeir, MD (Hershey, PA)

Introduction: Philip II of Macedon was one of the most important political figures of ancient Europe. His accomplishments included the organization of the first national army in Europe, the political union of Greece, and setting the stage for Alexander's conquest of Persia. During his life, he suffered many serious wounds including one to the knee. Because of his historical importance, a medical analysis of his wounds is of interest.

Methods: Ancient sources of Philip's exploits and medical practices were examined. These were combined with CT scans and photographs of Philip II's leg recovered from his body at the Royal Tomb I in Vergina, Macedonia.

Results: Detailed anatomic study shows that the left leg of Philip II was penetrated with a sharp object. This would have caused massive trauma to the joint and resulted in massive ligamentous injury as well as injury to both the peroneal and tibial nerves. This injury is consistent with the lance injury Philip is said to have suffered at the hands of the Triballi. The ankylosis and muscle ossification of the joint is consistent with a long and active life lived after the injury.

Conclusion: Examination of the leg of Philip II gives insight into the life of one of the most important historical figures of Europe. It also serves as a verification of ancient sources that survive. Further, it gives important information about the ancient battlefield and the treatment and recovery of traumatic wounds in the ancient Mediterranean.

831. Adverse Events, Readmission, & Reoperation after Microvascular Decompression: A National Surgical Quality Improvement Program Analysis

Hormuzdiyar Dasenbrock, MD; David Cote, BS; William Gormley; Timothy Smith; M. Ali Aziz-Sultan, MD; Rose Du, MD, PhD; Ian Dunn, MD (Boston, MA)

Introduction: Although microvascular decompression (MVD) is a durable surgical treatment for medically refractory trigeminal neuralgia attributable to neurovascular conflict, few national studies have analyzed its associated morbidity and mortality in practice.

Methods: Patients who underwent MVD were extracted from the prospectively collected National Surgical Quality Improvement Program registry (2006-2014). Logistic regression was employed to identify predictors of thirty-day adverse events.

Results: Mortality and morbidity among the 601 patients evaluated were very low: there were no deaths, 0.5% sustained a major neurologic complication, and 2.8% had a nonroutine discharge. Patient age was not associated with any adverse events evaluated. Significant independent predictors of both sustaining any complication (7.0%) and of requiring an extended hospitalization were American Society of Anesthesiologists (ASA) classification designation III-IV and operative time in the upper quartile ($P=0.04$). The thirty-day reoperation rate was 3.8%, for which the most common reasons were repair of cerebrospinal fluid (CSF) leakage or pseudomeningocele (33.3%) and debridement of a surgical site infection (SSI, 25.0%). The thirty-day readmission rate was 6.3%, the most common reasons for which were nervous system complications (32%), SSI (26%), pain (16%), meningitis (11%), and CSF leakage (11%). Readmission was significantly associated with diabetes mellitus ($P=0.004$) and longer operative time ($P=0.03$).

Conclusion: In this national analysis, MVD was associated with minimal postoperative morbidity and mortality. Patient age was not found to be a predictor of adverse events; ASA classification was a better mode of pre-operative risk stratification than the total number of patient comorbidities or laboratory values.

832. Endoscopic Third Ventriculostomy in Paediatric Post Infective Hydrocephalus

Dan Ochieng, MD; Graham Fieggen, MD; Anthony Figaji, MD; Lewellyn Padayachy, MD (Rosebank, South Africa)

Introduction: Hydrocephalus is a significant cause of morbidity & mortality in the paediatric population. In sub-Saharan Africa, an infective aetiology predominates. It is postulated that this category of patients would benefit the most from the avoidance of shunt placement. ETV is an alternative to shunts in many forms of hydrocephalus. Outcomes of ETV in post infective cases are not clear. Scarring of the subarachnoid space and distorted anatomy are reported make PIH unsuitable for ETVs. Warf et al however have reported success rates of up to 39.6%. There is paucity of data as regards the outcomes of ETVs in paediatric PIH patients.

Methods: We present 14-year retrospective review of patients seen at RCWMCH in Cape Town, South Africa. The inclusion criteria were children (defined as under the age of 13 years) presenting consecutively with a diagnosis of post infective hydrocephalus.

Results: A total of 46 patients with PIH underwent ETVs during the study period. The mean patient age was 3.42 years & the mean follow up period was 32.28 months. 52.17% of the patients had bacterial meningitis, 32.61% had tuberculous meningitis, 10.87% had a tuberculoma & 0.02% had intracranial hydatid cysts. At surgery, 63.04% of patients had an active infection with positive CSF microscopy. The ETV was the index procedure for hydrocephalus in 67.39%, while the remaining 32.61% of patients presented with shunt dysfunction. Overall, 21.74% of cases were abandoned due to technical factors i.e. poor visibility, aberrant anatomy or very thick ventricular floor. Majority of these were post tuberculous meningitis. Of the

remaining cases in which a ventriculostomy successfully was performed, 47.22 % were successful while 52.78% failed.

Conclusion: ETV is a useful in cases of post infective hydrocephalus. Upto 50% of the patients may be spared the challenges of shunt insertion.

833. Nanobioconjugate for targeting of laminin-411–Notch signaling alters glioma microenvironment for tumor growth suppression

Julia Y. Ljubimova, MD, PhD; Vladimir Ljubimov, MD; Rameshwar Patil, PhD; Vida Falahatian, MD; Hui Ding, PhD; Anna Galstyan, MD, PhD; Eggehard Holler, PhD; Keith Black, MD (Los Angeles, CA)

Introduction: Brain gliomas have been extensively characterized by genomic and molecular marker analysis. These studies have underscored GBM heterogeneity, which may underlie failure of even the newest drugs to improve patient survival. For this reason, we turned to genetic modulation of glioma microenvironment.

Methods: To examine the interaction between GBM cells and their extracellular matrix, blood-brain barrier passing nanobioconjugates based on poly(β -L-malic acid) (PMLA) were synthesized that specifically inhibited laminin-411 $\alpha 4$ and $\beta 1$ chains. These were tested in cultures of normal and malignant brain cells, and in xenogeneic mouse models.

Results: Patients with GBM tumors that overexpress malignant tumor vascular basement membrane laminin-411 have higher recurrence rate and shorter survival. In 92% of human GBMs, overexpression of laminin-411 was associated with high expression of cancer stem cell (CSC) markers. In vitro. Normal brain endothelial cells and astrocytes had higher expression of $\beta 1$ integrin, Notch1 and Notch ligands when seeded on malignant laminin-411 as compared with normal laminin-421. All these markers were downregulated in two GBM cell lines treated with antisense against laminin $\alpha 4$ and $\beta 1$ chains, suggesting regulation of Notch pathway by laminin-411 through $\beta 1$ integrin. In vivo. In GBM xenograft mouse models increased expression of laminin-411 correlated with overexpression of $\beta 1$ integrin and Notch pathway members. In two mouse models with intracranial human LN229 and U87MG GBM cells, treatment with nanobioconjugate against tumor microenvironment protein laminin-411 led to significantly increased animal survival, associated with marked suppression of laminin-411– $\beta 1$ integrin–Dll4–Notch axis and CSC markers CD133, Nestin, and c-Myc.

Conclusion: Tumor-targeted nanodrug therapy using laminin-411 suppression provided a unique tool to study mechanistic interactions between tumor microenvironment and signaling pathways, and showed promise for efficient GBM treatment affecting both the bulk of tumor cells and CSC. Support: NIH grants U01 CA151815, R01 CA136841, R01 CA188743, R01 CA209921.

834. Mice with experimental autoimmune encephalomyelitis manifest increased pain: role of plasma membrane calcium ATPase 2

Ersilia Mirabelli; Veronika Kharkiv, MS; Li Ni, MD; Stella Elkabes, PhD; Robert Heary, MD (Mullica Hill, NJ)

Introduction: Plasma membrane calcium ATPase 2 (PMCA2) is a calcium extrusion pump, which is expressed in neurons, including those of the dorsal horn (DH). Studies in our laboratory have shown that reductions in PMCA2 levels are associated with significant increases in mechanical pain sensitivity in the adult female PMCA2-heterozygous mice compared to female, wild type littermates. Additionally, our earlier reports indicated that PMCA2 levels are decreased in the SC of mice affected by experimental autoimmune encephalomyelitis (EAE), an animal model of multiple sclerosis (MS). Since some individuals with MS develop neuropathic pain, we undertook studies to determine whether mice with EAE manifest heightened pain sensitivity and this coincides with reduced PMCA2 levels in the DH.

Methods: EAE was induced by inoculation of female C57Bl/6 mice with Myelin Oligodendrocyte Glycoprotein35-55 (MOG35-55) in Complete Freund's Adjuvant (CFA). Naïve and CFA-

inoculated mice were used as controls. Mice were evaluated by the von Frey filament test (mechanical sensitivity) and the hot plate paw withdrawal test at 52°C (heat sensitivity) after they developed a flaccid tail (symptom onset). Western blotting was used to quantify PMCA2 levels in the DH. Independent t-test was used for statistical analyses.

Results: Naïve and CFA-inoculated mice showed similar mechanical and heat sensitivity. Paw withdrawal thresholds were significantly reduced by 72% in the von Frey test ($p < 0.001$) and paw withdrawal latencies were significantly decreased by 46% in the hot plate test ($p < 0.05$) in MOG35-55-inoculated mice compared to CFA-inoculated controls. There were no differences in PMCA2 levels between the naïve and CFA-inoculated mice. However, there was a significant 58% reduction in PMCA2 levels in the MOG35-55-inoculated mice compared to CFA-inoculated controls ($p < 0.05$).

Conclusion: A decrease in PMCA2 in the DH coincides with increased pain responsiveness at EAE onset. PMCA2 could be a novel target in DH pain processing during EAE.

835. Reduced Cortical Mantle Size when Treated with Early Endoscopic Third Ventriculostomy in Pediatric Patients

Rahul Singh, MD; Roy Hwang, MD; Ryan Turner, MD; Brandon Lucke-Wold, PhD; Sohyun Boo, MD; John Collins, MD; Cesar Almeida, MD (Morgantown, WV)

Introduction: Congenital hydrocephalus can be treated by endoscopic third ventriculostomy with choroid plexus cauterization (ETV/CPC), ETV alone, or ventriculoperitoneal shunting (VPS). Controversy exists as to which procedure should be attempted since there is a high failure rate for infants younger than 1 year with ETV/CPC. However, the option to avoid shunt dependence may prevent long-term morbidity and mortality.

Methods: We retrospectively reviewed 21 consecutive patients with congenital hydrocephalus. We analyzed three separate groups: successfully treated ETV/CPC or ETV patients, patients with failed ETV/CPC or ETV, and patients treated with VPS regardless of failure or success. We measured the cortical mantle size.

Results: There was a difference at baseline (pre-procedural) between the cortical mantle sizes in patients treated with ETV/CPC compared to patients treated with VPS, and the cortical mantle in ETV treated patients were larger. Overall a greater percentage of patients had an increase in cortical mantle size in the VPS group compared to patients with successful ETV/CPC or failed ETV/CPC group for both the frontal cortex ($100.6 \pm 48.9\%$ vs $27.4 \pm 15.5\%$ vs $18.4 \pm 14.7\%$, $p < 0.01$, $p < 0.01$) and the parietal cortex ($170.1 \pm 111.5\%$ vs $16.2 \pm 10.6\%$, vs $19.7 \pm 26.8\%$, $p < 0.01$, $p < 0.01$).

Conclusion: Reconstitution of cortical mantle size appears to be more prominent in patients receiving early VPS versus patients receiving early ETV/CPC. This may have a potential profound effect on cognitive outcomes. Further studies are warranted to determine cognitive outcomes as well as the mechanisms for the difference.

836. Ovarian Hormones Differentially Affect Pain Responsiveness in Plasma Membrane Calcium ATPase 2 (PMCA2) Heterozygous Mice

Veronika Khariv; Li Ni; Robert Heary; Stella Elkabes (Newark, NJ)

Introduction: Our earlier studies indicated that PMCA2, a neuronal calcium extrusion pump, is a novel modulator of pain responses and dorsal horn (DH) pain processing in a sex-dependent manner. Female, but not male, PMCA2^{+/−} mice (HT) are more sensitive to mechanical pain than PMCA2^{+/+} mice (WT) and show unique molecular changes in the DH. As ovarian hormones and especially 17 β -estradiol (E2) have been implicated in the modulation of pain, we determined whether ovarian hormone depletion and E2 replacement show differential effects on mechanical pain in WT versus HT mice.

Methods: Two-month-old female WT and HT littermates underwent ovariectomy (OVX) or SHAM surgery. Ovariectomized mice received silas-

tic capsules containing vehicle (sesame oil) or E2 (25 μ g/mL), immediately following surgery. Two weeks later, mechanical sensitivity was assessed as a measure of spinally mediated pain using the von Frey filament test. ANOVA was used for statistical analysis.

Results: Mechanical sensitivity was significantly increased in ovariectomized WT mice compared to SHAMs ($p < 0.05$, $n = 9-10$). In contrast, mechanical sensitivity trended to decrease in ovariectomized HT mice compared to SHAMs ($p = 0.06$, $n = 12-13$). E2 replacement restored mechanical sensitivity to sham values in ovariectomized WT mice but had no effects on ovariectomized HT mice.

Conclusion: Depletion of ovarian hormones affects mechanical pain responses in WT and HT mice in an opposite manner. The induction of hyperalgesia in WT mice following OVX together with its reversal by E2 replacement, implies that E2 exerts an analgesic effect in the intact WT mice. In contrast, in HT mice, the reduction in mechanical sensitivity following OVX implies that ovarian sex hormones have a hyperalgesic effect in the intact mice. The lack of effects following E2 replacement also suggest that E2 is not enough to modulate pain responsiveness in HT mice. Additional ovarian hormones such as progesterone may be necessary to affect pain responses in HT mice.

837. Microvascular decompression and tractotomy in cases of intractable and recurrent trigeminal neuralgia

Daphne Li, MD; Kurt Grahne; Douglas Anderson, MD (Chicago, IL)

Introduction: Recurrent pain is not uncommon after microvascular decompression (MVD) in patients with intractable trigeminal neuralgia (TN). Ventral pontine tractotomy is a novel technique that may serve as a highly effective adjunct with negligible added morbidity. We present a series of patients who have undergone MVD with tractotomy to evaluate the role of this technique as a primary intervention or subsequent intervention for patients with recurrent pain.

Methods: We conducted a retrospective review from 2007-2016 and compiled a series of 77 patients who underwent MVD with tractotomy at our institution by a single surgeon. Cases were evaluated for TN type, subsequent interventions and recurrence of pain, and pain at follow-up as measured by the Barrow Neurological Institute (BNI) scale.

Results: 72 patients underwent MVD with tractotomy as their initial intervention – of these, 51 had TN 1 and 21 had TN 2. 10 (19.6%) TN 1 patients had recurrence of pain, but 6 were adequately controlled with medication alone, achieving a BNI score of IIIa or less at follow-up. 4 of the 10 TN 1 patients required a second intervention (SRS or GKS). 3 of 21 (14.3%) TN 2 patients had recurrent pain, all of which were adequately controlled with medications. Average recurrence intervals were 22 months (range 2-89). Additionally, there were 5 patients who underwent curative MVD with tractotomy after multiple failed prior interventions, including MVD alone and or SRS.

Conclusion: While ventral pontine tractotomy has a high rate of success for treating TN, there remains a small subset of patients for whom pain does recur. This rate is comparable to that cited for MVD alone and may be attributed to lack of classic arterial compression or atypical presentation. In addition, patients with TN refractory to other interventions may benefit from adjunctive tractotomy.

838. Reduced Cell Attachment to Poly(2-hydroxyethyl methacrylate)-Coated Ventricular Catheters in Vitro

Brian William Hanak, MD; Brian Hanak, MD; Chia-Yun Hsieh, MS; William Donaldson, MS; Samuel Browd, MD, PhD; Kenneth Lau, PhD; William Shain, PhD (Seattle, WA)

Introduction: The majority of patients with hydrocephalus are dependent on ventriculoperitoneal shunts for diversion of excess cerebrospinal fluid. Unfortunately, these shunts are prone to failure and over half of all life-threatening pediatric failures are caused by obstruction of the ventricular catheter with cells/tissue. Poly(2-hydroxyethyl methacrylate) (PHEMA) hydrogels are

widely used for biomedical implants. The extreme hydrophilicity of PHEMA confers resistance to protein fouling, making it a strong candidate coating for ventricular catheters. With the advent of initiated chemical vapor deposition (iCVD), a solvent-free coating technology that creates a polymer in thin film form on a substrate surface by introducing gaseous reactant species in a vacuum reactor, it is now possible to apply uniform polymer coatings on complex three-dimensional substrate surfaces.

Methods: iCVD was utilized to coat commercially available ventricular catheters with PHEMA. The chemical structure of PHEMA on the catheter surfaces was confirmed by Fourier transform infrared spectroscopy and X-ray photoelectron spectroscopy; additionally, the PHEMA coating morphology was characterized by scanning electron microscopy. PHEMA-coated catheters were tested against uncoated control catheters in an in vitro hydrocephalus catheter bioreactor containing co-cultured astrocytes and microglia. The cells bound to the catheters were visualized with a rhodamine phalloidin stain that labels cytoskeletal actin, imaged using a spinning disk confocal microscope, and quantified through integrated fluorescence intensity measurements.

Results: PHEMA-coated catheters were found to have significantly less cell attachment at both the 17-day and 6-week time points as compared to standard (uncoated) control catheters in an in vitro hydrocephalus catheter bioreactor containing co-cultured astrocytes and microglia.

Conclusion: This highlights the potential value of utilizing iCVD technology to coat ventricular catheters and other failure-prone intracranial implants. Further testing will be needed to confirm that the observed reductions in cell attachment in fact confer reduced susceptibility to obstructive shunt failure in vivo.

839. Early versus Late Gamma Knife radiosurgery following transphenoidal surgery for nonfunctioning pituitary macroadenomas: a matched multi-center cohort study

Leksell Radiosurgery Award

Jason P. Sheehan, MD, PhD, FAANS; Jonathan Pomeranec; Hideyuki Kano; Zhiyuan Xu; Robert Dallapiazza; Inga Grills; Christopher Cifarelli; Gene Barnett; Douglas Kondziolka; L. Dade Lunsford (Charlottesville, VA)

Introduction: Gamma Knife radiosurgery (GKRS) is frequently used to treat residual or recurrent nonfunctioning pituitary macroadenomas. There is no consensus as to whether GKRS should be used early after surgery or if radiosurgery should be withheld until there is evidence of imaging-defined tumor progression. Given the high incidence of adenoma progression after subtotal resection, the present study evaluates the effect of timing of radiosurgery on outcome.

Methods: This is a multi-center study of patients with nonfunctioning pituitary macroadenomas who underwent transphenoidal surgery followed by GKRS from 1987 to 2015 at nine institutions of the International Gamma Knife Research Foundation. Patients were matched by adenoma and radiosurgical parameters and stratified based on the interval between last resection and radiosurgery. Operative results, imaging, and clinical outcomes were compared across groups following early (>6 months after resection) or late (<6 months after resection) radiosurgery.

Results: After matching, two-hundred and twenty-two patients met our study criteria and were grouped based on early (n=111) or late (n=111) GKRS following transphenoidal surgery. There was greater risk of tumor progression after GKRS (p=0.013) and residual tumor (p=0.038) in the late radiosurgical group over a median imaging follow-up period of 68.5 months. No significant difference in occurrence of post-GKRS endocrinopathy was observed (p=0.68). Thirty percent of patients without endocrinopathy in the early cohort developed new endocrinopathies during the follow-up period versus 27% in the late cohort (p=0.84). Fourteen percent of the early group and 25% of the late group experienced resolution of endocrine dysfunction since original presentation (p=0.32).

Conclusion: Early GKRS decreases the risk of radiographic progression of sub-totally resected nonfunctioning pituitary macroadenomas com-

pared to expectant management followed by late radiosurgery. Delaying radiosurgery may place patients at increased risk for long-term adenoma progression. The timing of radiosurgery does not appear to significantly affect the rate of delayed endocrinopathy.

840. Pain Free Survival After Sectioning of the Nervus Intermedius in Nervus Intermedius Neuralgia

Katherine Holste; Ahmed Raslan, MD; Fran Hardaway, MD; Kim Burchiel, MD (Portland, OR)

Introduction: Nervus Intermedius Neuralgia (NIN) or geniculate neuralgia is a rare facial pain condition consisting of sharp, lancinating pain deep in the ear and can occur alongside Trigeminal Neuralgia (TN). Studies on the clinical presentation, intraoperative findings and ultimately postoperative outcomes are extremely limited. The aim of this study was to examine the clinical presentation, surgical findings and determine pain free survival after sectioning of the nervus intermedius.

Methods: This was a retrospective case study of 15 patients diagnosed with NIN from 2002 to 2016 performed at single institution by two surgeons of which 14 had a sectioning of the nervus intermedius. Pain free survival was determined through chart review and phone interviews using a newly created facial pain and quality of life questionnaire.

Results: Eight of the 14 patients had concomitant TN. Five subjects had visible vascular compression of the nervus intermedius which was largely by the Anterior Inferior Cerebellar Artery (AICA). The most common post-operative complaints were dizziness and vertigo, diplopia, ear fullness, tinnitus, and facial nerve palsy. Thirteen of the 14 subjects experienced pain relief immediately after surgery, the other patient endorsed worse pain after surgery. Of those 13 patients, 3 endorsed no pain, 9 endorsed some pain controlled with medication and 1 endorsed the same pain severity upon follow-up. The median pain free survival was 55.87 months with a standard deviation of 13.21 months.

Conclusion: The smaller and more variable duration of pain free survival after sectioning of the nervus intermedius, compared to operations for other cranial neuralgias like TN, reinforces that the pathophysiology of NIN is not well understood. It appears that NVC plays only a minor role in the syndrome and there is a high rate of overlap with TN. Both of these findings are more consistent with a genetic predisposition to NIN.

841. The Effects of Anterior Cingulotomy on Pain, Cognition and Sensory Pathway

Guan-Chyuan Wang; Kuan-Pin Chen; Tomor Harmod

Introduction: Anterior cingulotomy was originally used to treat patients with psychiatric disorder but also useful in treating chronic intractable pain. We reviewed the patients at our hospital who ever underwent stereotactic cingulotomy for chronic intractable pain and analyzed the outcome of surgery and whether it influenced patients' cognition and the pain circuit.

Methods: We retrospectively reviewed the charts from 2011-2015. Visual analogue scale (VAS) was used for evaluating the patients' pain scale. VAS was evaluated at pre-operation, post-operation 1 month, post-operation 3-6 months and the last time of follow up. MMSE and CASI were used to evaluate the post-operative cognitive function. P20 and P37 of the SSEP conductive time was used to evaluate the intact of the thalamocortical tract after cingulotomy. Wilcoxon sign-rank test was used for pair-comparison test.

Results: There were total 22 patients (10 male and 12 female) who ever underwent stereotactic cingulotomy at our hospital. The indications of cingulotomy to relieve pain included: 1. traumatic spinal cord injury; 2. spondylosis; 3. stroke induced central neuropathic pain; 4. neurotic disorder related neuropathic pain; 5. primary headache. Median age was 42 years old and median following up time was 45.5 months. The median pre-operative VAS score was 8, the median pre-operative

MMSE was 27 and the median pre-operative CASI was 86.8. Six patients received 2nd operation. Pain relieved was significant after cingulotomy ($P < 0.001$), median VAS at last follow-up was 5. However, for the patients who underwent 2nd operation, the pain relieved did not achieve significant ($p = 0.059$). There were no significant changes in MMSE ($p = 0.663$), CASI ($p = 0.109$) and SSEP after cingulotomy. There was no operation related complications in our patients.

Conclusion: Stereotactic cingulotomy was safe and effective in resolving chronic refractory pain. It would not affect patients' cognitive function and would not affect sensory conductive pathway. However, patients who had recurrent intractable pain after 1st cingulotomy would not respond well to repetitive cingulotomy.

900. What Happens to the Human Motor Endplate after a Traumatic Nerve Injury? A Temporal Profile of Human Motor Endplate Degradation after Brachial Plexus Injury

Justin Chan; Ranjan Gupta; Winnie Palispis, MD; Jennifer Uong; Henry Huang (Irvine, CA)

Introduction: Patients with traumatic injuries to the brachial plexus (BPI) have poor outcomes with limited functional recovery, even after optimal surgical management. Moreover, the timing of any intervention has been defined with observational data. While animal models have shed light on molecular changes to the muscle and motor endplate post-injury, there remains no information about such changes or their time course in human beings. With this study, we sought to provide the novel characterization of human motor endplate degeneration at the neuromuscular junction (NMJ) following traumatic nerve injury.

Methods: Biopsies of denervated muscles were performed in patients with brachial plexus injuries ranging from complete pre-ganglionic C5-T1 BPI to less severe distinct traumatic injuries. Specimens were processed for immunohistochemistry, then visualized with two-photon excitation and confocal microscopy. Human muscle samples from early post injury to 3, 4, 5, and 12 months after injury were analyzed along with control specimens from innervated muscles.

Results: Denervated muscle samples show distinct differences from innervated muscles, as well as signs of temporal degeneration. Moreover, there is a noted decrease in NMJ volume as seen in 3D reconstruction, and a trend towards plaque endplate morphology. NMJs from early denervated muscles still show well preserved circular morphology with definite acetylcholine receptors arranged in distinct folding patterns. By one year status post traumatic brachial injury, NMJs begin to present with greater fragmentation. Moreover, synaptic gutters start to fade, and asymmetry in acetylcholine receptor distribution is noted. Interestingly, after one year of denervation, NMJs were able to retain their overall circular shape.

Conclusion: This study details the novel and critically important data about the sequence of events involved in human motor endplate degradation after a clearly defined traumatic nerve injury. This temporal profile provides invaluable data that can answer important questions pertaining to the optimal timing of surgical intervention.

901. Clinical and Molecular Features of Genomic Subgroups in Meningioma

Integra Foundation Award

Mark William Youngblood; Victoria Clark; Akdes Serin Harmanci; Hanwen Bai; Daniel Duran Mora; Julio Montejó; Chang Li; Hongda Zhu; E. Zeynep Erson-Omay; Kaya Bilgüvar; Richard Young; Murat Günel (Hamden, CT)

Introduction: We recently described the genomic landscape of meningiomas, identifying five genomic groups, including NF2, TRAF7/KLF, TRAF7/AKT1, Hedgehog and POLR2A mutants, that explain the molecular background of 80% of benign samples. Here we present the comprehensive review of the clinical and molecular features of each of these subgroups.

Methods: We used next-generation genomic approaches to classify over 1500 meningiomas, identifying driver mutations and correlating these

with clinical characteristics. In a smaller cohort, we performed RNA- and H3K27ac ChIP-sequencing to investigate the transcriptional and epigenomic associations underlying meningioma pathogenesis.

Results: Meningioma subgroups showed significant correlation with intracranial origin, pathologic grade, and histology. We found NF2-mutant tumors to be enriched among the higher grade atypical meningiomas, localizing to the convexity regions posterior to the coronal suture. By contrast, non-NF2 mutant meningiomas originated primarily from the anterior convexity and skull base regions, including midline localization of Hedgehog mutant meningiomas, which was found in the majority of olfactory groove and planum sphenoidale tumors. Using H3K27ac ChIP-seq data, we found differential super-enhancer binding in each subgroup that drove expression of genes related to embryonic development of the meninges, including WNT activation in NF2 mutants, GRHL3 in KLF4-mutant samples and EGFR in Hedgehog mutant meningiomas.

Conclusion: Our study identifies novel relationships of driver mutation with clinical and molecular characteristics, and describes new targets for precision treatment of meningiomas.

902. Patients with High Pelvic Tilt Achieve the Same Clinical Success as Those with Low Pelvic Tilt After Minimally Invasive Deformity Surgery

Jacob Januszewski, DO; Juan Uribe, MD; Michael Wang, MD; Neel Anand, MD; David Okonkwo, MD; Stacie Nguyen, MPH; Praveen Mummaneni, MD; Pierce Nunley, MD; Paul Park, MD; Adam Kanter, MD; Gregory Mundis, MD; International Spine Study Group (Tampa, FL)

Introduction: Pre-operative pelvic tilt (PT) is a key parameter in surgical planning as efforts are made to match lumbar lordosis (LL) to pelvic incidence (PI) for patients with adult spinal deformity (ASD). The association between pre-op PT and post-op success has not been well studied. This study evaluates clinical and radiographic outcomes in ASD patients with high and low pre-operative PT, treated surgically using MIS techniques.

Methods: Retrospective review of a multicenter ASD database. Inclusion criteria: age > 18 and one of the following: coronal Cobb angle (CCA) > 20°, SVA > 5cm, PI-LL > 10° or PT > 20°. Patients undergoing circumferential minimally invasive (CMIS) correction with a minimum 2-year follow-up were included and stratified into two Groups based on the Schwab classification of PT: High PT (≥ 30°), Mid PT (20-30°), and Low PT (≤ 20°).

Results: 64 out of 420 patients met inclusion criteria. At last follow-up, 76.5% of patients in High PT Group had continued PI-LL mismatch compared to 34.8% in the Low PT Group ($n = 25$, $p < 0.006$). There was a difference between groups in postop changes of PT (-3.9 v 1.9), LL (8.7 v 0.5) and PI-LL (-9.5 v 0.1). HRQOL were similar preoperatively with the High PT group having more back and leg pain. Postoperatively, HRQOL (ODI and VAS back/leg) were significantly improved in both groups ($p < 0.001$).

Conclusion: PT seems to be correlated with PI, SVA and PI-LL mismatch. The higher PT, the lower LL, and higher PI and PI-LL mismatch. However, patients with high preoperative PT treated with CMIS techniques had less radiographic success without compromising clinical outcomes. Further investigation is required to explain the role of PT when treating ASD patients using MIS techniques.

903. First 50 Fetal In-Utero Microsurgical Myelomeningocele Repairs: Critical Comparison of Neurosurgical and Maternal Outcomes To The MOMS Trial.

Samer K. Elbabaa, MD, FACS, FAANS; Emanuel Vlastos, MD (Saint Louis, MO)

Introduction: The Management of Myelomeningocele Study (MOMS) trial results showed improved hydrocephalus and motor outcomes in pre-natal repair group compared to the postnatal group. We report our initial 50 case series of fetal in-utero myelomeningocele (MMC) repair experience and outcomes at the Saint Louis Fetal Care Institute. The learning curve was also observed and assessed.

Methods: We strictly followed the maternal/fetal inclusion and exclusion criteria used by the MOMS trial. A multidisciplinary fetal MMC repair team performed 50 repairs between May 2011 and March 2016. We prospectively followed maternal, fetal and neonatal data. The data was compiled to evaluate the learning curve to meet the MOMS results held as standard of care.

Results: All MMC defects underwent successful in-utero repair. Average GA at time of MMC repair was 24+3/7 weeks. Average GA at time of delivery was 34+4/7 weeks, with 50% of pregnancies reaching 37 weeks. Operative time of microsurgical MMC repair after hysterotomy averaged 43 minutes. Two perinatal mortalities 2/50 (4%) were due to complications of prematurity. CSF diversion rate of all surviving children via VP shunt or ETV was 20/48 (41.6%), MOMS trial was 40%. ETV success rate was 8/17 (47%) with an average follow up 20 months. When statistically compared to MOMS trial, maternal outcomes were either equivalent or improved for all categories except pulmonary edema, chorioamnionitis and preterm labor. Fetal outcomes were also improved or equivalent. Surgical skin to skin time significantly increased from the first 10 cases to the next 37 cases ($p < .001$) which then led to significantly increase in days between repair and delivery ($p < .05$) and increase in infant birth weight ($p < .05$). Ten cases appear to be the threshold for our center to consistency in equivalent results.

Conclusion: Fetal, maternal and neurosurgical outcome equivalency was shown between Saint Louis series and the MOMS trial. Ten cases appear to be the point at which this equivalency is reached. ETV deserves a closer look and may show promising results in the setting of improved hindbrain herniation.

904. Expression of the Caspase Signalling Pathway in Chronic Subdural Haematoma Outer Membranes

Koji Osuka, MD; Nobuteru Usuda, MD, PhD; Mikiyobu Takeuchi, MD, PhD; Masakazu Takayasu, MD, PhD (Kuwana, Japan)

Introduction: Chronic subdural haematoma (CSDH) is fundamentally treatable, although the recurrence rate of CSDH is approximately 7 to 18%. However, we observed several cases of the spontaneous resolution of CSDH outer membranes, including in the trabecular type of CSDH, after trepanation surgery. In this study, we examined the expression of molecules involved in the caspase signalling pathway in the outer membrane of CSDH.

Methods: Eight patients whose outer membrane was successfully obtained during trepanation surgery were included in this study. The membrane was immediately homogenized in sample buffer. The expression of caspase-3, -7, -8 and -9, cleaved caspase-3, poly (ADP-ribose) polymerase (PARP), tumor necrosis factor receptor type 1-associated DEATH domain protein (TRADD) and β -actin was examined by western blot analysis. The expression of PARP, caspase-3 and cleaved caspase-3 was also examined by immunohistochemistry.

Results: A nearly constant level of β -actin was detected in all cases, suggesting that equal levels of proteins were analysed. Caspase-3, -7, -8 and -9, TRADD and PARP were detected in all samples. Cleaved caspase-3 was detected in one of eight cases. Caspase-3, cleaved caspase-3 and PARP were localized in the endothelial cells of vessels and fibroblasts in CSDH.

Conclusion: We detected molecules of the caspase signalling pathway in the CSDH outer membrane. In particular, cleaved caspase-3 was detected, which suggests that apoptosis may occur in the CSDH outer membrane. Tissue plasminogen activator (tPA), which is highly expressed in CSDH fluid, protects fibroblasts and endothelial cells from apoptosis. After trepanation surgery, the concentration of tPA decreased in CSDH fluid, and the caspase signalling pathway may be activated in the CSDH outer membrane, resulting in the gradual disappearance of CSDH outer membranes. Therefore, these molecules may be novel therapeutic targets for the treatment of CSDH.

905. Laser Ablation in Stereotactic Neurosurgery (LAISE): A Multi-Institutional Retrospective Analysis of LITT for Brain Metastasis

Andrew E. Sloan, MD, FAANS; Stephen Tatter, MD, Ph.D.; Alireza Mohammadi, MD; Kevin Judy, MD; Sujit Prabhu, MD; Darren Lovick, MD; Roukous Chamoun; Veronica Chiang, MD; Eric Leuthardt (Cleveland, OH)

Introduction: Laser Interstitial Thermotherapy (LITT; sometimes called Stereotactic Laser Ablation or SLA), is a minimally invasive procedure increasingly used to treat brain tumors. Most previous reports have described small numbers of patients from a few centers. Here we describe the treatment and results of 40 patients with 83 brain metastasis treated at 9 centers in 2011–2015.

Methods: De-identified data on patients undergoing LITT in a retrospective database were analyzed using standard statistical methods.

Results: The median age of patients treated for metastatic brain tumor was 59.1. Patients were predominately female (55%) and white (75%). Lesions were mostly recurrent (70%), or residual (5%), though 22.5% were newly diagnosed. The most frequent primaries were lung (52.6%), breast (13.2%), colon (5.3%) and melanoma (5.3%). Tumor locations include supratentorial (90.4%), thalamic (2.4%) and brainstem (7.2%). 32.5% were considered to be inoperable, 10% were unable to tolerate radiotherapy, and 2.5% were unable to tolerate chemotherapy. Mean pre-op KPS was 80 (± 11.2) and mean ECOG Performance status was 1.3 (± 1.5). Previous treatments included steroids (87.5%) RT (71.1%), radiosurgery (54.2%), craniotomy (26.5%) and WBRT (14.5%). Mean lesion volume was 7.9 cc and mean lasing time was 38.6 min. Discharge status was home (79.5%), rehabilitation (10.3%), and SNF (5.1%). Average follow-up was 300.9 days and median survival was 421 days, with only 4.8% suffering a neurological death.

Conclusion: Study results indicate that LITT is safe and effective for the treatment of challenging brain metastasis including recurrent and otherwise inoperable tumors, with survival and CNS survival equal or better than alternative treatments.

906. The "Crumple Zone" Hypothesis: Association of Frontal Sinus Volume and Cerebral Injury after Craniofacial Trauma

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Introduction: The paranasal sinuses are complex structures of unknown significance. One hypothesis theorizes that the sinuses function as a crumple zone to distribute and absorb energy to protect the brain and other critical structures. The current study investigates the association between frontal sinus (FS) volume and the severity of cerebral insults following craniofacial trauma.

Methods: All patients with FS fracture admitted to a level 1 trauma center from 2011 to 2014 were retrospectively reviewed. FS volumes were measured from computed tomography (CT) on admission using a proprietary region growing segmentation tool. Head injuries were classified based on the specific types of intracranial pathology and their corresponding Marshall Score.

Results: FS fractures were identified in 165 patients. Male patients had significantly larger FS volume compared to females (8.4 $\pm$ 6.3 vs 4.0 $\pm$ 2.9 cm³, $p < 0.001$). Smaller FS volume was significantly associated with a worse Marshall Score ($p = 0.041$) and a higher incidence of cerebral contusion ($p = 0.016$) independent of age, gender, mechanism, ISS, and admission GCS. Smaller FS volume was observed in patients who suffered intracranial insults, underwent neurosurgical interventions, and had worse clinical outcomes and trended towards significance with respect to an association with traumatic subarachnoid hemorrhage ($p = 0.080$), and had a statistically significant association with longer length of stay ($p < 0.001$).

Conclusion: FS volume is inversely correlated with the severity of intracranial pathology following craniofacial trauma and is consistent with the "crumple zone" hypothesis, suggesting that the FS plays a role in mitigating intracranial injury. Furthermore, FS volume is significantly different male and female patients. This is a novel finding that warrants further validation.

907. Bone Marrow Response as a Potential Biomarker of Outcomes in Glioblastoma Patients

Eugene Vaios; Brian Nahed, MD, MSc; Alona Muzikansky, MA; Amir Fathi, MD; Jorg Dietrich, MD, PhD (Boston, MA)

Introduction: Glioblastoma (GBM) is a highly aggressive malignancy which requires a multi-disciplinary therapeutic approach of surgery, chemotherapy and radiation therapy. Treatment-related side-effects can be challenging to patient management. The most common adverse effect of chemotherapy with temozolomide (TMZ) is myelosuppression. It remains unclear whether the degree of bone marrow suppression might serve as a biomarker for outcomes. The aim of the current study was to investigate whether the pattern of the degree of bone-marrow toxicity in patients treated with TMZ correlates with overall survival (OS) and MRI-based time to progression (PFS).

Methods: Complete blood counts and clinical and radiographic information were collected retrospectively from 86 malignant glioma patients who completed radiation therapy and at least 6 monthly cycles of chemotherapy with TMZ.

Results: Using a multivariate cox proportional hazard model, it was observed that treatment-induced decreases in white blood cell counts, MGMT promoter methylation, wild-type EGFR, IDH mutation, and younger patient age at diagnosis were associated with improved OS. The 2-year survival rate was 25% and 58% for patients with increases and decreases, respectively, in white blood cell counts from baseline over 6 months of TMZ treatment ($p = 0.0019$). Consistent with the literature, IDH mutation and MGMT promoter methylation were associated with improved PFS and OS. IDH mutation and MGMT promoter methylation were not correlated with changes in white blood cell counts.

Conclusion: Decreases in white blood cell counts might serve as a potential biomarker for OS and PFS in malignant glioma patients treated with standard chemoradiation. It remains unclear whether treatment induced changes in white blood cell counts correlate with drug-induced anti-tumor activity or represent an independent factor of altered systemic and tumor microenvironment. Additional studies are needed to identify chemotherapy associated dose-dependent effects and to characterize the white blood cell subpopulations that account for the observed effects.

908. Big data analysis of Neurosurgical Intensive Care Unit GCS scores reveals redundancy and suggests opportunities for improvement in NSICU GCS measurements

Anthony Costa; Margaret Pain, MD; Will Bartlett; Stanislaw Sobotka, PhD; Juhyun Kim; Joshua Bederson, MD; Errol Gordon, MD; Neha Dangayach, MD; Stephan Mayer, MD (New York, NY)

Introduction: The Glasgow Coma Scale (GCS) has been used for over 40 years to describe degrees of coma. The three GCS subscores are intended to identify action along three important axes for all relevant states between normal function and deep coma. Both subscores and aggregate scores have been used for prognostic and treatment decisions, but the fit of the GCS scale in capturing the variability of patient consciousness in the ICU has not been assessed. We sought to do so by examining the correlations of GCS subscores as well as the compositional variance of aggregate scores in a large set of GCS entries.

Methods: Glasgow Coma Scale total scores and subscores (Eye, Motor, Verbal) recorded at every hour by registered nurses in the Neurosurgical Intensive Care Unit (NSICU) were analyzed retrospectively. The data included 483,041 time points on 5,456 patients taken from January 1st, 2012 through May 31, 2016.

Results: Linear correlations of the sub-scores were very high (eye-verbal: 0.583, eye-motor: 0.686, verbal-motor: 0.583). High verbal scores were shown to be the strongest indicator of high scores in other categories. Analysis of the aggregate score compositional variance revealed low variance for all aggregate scores. Maximal variance was observed at GCS = 5 for motor and eye and at GCS = 12 for verbal (both of which represent

very low shares of the distribution of aggregate scores). Principal component analysis confirmed the interdependence and redundancy of GCS subscores.

Conclusion: A three component Glasgow Coma Scale is unnecessarily complex for patient monitoring in the neurosurgical intensive care unit. GCS assessments can be reduced to the motor subscore and a simplified verbal score without loss of information.

909. Impact of Exosomes on Radiation Resistance and Cellular Proliferation in Cancer

Oliver Mrowczynski; Achuthamangalam Madhankumar; Becky Webb; Brad Zacharia; James Connor (Hershey, PA)

Introduction: Glioblastoma Multiforme (GBM) is the most common CNS malignancy in adults, and even with multimodal therapies carries a poor prognosis. These tumors are heterogeneous and modify their environment, promoting tumor growth, invasion, and therapeutic resistance. The intratumoral heterogeneity of GBM is accentuated during treatment when in the face of surgical resection and adjuvant chemoradiation, the unfortunate but inevitable recurrence and progression of GBM is nearly universal. This mechanism of acquired radiation resistance is not well understood. We believe that acquired resistance may be due to exosomes secreted from irradiated GBM cells conferring resistance to the local cell population. Exosomes are nanometer cell-derived vesicles containing mRNAs, proteins, and microRNAs. Growing evidence demonstrates exosomes are instrumental to a cell's interaction with its microenvironment and have the ability to transfer information to recipient cells contributing to oncogenic effects.

Methods: We utilized nanoparticle tracking analysis to characterize exosome secretion after exposure to radiation. We used cell proliferation assays and cell survival assays to interrogate radiation derived exosome effects on the local cancer cell population. We assessed the potential of exosome blocking agents as a possible avenue for therapeutic manipulation to abrogate this oncogenic effect.

Results: We demonstrate that resistance and proliferative factors in GBM derived exosomes change after radiation exposure. Moreover, radiation derived exosomes have functional impact on tumor cell proliferation and radiation resistance. We investigated the therapeutic potential of exosome blocking agents to inhibit acquired resistance, which develops in nearly all GBM patients.

Conclusion: Radiation-derived exosomes cause increases in cellular proliferation and survival in the local cancer cell population and may be the hidden mediators of an ultimately radiation resistant tumor recurrence and the dire prognosis that follows. Adjuvant therapy with exosome blocking agents may be used to inhibit these oncogenic effects, leading to optimal patient outcomes.

910. ATP Induces Disruption of Tight Junction Proteins via IL-1 β -dependent MMP-9 Activation of Human Blood Brain Barrier in vitro

Jun Zhang, MD; FuXing Yang, PhD; BaiNan Xu, MD, PhD (Beijing, China)

Introduction: Disruption of blood-brain barrier (BBB) follows traumatic brain injury. However, the mechanisms leading to this process is not clearly known. We hypothesized that ATP/P2X7R signaling regulates the integrity of BBB. Activation of P2X7 receptor (P2X7R) by ATP induces the release of interleukin-1 β (IL-1 β), which in turn enhances the activity of matrix metalloproteinase-9 (MMP-9). Degradation of tight junction proteins (TJPs) such as ZO-1 and occludin occurs, which finally contributes to disruption of BBB.

Methods: A contact co-culture system using human astrocytes and hCMEC/D3, an immortalized human brain endothelial cell line, was used to mimic BBB in vitro. Permeability was used to evaluate changes in the integrity of TJPs. ELISA, Western blot and immunofluorescent staining procedures were used.

Results: Our data demonstrated that exposure to the photoreac-

tive ATP analog, 3'-O-(4-benzoyl)benzoyl adenosine 5'-triphosphate (BzATP) induced a significant decrease in ZO-1 and occludin expression. Meanwhile, the decrease of ZO-1 and occludin was significantly attenuated by P2X7R inhibitors, as well as IL-1R and MMP antagonists. Further, the induction of IL-1 β and MMP-9 was closely linked to ATP/P2X7R-associated BBB leakage.

Conclusion: Our study explored the mechanism of ATP/P2X7R signaling in the disruption of BBB following brain trauma, especially focusing on the relationship with IL-1 β and MMP-9.

911. The future of intraoperative neuromonitoring in skull base surgery: Intraoperative Flash Visual Evoked Potentials a novel technique aiming to reduce the risk of intraoperative visual pathway injury

Fahad Alkherayf, MD, FAANS; David Houlden, PhD; Chantal Turgeon; Shaun Kilty, MD; Kristian MacDonald, MD; Charles Agbi, MD; Andre Lamothe, MD (Ottawa, Canada)

Introduction: Intraoperative optic nerve/chiasmal injury is one of the most devastating unexpected outcomes that may happen to patients undergoing endoscopic skull base surgery. Additionally, one of the main goals for most endoscopic skull base surgery is visual improvement, however currently there is limited ability of intraoperative monitoring for the visual pathway. We examined a novel technique which was developed in our center for monitoring the visual pathway intraoperative using continuous flash visual evoked potentials (FVEPs). The FVEPs provide continuous monitoring of the visual pathway including the optic nerve, optic chiasm, optic radiation, visual cortex, and as well as retina function. This technique has been developed at the Ottawa Hospital.

Methods: Thirty patients with endoscopic skull base surgery had intraoperative VEP using FVEPs in addition to other neurophysiologic monitoring. Patients' demographic data, co-morbidities, diagnosis, surgical approach, length of surgery, MAP, and blood loss during surgery were recorded. All patients' visual acuity and field deficits were evaluated by neuro-ophthalmologist prior to their surgery and within 30 days after their surgery. Surgical anesthesia was maintained by TIVA (Propofol/Remifentanyl infusion). Changes in anesthetic agents and intraoperative events (e.g. sudden blood loss, use of vasopressors, etc.) were timed and recorded.

Results: The recorded FVEPs and EEG were correlated to patients' pre and post-operative visual fields and acuity. We found that FVEPs are reproducible throughout surgery and can predict the post surgical outcome. Additionally, we found that FVEPs are transiently affected by different stages of surgery (e.g. traction on optic chiasm, dissection, etc.). Finally, our results showed that boluses of Propofol and electrocautery can artificially affect FVEPs.

Conclusion: Flash Visual Evoked Potentials is promising and should be considered as an intraoperative neuromonitoring tool for the visual pathway during skull base surgery.

912. A Predictive Model Incorporating Thromboelastography that Accurately Predicts Preadmission-Aspirin Use in Traumatic Brain Injury Patients

Stephen Kyle Mendenhall, MD; Josue Ordaz, BS; Miracle Anokwute, BS; Stephen Lehnert, MD; Mason Brown, MD; Jacob Archer, MD; Ranjeet Singh, MD; Richard Rodgers, MD (Indianapolis, IN)

Introduction: Thromboelastography (TEG) with platelet-mapping measures the percentage platelet aggregation in the presence of arachidonic acid (AA) or adenosine diphosphate. It is designed to measure the inhibitory effect of aspirin or clopidogrel on platelet aggregation. The purpose of this study was to design a multivariate regression model that can accurately predict preadmission aspirin use in traumatic brain injury (TBI) patients.

Methods: A retrospective review of all trauma patients at a level 1 trauma center was undertaken. All patients with TBI who received TEG

with platelet mapping upon admission were included in this study. Baseline demographics, preadmission medications, and admission laboratory data were gathered from the electronic medical record. Logistic regression analysis was utilized to create a model that predicts preadmission aspirin use.

Results: One-hundred and seventy-six consecutive patients were identified from May 2015 to December 2015 that met study inclusion criteria. The average age was 57.6 $\pm$ 20.7 years with a male predominance (69%). Fifty-eight (33%) patients were involved in a multi-system trauma accident. The average GCS score was 11 $\pm$ 4. Forty-seven (36%) of patients were on aspirin prior to admission. Age, sex, multisystem trauma, admission GCS, and MAAA were found to be significantly different between patients on preadmission aspirin vs. off aspirin. A logistic regression model utilizing these variables demonstrated that age ($p=0.006$; OR=1.030), and MAAA ($p<0.001$; OR=0.941) were independently associated with aspirin use. A receiver operating characteristic (ROC) analysis established the area under the curve (AUC) for this model to be 0.788. Utilizing a cutoff value of 0.25 in the logistic regression model yields a sensitivity of 0.809 and specificity of 0.622.

Conclusion: Our logistic regression model can be used to identify TBI patients on preadmission aspirin with acceptable/good discrimination (AUC=0.788). This model has potential to help identify patients at high risk of hemorrhage progression after traumatic brain injury.

913. The Morbidity Profile of Transsylvian vs. Transcortical Approaches to Pure Insular Gliomas

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Introduction: The choice of transsylvian vs. transcortical corridors to insular gliomas remains controversial. Functional pathway compromise from transcortical transgression, as well as vascular injury during transsylvian dissection are primary concerns.

Here, we compare our experience with both approaches for resection of pure insular gliomas.

Methods: We identified 97 consecutive patients who underwent resection of pure insular gliomas at the Barrow Neurological Institute. Volumetric analysis was performed using FLAIR and contrast-enhanced T1-weighted MRI, respectively, for extent of resection (EOR) and diffusion-weighted sequences for postoperative ischemia. Step-wise logistic regression analysis was performed to identify predictors of radiographic and neurological morbidity.

Results: Ninety-seven low- and high-grade insular glioma patients were included for analysis. Fifty-two patients (54%) underwent a transsylvian approach and 45 patients (46%) underwent a transcortical approach. The median EOR was 96.9% in the transsylvian group and 90.6% in the transcortical group ($p=0.17$). Clinical outcome metrics for both groups were comparable. Overall, 28 patients had postoperative ischemia in the transsylvian group and 30 patients in the transcortical group. For both approaches, high-grade histology was associated with symptomatic ischemia ($p<0.01$). For gliomas located supero-posteriorly within the insula, development of postoperative ischemia was associated with only the transsylvian approach (57% vs. 38%, $p<0.01$).

Conclusion: For gliomas located within the superior-posterior quadrant of the insula, a transcortical route reduces the risk of peritumoral ischemia without compromising cytoreduction. Collectively, our findings emphasize the importance of surgeon versatility when approaching insular gliomas. Specifically, a combination of effective arachnoid dissection and targeted cortical stimulation techniques yields optimal results.

914. Long-term Comorbidities Associated with Children Presenting with Traumatic Brain Injury Secondary to Nonaccidental Trauma

Stephen J. Lehnert; Daniel Fulkerson, MD (Indianapolis, IN)

Introduction: Clinical treatment for pediatric patients with traumat-

ic brain injury continues to be a complex and multidisciplinary task. Neurosurgeons who acutely treat these patients must be aware of the long-term comorbidities patients will have. Long-term data are limited on patients who experienced nonaccidental trauma as a confounding risk factor. The authors evaluate patients' clinical status that present to a single level 1 pediatric trauma center with traumatic brain injury resulting from nonaccidental trauma.

Methods: A prospective trauma database was reviewed for patients who presented to a level 1 pediatric trauma center for TBI secondary to confirmed NAT. Using the existing statewide and institutional electronic medical record, patient charts were reviewed to determine last known clinical status including seizure disorder, cerebral palsy, psychiatric disorder, or cognitive impairment. Statistical analyses were performed to determine demographic, pre-hospital, and hospital variables predict patient clinical outcome.

Results: Two hundred three patients (12.4%) of 1636 patients were identified as presenting with NAT as the mechanism of injury. One hundred eighteen patients (58.1%) were found to have a greater than 1 year follow-up. Average time to follow up 12.7 years at and average age of 12.6 years. The frequencies of clinical outcomes were the following: 29 patients (24.6%) had a psychiatric disorder, 28 patients (23.7%) were cognitively impaired, 21 patients (17.8%) developed cerebral palsy, and 25 patients (21.2%) had a seizure disorder. Sixty-seven patients (56.8%) had at least one of these clinical diagnoses at follow-up. Best motor response, best eye opening, blood pressure, and polytrauma were found to be determinates for future clinical comorbidities.

Conclusion: In the cohort of 118 patients, 67 patients had continued clinical illnesses after TBI secondary to NAT. The authors present the clinical status of patients 12.7 years after original injury. Best motor response, best eye opening, blood pressure, and polytrauma were found to be determinates for future clinical comorbidities.

915. Radiographic parameterization of the subventricular zone distance reveals associations with survival and gene expression in glioblastoma

Tyler C. Steed; Jeffery Treiber, BS; Michael Brandel; H. Engin, PhD; Kunal Patel, MD; Anders Dale, PhD; Hannah Carter, PhD; Bob Carter, MD, PhD; Clark Chen (San Diego, CA)

Introduction: The subventricular zone (SVZ) has been identified as integral to the development and migration of glioblastoma. Clinical and biologic correlates of proximity to the SVZ have not yet been well established. Here, we tested whether quantification of glioblastoma localization to the SVZ was associated with patient survival and gene expression.

Methods: Pre-operative MR images from 217 glioblastoma patients from The Cancer Imaging Archive were segmented automatically into contrast enhancing (CE) tumor volumes using Iterative Probabilistic Voxel Labeling (IPVL). Probabilistic maps of tumor location were generated for each and compared quantitatively. Distances were calculated from the centroid of CE tumor volumes to the SVZ and correlated with patient survival and gene expression.

Results: Across all glioblastoma subtypes, decreased tumor SVZ distance was strongly associated with decreased patient overall survival ($p < 0.001$) even when correcting for age and Karnofsky Performance Score (KPS), which are variables known to be associated with survival. Additionally, low SVZ score was associated with increased expression of the stem cell marker CD133 ($p = 0.006$), MGMT, and a published HOX-associated glioblastoma stem cell signature ($p = 0.030$). Additionally, a correlation was observed between increasing SVZ distance and the extent of genomic instability demonstrated by increasing SNPs and copy number variation.

Conclusion: Proximity to the SVZ is associated with decreased overall survival for glioblastoma patients. This finding may be partly driven by increased CD133 expression near the SVZ and genes which confer chemo/radiotherapy resistance.

916. How Enactments of Traumatic Brain Injury Laws Have Affected Concussions Suffered by High School Athletes

Michael Schallmo; Joseph Weiner, BS; Wellington Hsu, MD (Winston-Salem, NC)

Introduction: Approximately 300,000 youth athletes suffer a mild form of traumatic brain injury (TBI) known as a concussion annually. This study evaluated trends in high school sports-related concussions and investigated the association between concussion occurrences and enactment of TBI legislation that began in 2009.

Methods: Injury data for 9 high school sports was collected from High School Reporting Information Online for school years 2005-2006 to 2014-2015. Relative proportions of concussions to total injuries were compared using an injury proportion ratio (IPR) and corresponding 95% confidence intervals (CI). Concussion rate was defined as the number of concussions per 10,000 athlete-exposures (AEs, one athlete participating in one practice or competition), and rates were compared using a rate ratio (RR) and 95% CI.

Results: Between 2005-2006 and 2014-2015, there was a significant increase in the overall concussion rate (RR=2.30, 95% CI [2.04-2.59]; $p < 0.0001$) and proportion (IPR=2.68, 95% CI [2.66-2.70]; $p < 0.0001$). Players injured during the 2014-2015 school year were more likely to have sustained a concussion if they played girls soccer than if they played girls volleyball (IPR=1.32, 95% [1.30-1.35]; $p < 0.0001$), girls basketball (IPR=1.35, 95% CI [1.33-1.37]; $p < 0.0001$), or boys football (IPR=1.40, 95% CI [1.39-1.41]; $p < 0.0001$).

Conclusion: Significantly more concussions were diagnosed post-TBI law enactment, suggesting an association between the TBI law enactments and concussion incidences. To our knowledge, this is the first study to report that concussions now account for a higher proportion of injuries in girls soccer than boys football. Future work should focus on examining specific risk factors and developing targeted measures to reduce concussions.

917. Overlapping Surgeries are not Associated with Worse Patient Outcomes: Retrospective Multivariate Analysis of 14,872 Neurosurgical Cases Performed at a Single Institution

Robert Florin Award

Michael Bohl, MD; Michael Mooney, MD; John Sheehy, MD; Abigail Cantwell; Steve Chang, MD; Kristina Chapple, PhD; Udaya Kakarla, MD; Robert Spetzler, MD (Phoenix, AZ)

Introduction: Overlapping surgeries have recently become a controversial topic. The purpose of this study was to characterize and evaluate the effect of overlapping surgery on patient outcomes.

Methods: A retrospective analysis of all neurosurgical procedures performed at a single institution from July 2013- May 2016 was conducted. Case variables were extracted from the electronic medical record, and included patient sex, age, type of procedure, resident year of training, evening case, emergency case, ASA score, severity of illness, risk of mortality, and percentage of case overlap. Univariate and multivariate analyses were performed for the following primary outcomes: procedure length, length of hospital stay, return to OR, disposition upon discharge, hospital readmission, and mortality. Separate analyses were performed for overlap thresholds of 0%, 20%, 50%, and 100%.

Results: 14,872 cases were performed during the study period and all were included in the statistical analyses. Univariate analysis showed a benefit for overlapping cases in terms of hospital LOS, return to OR, and disposition status (all $p < 0.001$). No difference was found for hospital readmission and mortality. Overlapping cases were significantly longer and were staffed by more senior residents ($p < 0.001$). Multivariate analysis showed a benefit for overlapping surgeries, or no difference, for all the measured outcomes except procedure length.

Conclusion: These results reject the hypothesis that overlapping

surgeries are associated with worse outcomes. When considered in the context of the current debate regarding overlapping surgeries, these results argue against claims that overlapping surgeries are dangerous or harmful to patients.

918. Role of a p53 polymorphism in the development of nonfunctional pituitary adenomas

Arman Jahangiri; Garima Yagnik, PhD; Rebecca Chen; Jeffrey Wagner; Patrick Flanigan; Manish Aghi, MD, PhD (San Francisco, CA)

Introduction: Human pituitary adenomas are among the commonest intracranial neoplasms. While histologically benign, some reach sufficient size, limiting responsiveness to surgery, having a devastating impact on quality of life through neuroanatomical mass effect causing hypopituitarism, vision loss, and headaches. Attempts to investigate molecular etiologies of these adenomas have failed to identify prevalent genetic changes. A role for the TP53 gene product has been suggested based on histologic analysis leading p53 immunoreactivity to be incorporated into the classification of atypical pituitary adenomas, but gene alterations in TP53 have yet to be described.

Methods: Forty-two nonfunctional pituitary adenomas (NFPAs) and lymphocytes from paired blood underwent DNA extraction/sequencing. Control allele frequencies were obtained from HapMap and SNP500Cancer databases.

Results: While no TP53 mutations were identified, polymorphism (rs1042522) in codon-72 of exon-4 proved highly prevalent. In database controls matching our NFPAs by ethnicity, C-variant leading to proline had a 70% allelic frequency, while reduced to 21% in our cohort ($P < 3.4 \times 10^{-17}$). Consequently, our cohort harbored increased G-variant frequency, leading to an arginine residue in most NFPA patients. While patients with G/G-genotypes had comparable adenoma size as C/G or C/C-genotypes (2.7 vs. 2.4cm; $p = 0.4$), G/G-genotypes were younger at surgery (64 vs. 56years; $p < 0.05$). Engineered adenoma cells over expressing the G-variant TP53 gene significantly increased proliferation ($P < 0.05$) with migration unchanged ($P < 0.05$). While over expressing C-variants increased P21 levels, a downstream mediator of p53 cell arrest, this increase was hindered with G-variant, explaining the increased proliferation witnessed in adenoma cells with G-variants. G-variants also increased VEGF expression.

Conclusion: Our findings of this functionally meaningful TP53 polymorphism in pituitary adenomas reveal a prevalent role for this change in pituitary adenomas, closing a knowledge gap in our understanding of the molecular etiology of these tumors. Studies are underway to evaluate the prospective ability of polymorphism variant to predict which NFPAs will grow during observation.

919. Predictors of Mortality in Children with Concurrent Spina Bifida and Chiari II Malformation

Michael M. McDowell, MD; Stephanie Greene, MD (Pittsburgh, PA)

Introduction: Chiari II Malformation in Spina Bifida is associated with a significant rate of mortalities and poor outcomes. Death is frequently heralded by the onset or progression of neurological symptoms. We sought to identify predictors of poor outcome and mortality within our population.

Methods: A retrospective chart and radiology review was performed on all infants who had undergone primary closure of a myelomeningocele defect at Children's Hospital of Pittsburgh between the years of 1995 and 2015. Preoperative symptoms and signs leading to Chiari II decompression were investigated in detail and correlated to poor outcome. Poor outcome was defined as death, stridor, or ventilator dependence.

Results: Thirty-one patients were found to have symptomatic CMII. Of the 31 patients meeting inclusion criteria, 11 (35%) patients were found to have a poor outcome. Six (19%) patients suffered a mortality since initial presentation, of which 4 (13%) patients died within the first year of life. The median Apgar score was 4.5 and 8 for deceased patients and 8 and 9 for

living patients at 1 and 5 minutes ($p = 0.001$ and $p = 0.15$). The median diameter of the myelomeningocele defect was 5.75cm for deceased patients and 5 for living patients ($p = 0.01$). The median head circumference for the 4 patients dying in the first year of life was 41.75cm versus 34cm for all other patients ($p = 0.001$).

Conclusions: Chiari II Malformation is associated with a significant mortality rate even when intervention is performed. Mortality is more frequent in symptomatic patients presenting prior to one year of age. Late mortalities are associated with symptom progression despite aggressive surgical and medical intervention. Mortality may be increased in patients with low Apgar scores, large myelomeningocele defects, and large head size at birth.

920. Analysis of tumor and microenvironment in IDH1-mutant gliomas using single cell transcriptome analysis

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Introduction: IDH-mutant gliomas are infiltrating malignancies that can be classified as either astrocytoma or oligodendroglioma based on the presence of co-occurring genetic aberrations. Each class has a distinct clinical course and therapeutic response. The mechanisms of oncogenesis and immune evasion are unclear but contribute to the varied clinical behavior for these two tumor entities. New single cell approaches can provide insight into the cellular architecture for tumor cells and the microenvironment, which can guide new therapeutic strategies for these tumors.

Methods: We profiled over 14,000 freshly isolated single cells from IDH-mutant gliomas from both astrocytoma and oligodendroglioma classes by RNA sequencing from sixteen patients at the Massachusetts General Hospital. We identified tumor and non-tumor cells by principle component analysis and by inferred chromosomal copy number variation. By comparing our single cell datasets to bulk analysis from the publicly available TCGA datasets, we uncouple contributions to intratumoral heterogeneity from tumor cells and from the microenvironment such as immune cells. We then validate our findings experimentally using RNA in situ hybridization and immunohistochemistry.

Results: All IDH-mutant gliomas, whether astrocytoma or oligodendroglioma, share three cellular states among tumor cells, which includes differentiated oligodendrocytic- and astrocytic-like tumor subpopulations and a rarer subpopulation of stem-like tumor cells. Interestingly, the distribution of states differs markedly between these two glioma subtypes, with an impressive expansion of the undifferentiated stem-like compartment in astrocytomas relative to oligodendrogliomas. The proportion of proliferating cells and the expression of immune and endothelial genes also vary with respect to with tumor subtype and grade, highlighting important implications for chemotherapeutic and immune modulating intervention.

Conclusion: Our work defines a cellular architecture of IDH-mutant gliomas and provides a framework to understand the contributions of tumor cells, microenvironment, and genetics to intratumoral heterogeneity in oligodendrogliomas and astrocytomas.

921. Calpain Inhibition Improves Brain White Matter Damage in a Mouse Model of Subarachnoid Hemorrhage

R. Loch Macdonald, MD, PhD, FAANS; Tian Nie; Jinglu Ai, MD, PhD; Charles Lee, BSc (Berkeley Heights, NJ)

Introduction: Subarachnoid hemorrhage (SAH) is associated with high mortality and morbidity. Most studies have been done are focused on cerebral vasospasm or grey matter of the brain. Clinical evidence shows that brain white matter injury plays a role in secondary complications after SAH. This project is to investigate the role of calpain activation after SAH, and to evaluate the neuroprotective effect of a calpain inhibitor treatment on brain white matter injury.

Methods: 30g CD1 mice were used in groups: Naïve, SAH, sham, SAH

plus calpain inhibitor MDL28170 or vehicle. SAH was created by prechiasmatic injection of 120 μ L of blood. MDL28170 or vehicle (100 μ L i.p.) was administered at 1, 3, 5 and 7 hours post-SAH induction. Neurobehavioral assessment (modified Garcia Score) was conducted for 2 days post-SAH. Corpus callosum injury was assessed with electrophysiological recording of compound action potential (CAP). Brain slices were subsequently used for transmit electron microscopy, where myelinated axon density was quantified to correlate with electrophysiology and behavioral assessment. **Results:** SAH resulted in significant decrease in CAP peak amplitudes as compared to sham operated, MDL28170 restored the CAP to sham level ($p < 0.05$, two-way ANOVA). MDL28170 also restored the increased latency of myelinated axons caused by SAH to sham level. Compared to sham operated, SAH group has significant lower myelinated axon density, and MDL28170 treatment returned that back to sham level. MDL28170 also improved behavior score of SAH animals.

Conclusion: The data suggests that SAH damages both structure and function of myelinated and non-myelinated axons in the corpus callosum, where calpain activation may play a role. Calpain inhibitor MDL-28170 effectively prevents the damage, and restore the function of axons back to normal level, and improved behavioral score. These results indicate that calpain inhibitor may be a viable treatment for brain white matter injury after SAH.

922. Differences in the MicroCT Morphology and mRNA Expression in the Sagittal Suture of Normal and Craniosynostotic Bone

Rafael A. Vega, MD; Ann Ritter, MD; Garrett Cyprus, BS; René Olivares-Navarrete (Richmond, VA)

Introduction: Cranial suture patterning and development is a highly regulated process that is not entirely understood. While studies have investigated the differential gene expression in different sutures little is known about gene expression changes in suture fusing. The aim of this study was to examine gene expression in patent, fusing, and fused areas along minimally invasive sagittal suture specimens.

Methods: Cells were isolated from bone collected from patients undergoing minimally invasive craniotomies at the Children's Hospital of Richmond under IRB approval. Seven minimally invasive samples (6 months) and four fetal demise sample (control) were analyzed by micro-computed tomography (microCT) to evaluate sutural patency. The areas, documented as open, fusing, or fused, were harvested and mRNA was extracted, and gene expression for bone-related proteins, osteogenic, angiogenic, TGF- β superfamily and Wnt signaling were analyzed by qPCR.

Results: MicroCT demonstrates that there are variable areas of closure along the length of the sagittal suture in the form of a zipper. When comparing fetal demise to surgical samples, there was a significant difference in genes for Wnt signaling, TGF- β , angiogenic and osteogenic factors, bone remodeling and nuclear rigidity in mRNA isolated from fusing and fused areas as compared to patent areas ($p < 0.05$).

Conclusion: In sagittal craniosynostosis, the sagittal suture has variable areas of being open, fusing and fused. These specific areas have different mRNA expression. The results suggest that BMP2, FGFR3, and several other signaling pathways play a significant role in the regulation of suture fusion as well in the maintenance of patency in the normal suture.

923. Microsurgical and Endovascular Aneurysm Training in a Chicken Thigh and Leg Pulsatile Model

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Introduction: Current neuro-vascular training models include either animal in vivo aneurysm models, silicone circuits or computer simulation. We describe an endovascular and microsurgical training model using a chicken thigh and leg that is readily available from your local grocery store.

Methods: Twenty chicken thigh and leg models were obtained for

anatomical analysis. Angiography was also utilized to understand the anatomy. Aneurysms were created at the thigh-leg junction using previously described microvascular techniques. Proximal cannulation with a 5-French catheter was achieved and connected to a hemostatic valve with a pump to simulate pulsatile flow. For microsurgical clipping training, three types of aneurysms were also created to reproduce anatomy seen in MCA, ACoA and PCoA aneurysms.

Results: The average cost per specimen was \$1.7 +/- .3. The diameter of the proximal femoral (ischial) artery was 2.4mm +/- .2mm and working length was 9.5cm +/- .7cm. Distal catheterization of aneurysms with microcatheters was successful in all cases, (n=6). Successful deployment of coils and a stent was achieved under fluoroscopic guidance. Gross over-sizing of coils and other mistakes with microwires did lead to aneurysm rupture. For aneurysm clipping exercises, each examiner performed an exploration of the pulsatile aneurysm, application and re-application of a variety of clips and then final inspection of the branching vessels to confirm patency.

Conclusion: The chicken thigh and leg model provides training opportunities in microsurgical suturing, endovascular techniques at aneurysm obliteration and microsurgical reconstruction of aneurysms. Further studies measuring improvement in technical aneurysm management and comparison to other training models are warranted.

924. Use of a Preoperative Bundle to Prevent Pediatric Neurosurgical Infections

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Introduction: Post-operative infections are associated with prolonged hospitalization, IV antibiotics, additional surgery for removal or replacement of infected hardware, and decreased patient satisfaction. Groups such as the HCRN have created and tested standardized infection prevention protocols to decrease the rate of infection after cerebrospinal fluid shunt surgery, with recent published multi-center results showing an average rate of infection of 5.7% after shunt surgery. One etiology for postoperative infection is an inadequate patient preparation with contamination occurring during the initial draping period prior to making an incision. A single pediatric neurosurgeon created and tested an improved infection bundle at our institution. A major modification of the HCRN bundle is that the attending surgeon prepped and draped each patient himself. He used gloves explicitly for draping, and removed these gloves prior to the start of surgery.

Methods: A single pediatric neurosurgeon implemented a preoperative bundle in August 2013 as part of a hospital engagement network study. Bundle completion through December 2015 was prospectively assessed, and post-operative infections were prospectively recorded. The bundle included double gloving, wearing and disposing of draping gloves, giving antibiotics prior to surgical incision, cleaning skin with alcohol and chlorhexidine prior to a Chloroprep skin preparation, attending surgeon performing prep and drape himself, and 24 hours of post-operative antibiotics. A retrospective chart review was performed to ensure all infections were captured.

Results: We evaluated 238 surgeries performed on patients < 18 years of age during this time period. Bundle compliance was 96%. Post-operative infection rate was 1.7%.

Conclusion: Our infection bundle provided a rate of infection below rates published in the literature. The use of draping gloves combined with having the attending surgeon prep and drape patients may help prevent post-operative infections. Adding these techniques to bundles used for future studies should be considered.

925. Ventral capsular / ventral striatal deep brain stimulation for the affective sphere of neuropathic pain: a first-in-human prospective, randomized double-blinded placebo-controlled trial

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John Ozinga, PA; Ela Plow, PhD; Cynthia Kubu, PhD; Paul Ford, PhD (Cleveland, OH)

Introduction: To date, all large deep brain stimulation (DBS) studies have targeted the somatosensory system for the management of chronic neuropathic pain with mixed results. We hypothesized that targeting neural pathways underlying emotion and affective behavior could alleviate the suffering and disability associated with chronic pain.

Methods: To test our hypothesis, we conducted a first-in-human prospective, double-blinded, randomized, placebo-controlled, double-arm crossover DBS study targeting the ventral striatum / anterior limb of the internal capsule in 10 patients with post-stroke pain syndrome. We evaluated outcomes in with the Short-Form McGill Pain Questionnaire, depression and anxiety scales as well as the Pain Disability Index (PDI).

Results: We observed statistically-significant differences in multiple outcome measures related to the affective sphere of chronic pain. Active DBS versus sham stimulation was associated with an increased probability of response (i.e. $\geq 50\%$ improvement) in the Montgomery-Asberg Depression Rating Scale (44% DBS ON v. 19% DBS OFF, $p=0.02$), Beck Depression Inventory (45% DBS ON v. 27% DBS OFF, $p=0.004$), the Affective Pain Rating Index (39% DBS ON v. 18% DBS OFF, $p=0.002$) and Present Pain Intensity (10% DBS ON v. 3% DBS OFF, $p=0.002$) of the Short-form McGill Pain Questionnaire. There were no significant differences in disability indexed by the PDI.

Conclusion: The results of our double-blind study indicated that DBS of the ventral capsule and ventral striatal area can effectively modulate the affective sphere of chronic pain, thereby benefiting select patients. The results indicate that it may be possible to improve clinical outcomes by shifting our focus from sensory pathways towards networks related to the affective sphere of pain. Our ultimate goal is to reduce pain-related disability and promote social and occupational rehabilitation from chronic pain.

926. Robotically-Assisted Cerebral Angiography and Intracranial Intervention: Initial Experience with the Magellan Catheter System

Christopher Carroll, MD; Ryan Tackla, MD; Shawn Vuong, MD; William Jeong, MD; Joseph Serrone, MD; Andrew Ringer, MD (Cincinnati, OH)

Introduction: Robotically-assisted angiography recently became available and has been implemented for both diagnostic and interventional management of extra-cranial vascular disease. Animal studies demonstrated that robotically-assisted angiography is, at least, as safe as manual techniques. Robotically-assisted catheter navigation may cause less endothelial trauma, thereby reducing the risk for embolic events. To our knowledge, there is only one report of robotic-assisted cerebral angiography (RACA) in 15 patients and no report to-date on the feasibility or safety of robotically-assisted intracranial intervention (RAII).

Methods: During a 15-month period (2/2015-5/2016) consecutive patients undergoing RACA or RAIL with the Magellan robotic catheter system were prospectively followed at a single-institution. Traditional manual angiography and/or intervention in seven of the patients served as a control. Prospectively collected data included procedure time, fluoroscopy time, procedural success, contrast volumes, and peri-procedural complications.

Results: Twenty-three patients underwent RACA (N=9) or RAIL (N=18). RACA had a mean procedure time of 72.2 ± 41.4 min; mean fluoroscopy time of 27.3 ± 22.1 min.; and mean contrast volume of 84.0 ± 23.0 mL. RAILS had a mean procedure time of 154.0 ± 79.72 min; mean fluoroscopy time of 52.3 ± 29.5 min.; and mean contrast volume of 177.5 ± 49.7 mL. There was no significant difference in procedure time, fluoroscopy time, or contrast volume for RACA versus matched manual angiography controls ($p < 0.05$). After the senior author's first five procedures the difference between manual and robotically-assisted procedure and fluoroscopy times became negligible. One coil-embolization was aborted due to lack of aneurysm access; one coil-embolization was converted to flow diverting stent placement. No perioperative complications were encountered.

Conclusion: Application of the Magellan robotically-assisted catheter system to cerebral angiography and cerebrovascular interventions is tech-

nically feasible and does not appear to increase risk to the patient. After a short-learning curve, procedure time, fluoroscopy time, and contrast volumes did not differ significantly from manually-performed diagnostic cerebral angiography controls.

927. Auditory-Cued Naming as an Optimal Paradigm for the Mapping of Human Language

Cihan M Kadipasaoglu; Thomas Pieters, MD; Matthew Rollo; Joshua Breier, MD; Nitin Tandon, MD (Houston, TX)

Introduction: Cortical stimulation mapping remains an integral component for language localization to facilitate maximally safe resection of neoplasms and seizure foci in the dominant hemisphere. Visual object naming has been the standard technique used for such mapping, despite limitations in that auditory processes and working memory intrinsic to phonology are not mapped. In contrast, auditory-cued naming paradigms engage broader language networks involving auditory processing, semantics, working memory, phonology, and articulation.

Methods: We performed a systematic prospective data collection in 56 patients undergoing either intra-operative (awake craniotomy) or extra-operative (with implanted subdural electrodes) language mapping (Ojemann stimulator, 5 – 10mA, 50 Hz, 2-4s trains), using a battery of tasks (auditory cued naming and repetition, visual naming, and simple articulation). Testing was performed with a neuropsychologist, with concurrent ECoG to detect after-discharges. A depolarization model of current spread was generated (derived from experimental mammalian epileptical stimulation studies) to compute a point probability for presence of linguistic function on subject-specific 3D cortical surface models. A surface-based co-registration algorithm was implemented to co-localize positive language sites across subjects to generate a population map for this large cohort.

Results: Comparison of positive language sites combined across all tasks against auditory naming alone revealed no significant differences ($p < 0.01$) in essential language regions: Broca's area, superior temporal gyrus, posterior medial temporal gyrus, and posterior middle frontal gyrus. Interestingly, auditory naming was also proficient at identifying ventral temporal sites traditionally viewed as part of the ventral visual stream (i.e. basal-temporal-language-area). No other task fully engaged all of these regions.

Conclusion: Auditory-cued naming paradigms effective for localization of the broader language network. Given finite time for stimulation in patients, the availability of such an efficient paradigm is of importance for predicting the likelihood of language in specific cortical sites so that functional deficits following resections may be minimized.

928. Natural History of Patients with Hemorrhagic Moyamoya Disease : A Long-term Follow-up study

Xingju Liu, MD (Beijing, China)

Introduction: Very little is known about the long-term prognosis of patients with hemorrhagic moyamoya disease (MMD). We did an extensive observational study to learn the natural course of patients with hemorrhagic MMD in China.

Methods: Thirty-six patients with hemorrhagic MMD treated without bypass surgery between 1985 and 2007 were included. All patients were followed up until death or until 2015. The rate of recurrent hemorrhage over long-term follow-up was recorded. Annual and cumulative incidences of rebleeding and risk factors for rebleeding were studied using Kaplan–Meier survival analysis and cox regression model.

Results: The median follow-up time was 11.7 (range, 5–27) years. During 423.7 person-years, 16 patients experienced twenty-two episodes of rebleeding, giving an average annual incidence of 5.2%. Five patients died on account of rebleeding. Most episodes of rebleeding occurred within 10 years after first stroke. The annual risk of rebleeding increased gradually from 2.78% in the first five years to 7.8% in the 10 years after first bleeding. The cumulative rate of rebleeding was 11.1% at 5 years, 33.0% at 10 years,

and 62.0% at 15 years. Age, gender, types of first bleeding, DSA stage, and complication with aneurysm were not associated with any increased risk of rebleeding in either univariate or multivariate analysis.

Conclusion: The natural history of rebleeding in patients with hemorrhagic MMD is dynamic. Rebleeding events are common and the risk of rebleeding increases within a very long-term follow-up.

929. Alpha7 Nicotinic Acetylcholine Receptor Stimulation Attenuates Neuroinflammation in Murine Intracerebral Hemorrhage

Paul Krafft; Devin McBride; William Rolland; Tim Lekic; Jerry Flores; John Zhang (Loma Linda, CA)

Introduction: Accounting for high mortality and morbidity rates, intracerebral hemorrhage (ICH) remains one of the most detrimental stroke subtypes without a specific therapy. Neuroinflammation contributes to ICH-induced brain injury and is associated with unfavorable outcomes. This study aimed to evaluate whether $\alpha 7$ nicotinic acetylcholine receptor ($\alpha 7$ nAChR) stimulation ameliorates neuroinflammation after ICH.

Methods: Male CD-1 mice and Sprague-Dawley were subjected to intracerebral injection of autologous blood or bacterial collagenase. ICH animals received either $\alpha 7$ nAChR agonist PHA-543613 alone or combined with $\alpha 7$ nAChR antagonist methyllycaconitine (MLA) or Janus kinase 2 (JAK2) antagonist AG490. Neurobehavioral deficits were evaluated at 24 hours, 72 hours, and 10 weeks after ICH induction. Perihematomal expressions of JAK2, signal transducer and activator of transcription 3 (STAT3), tumor necrosis factor α (TNF- α), and myeloperoxidase (MPO) were quantified via Western blotting. Histologic volumetric analysis of brain tissues was conducted after 10 weeks following ICH induction.

Results: PHA-543613 improved short-term neurobehavioral (sensorimotor) deficits and increased activated JAK2 and STAT3 expressions while decreasing TNF- α and MPO expressions after ICH. MLA reversed these treatment effects. PHA-543613 also improved long-term neurobehavioral (sensorimotor, learning, and memory) deficits and ameliorated brain atrophy after ICH. These treatment effects were reduced by AG490.

Conclusion: $\alpha 7$ nAChR stimulation reduced neuroinflammation via activation of the JAK2-STAT3 pathway, thereby ameliorating the short- and long-term sequelae after ICH.

930. Conceptual Processing in the Basal Temporal Language Area

Kiefer Forseth; Nitin Tandon, MD (Houston, TX)

Introduction: The seemingly effortless human capability to access and relate concepts – a cognitive process termed semantics – is integral to human language. Despite many years of functional imaging research, it is still unclear where in the brain sub-lexical semantic processing occurs. In addition to Broca's area, ventral temporal cortex (also known as the basal temporal language area – BTLA) has been proposed as a hetero-modal convergence node for semantic processing, but no firm evidence exists for this idea. Susceptibility artifacts render this area difficult to study with functional imaging.

Methods: We used electrocorticography (ECoG) and CSM in a large cohort ($n = 25$) to study semantic contrasts in the auditory and visual domains. Electrode recording zones were estimated on the cortical surface. Each individual cortex was registered to a standard space with a surface-based nonlinear transform to optimize topographical accuracy. In this standard space, we implemented a mixed-effects multilevel analysis (MEMA) to identify anatomic substrates of neural processes consistent across the study population. In the same space, we aggregated CSM results from all stimulated pairs of electrodes.

Results: Direct spectral measures of cortical activity from ECoG revealed a distinct cognitive network state for semantic processing indexed by coherent activity linking the anterior fusiform and Broca's area. Additionally, transient dysfunction of the same anterior fusiform region (and Broca's area) induced by CSM disrupted both visual and auditory cued naming. The ventral anterior fusiform region identified by both ECoG and

CSM corresponds to the center of the BTLA.

Conclusion: We connect a functionally derived cortical map of semantic cognition with the BTLA as defined by CSM. The role of this region in language is currently underappreciated in the neurosurgical community and its systematic individualized localization and preservation would likely improve cognitive outcomes after resections in the dominant temporal lobe.

931. Applications of the Apollo Detachable Tip Microcatheter for Endovascular Embolization of Arteriovenous Malformations and Arteriovenous Fistulas: The BNI Experience

Bruno Cesar Flores, MD; Alfred See, MD; Andrew Ducruet, MD; Felipe Albuquerque, MD (Phoenix, AZ)

Introduction: Liquid Embolic Agents have revolutionized the endovascular management of AVMs and AVFs. Nonetheless, since 2005 the Food and Drug Administration has received more than 100 reports of microcatheter breakage or entrapment related to Onyx embolizations. In 2014, the Apollo became the first detachable tip microcatheter available in the US. Only a few small reports on its safety have been published.

Methods: Retrospective review of the BNI database was conducted. All patients that underwent endovascular embolization using the Apollo microcatheter were identified. Patient and lesion demographics were collected. In addition, and Apollo-specific variables were analyzed.

Results: From July/2014 to July/2016, 132 Apollo catheterizations were performed in 35 patients. Mean patient age was 35.2 years. The most frequent presentation was hemorrhage (34.3%). The majority of the lesions were AVMs (91.4%, mean diameter: 35.6mm). The median Spetzler-Martin Grade was 3. Twenty five patients underwent surgical resection, and good functional outcomes (mRS 0-2) achieved in 88.2%. Microcatheterization was successful in 128 pedicles. The majority of the patients (68.6%) underwent one embolization session. The mean number of pedicles per session was 2.81. Onyx 18 was used in 56.3%, nBCA in 29.7%, and Onyx 34 in 14% of the embolizations. In 45.7% of the patients, obliteration greater than 75% was achieved. Tip detachment was seen in 17.4%; the microcatheter was retrieved intact in 65.2% of the catheterizations. No unintended catheter fractures or Apollo-related morbidity were seen. One patient died from intra-procedural complications unrelated to microcatheter selection.

Conclusion: The use of the Apollo detachable tip microcatheter for embolization of AVMs and AVFs is associated with high successful catheterization and obliteration rates, low morbidity and mortality. The microcatheter was retrieved in all cases, even following prolonged injections in distal branch pedicles often with significant reflux. The current study represents the largest case series on the Apollo application for neurointerventional procedures.

932. Major Complications Following Microvascular Decompression: 6-Year Incidence and Predictive Risk Factors

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Introduction: Microvascular decompression (MVD) for the treatment of trigeminal neuralgia is effective in relieving severe facial pain. MVD of other cranial nerves to relieve facial spasm or refractory pain is also rising. Currently, there are no studies reporting specific patient risk factors for complications following these procedures. The purpose of this study was to describe the incidence and predictive risk factors for major complications following MVD.

Methods: Current Procedural Terminology (CPT) and ICD9 codes were applied to the 2008-2014 National Surgical Quality Improvement (NSQIP) database in order to identify all patients undergoing a craniectomy for section or decompression of cranial nerves. Demographics, comorbidities, and perioperative variables were collected for each patient. Univariate statistics with subsequent binary logistic regression analyses were used to explore the relationship between these perioperative factors and adverse events.

Outcome variables of interest included major (Clavien IV) complications along with mortality as well as prolonged hospital length of stay (LOS). Significant variables such as demographics, comorbidities, operative time, body mass index (BMI), and American Society of Anesthesiologists (ASA) score were controlled for in each model. The c-statistic was computed to assess the predictive capacity of the models.

Results: 663 patients were identified. Of these, 39 (5.9%) sustained a major complication, including 4 (0.6%) deaths. Independent predictors of major adverse events included preoperative bleeding disorder (OR=32.5, P=0.014), functional dependency (OR=12.7, P=0.015), and prolonged operative time (OR=1.01, P=0.001). Predictors of prolonged LOS were hypertension (OR=1.55, P=0.016), and operative time (OR=1.01, P<0.001). The c-statistic values for the models were 0.79 and 0.66, respectively.

Conclusion: Bleeding disorders, functional status, hypertension, and prolonged operative time were predictors of suboptimal outcomes following MVD. Understanding these risk factors gives providers the ability to provide additional perioperative resources to these patients in order to reduce the incidence of adverse events and prolonged LOS following MVD.

933. Distinct Transcriptional Modules Define Cerebral Aneurysm Formation and Aneurysm Rupture

Tej Azad; James Pan; Omar Choudhri (Floyds Knobs, IN)

Introduction: Analyzing genes involved in formation and rupture of intracranial aneurysms (ICA) can enhance knowledge about the pathogenesis of aneurysms and identify novel treatments. We conducted an integrated multi-cohort study of gene expression to better understand the transcriptional mechanisms underlying ICA biology.

Methods: We systematically queried the NCBI Gene Expression Omnibus for microarray studies of ICAs. We identified 132 samples from six independent data sets, including 25 normal cerebral vessels (NV), 31 ruptured aneurysms (RA), and 20 unruptured aneurysms (UA). We conducted an integrative gene expression analysis by combining effect sizes and p-values to analyze aneurysm formation (UA vs. NV) and aneurysm rupture (RA vs. UA). Differentially expressed genes (DEGs) were analyzed using Ingenuity Pathway Analysis (IPA, Qiagen, Inc.).

Results: We found 622 (2.70%) DEGs, 268 overexpressed and 354 underexpressed, between aneurysmal and normal vasculature and 95 (0.367%) DEGs, 43 overexpressed and 52 underexpressed, between ruptured and unruptured aneurysms with FDR (False Discovery Rate) < 0.05. Notably, only three genes (IPP, CMTM6, and MAST4) were shared between these two gene sets. For aneurysm formation, the most enriched biological pathway was EIF2 signaling (p=3.26e-06) DNA double-strand break repair by homologous recombination (p=2.88e-04), whereas for aneurysm rupture the most enriched pathways were clathrin-mediated endocytosis signaling (p=9.6e-03) and formaldehyde oxidation II (p=1.30e-02). Moreover, we found that aneurysm formation was enriched for genes involved in cellular growth and proliferation (p=3.74e-03) and free radical scavenging (p=9.36e-07) while aneurysm rupture was significantly enriched for genes involved in molecular transport (p=4.49e-02) and cell death and survival (p=8.5e-04).

Conclusion: Our results provide evidence for aneurysm formation and rupture as distinct pathophysiologic processes with dissimilar transcriptional modules, biological functions, and signaling pathways. Our integrative analysis takes advantage of the marked variation between individual studies of ICAs to reveal fundamental differences in the biology of aneurysm formation and rupture.

934. Neurophysiological analysis of subthalamic deep brain stimulation for Parkinson's disease between general and local anesthesia: pattern shift of physiological signatures by anesthesia

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Introduction: STN-DBS under general anaesthesia (GA) is an alterna-

tive approach, but detailed analysis of long-term clinical outcomes and physiological features of MER between GA and LA for STN-DBS is lacking.

Methods: 19 consecutive PD patients with similar motor disabilities underwent placement of STN DBS electrodes under either GA with sevoflurane (n = 10) or LA (n = 9). Both groups received similar intraoperative MER of the STN identified on pre-operative imaging. Clinical evaluation included both pre-operative and post-operative Unified Parkinson's Disease Rating Scales (UPDRS), Mini Mental Status Examination and Beck Depression Inventory. Microelectrode recordings were analysed for neuron spiking rate and oscillatory dynamics along the recording trajectory through the STN.

Results: Clinical outcomes at five years were similar for both groups. UPDRS part III improved (55.4±15.8% improvement in UPDRS part III in GA in DBS on/ Med on/ DBS off Med off status and 51.1±17.1% in LA), dyskinesia and levodopa equivalent dosage was reduced. Cognitive and psychiatric status remained stable and there is no difference of adverse effects between two groups. Final coordinates of active contacts and clinically determined stimulation parameters were also no different between groups. On MER recordings, STN firing rates and amplitudes were similar between LA and GA. However, distinct dorsolateral beta (13-30 Hz) and ventromedial gamma (30-100 HZ) oscillations were detected in the STN only for the LA condition. Under general anesthesia, lower frequency (delta 0.5-4 Hz, theta 4-8 Hz, alpha 8-12 Hz) spike oscillations predominated.

Conclusion: In our cohort, long-term outcomes were equivalent for STN-DBS placed under GA and LA. GA with sevoflurane disrupted characteristic beta-frequency spike oscillations, but did not disrupt the detection of dorsal and ventral STN borders. STN-DBS under inhaled anesthesia should be considered for patients for whom electrode implantation under LA is not feasible.

935. Declining Complication Rates with Flow Diversion of Anterior Circulation Aneurysms after Introduction of Pipeline Flex

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Introduction: Second generation Pipeline embolization device (PED Flex) has several design upgrades, including improved opening and resheathability, in comparison to PED Classic. We investigated whether PED Flex is associated with less complications in a large single-institution series of anterior circulation aneurysms treated by flow diversion.

Methods: A prospective, IRB-approved database was analyzed for all patients with anterior circulation aneurysms treated by flow diversion at our institution. All treatments were performed by one of two dual-trained cerebrovascular/endovascular neurosurgeons. PED Classic was used from August 2011-January 2015, and PED Flex was used since February 2015.

Results: 513 PED procedures (252 Classic, 261 Flex) were performed for anterior circulation aneurysms during the study period. 82% of patients were female, with average age 56 years and average aneurysm size 6.8mm. 16% of patients had prior SAH, and 18% of aneurysms had prior treatment. The distribution of aneurysms included 81% ICA, 14% ACA, and 4% MCA. Procedural success was achieved in 96.7% of cases (95.6% of Classic and 97.7% of Flex cases). Device caking/removal occurred in 15.8% of Classic and 2.9% of Flex cases. With PED Classic, there were 5 major ischemic strokes (2.0%), 6 ICH (2.4%), and 4 SAH (1.6%), collectively resulting in 4 mortalities (1.6%). With PED Flex, there were 0 major ischemic strokes, 3 ICH (1.1%), and 2 SAH (0.8%), collectively resulting in 2 mortalities (0.8%). Major morbidity or death occurred in 3.9% of cases overall, 6.0% of Classic cases, and 1.9% of Flex cases (p=0.018). Minor morbidity (minor ischemic stroke, TIA, transient CN palsy, dissection, groin hematoma, infection) occurred in 27 Classic cases (10.7%) and 20 Flex cases (7.7%).

Conclusion: Flow diversion of anterior circulation cerebral aneurysm is associated with an overall low rate of major complications. The complication rate is significantly lower since the introduction of second generation PED Flex.

936. Venous Thromboembolism Complications in Patients with Spontaneous Intracerebral Hemorrhage: A Multicenter Cohort Study

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Introduction: Patients with spontaneous intracerebral hemorrhage (ICH) are predisposed to venous thromboembolic (VTE) complications, such as deep vein thrombosis (DVT) and pulmonary embolism (PE). In this multicenter cohort study, we evaluated the rate of VTE complications in ICH patients during acute hospitalization and identified potential risk factors.

Methods: We analyzed prospectively collected data from 19 centers and 41 sites that participated in the Ethnic/Racial Variations of Intracerebral Hemorrhage (ERICH) study, from August 2010 to February 2016. We compared ICH patients with VTE complications to those without VTE complications. Statistical analyses were performed to determine predictors of VTE complications and poor outcome (modified Rankin Scale ≥ 4) at discharge and three-month follow-up.

Results: Of the 2,902 ICH patients who were eligible for analysis, 87 (3.0%) had VTE complications: 57 (2.0%) had only DVT, 19 (0.7%) had only PE, and 11 (0.4%) had both. In the multivariable logistic regression analysis, the strongest independent predictor of VTE complication was a prior history of VTE (OR=6.8; $P<0.0001$), followed by intubation (OR=4.0; $P<0.0001$) and presence of IVH (OR=1.8; $P=0.0157$). After controlling for ICH volume and location, IVH, age, and presenting Glasgow Coma Scale, the occurrence of VTE complications was an independent predictor of poor outcome at discharge (OR=2.9; $P=0.002$) and three-month follow-up (OR=2.1; $P=0.02$).

Conclusion: Although VTE complications are uncommon after ICH, they are associated with significantly worse outcomes. Further studies will be needed to determine the optimal treatment regimen for the prevention and treatment of VTE complications in ICH patients.

937. The Therapeutic Challenge to Large Arteriovenous Malformations: Volume-Staged or Single-Session Gamma Knife

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Introduction: Generally, arteriovenous malformations (AVM) with large nidus (≥ 10 ml) are considered less appropriate targets for stereotactic radiosurgery (SRS) because of possible increase in radiation-induced adverse events (AEs); however, surgeons sometimes need to manage such large AVMs. Clarifying the efficacy of SRS is important.

Methods: The outcomes of 105 consecutive patients with AVMs larger than 10 ml in volume treated with SRS were retrospectively analyzed. Our institution has performed volume-staged gamma knife (VSGK) and single-session gamma knife (SSGK) to those with 10–20 ml and >20 ml, respectively.

Results: After excluding 19 cases with incomplete data, 86 patients were analyzed (VSGK, $n = 17$; SSGK, $n = 69$). The mean follow up period, maximal diameter, volume were 74 months, 42mm, and 20 ml, respectively. Spetzler-Martin grade was II, III, and IV-V in 19 (22%), 41 (48%), and 25 (29%), respectively, and 41% were hemorrhagic. Obliteration rates were 71% and 80% at 5 and 6 years, respectively in SSGK cohort; 38% and 54% at 6 and 7 years, respectively in VSGK cohort. Post-treatment hemorrhage was observed in 14 patients (SSGK, $n = 9$; VSGK, $n = 5$), resulting in severe, moderate, mild, and no deficit in 6, 3, 1, and 4 patients, respectively. AEs were observed in 10 patients and the outcomes were moderate, mild, and no deficit in 1, 3, and 6 patients, respectively. Event free survival rates were 85% and 77% at 2–5 years and 10 years, respectively in SSGK; 82%, 70%, and 60% in 2, 5, and 10 years, respectively in VSGK cohort.

Conclusion: SSGK for medium to large AVMs (10–20 ml) is feasible

with acceptable safety profile. VSGK to further large nidus (≥ 20 ml) is still a matter of debate and should be performed after due consideration of natural history and propensity of hemorrhage.

938. Differentiating Traumatic Brain Injury and Post Traumatic Stress Disorder with the use of Diffusion Tensor Imaging and Volumetric Analysis

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Introduction: The prevalence of concomitant TBI and PTSD often complicates the clinical diagnosis and treatment of patients, particularly those in the military. Multiple studies have shown alterations in DTI in TBI patients using Fractional Anisotropy (FA). The suggestion of volumetric differences of the amygdala and hippocampus have been found in PTSD. We collected data from 227 Veterans with TBI, PTSD or both. In addition to FA, we measured mean (MD), axial (AD) and radial diffusivity (RD) as well as Voxel-Based Morphometry of brain structures in these patients. Our objective is to further delineate the radiographic differences in these two conditions, as much of the clinical presentation can be difficult to discern.

Methods: The FMRI's Integrated Registration and Segmentation Tool was used to determine Volumetric segmentation. DTI analysis was performed using the FMRI's Diffusion Toolbox. Probabilistic tractography was conducted at the single-subject level in all pairwise comparisons generating a structural connectivity map using a two-region of interest approach in all participants. Diagnosis of TBI severity was established using Alteration of Consciousness, Loss of Consciousness, and Post-traumatic amnesia. PTSD status was established by using a criteria cutoff of 45 or more on the PCL-C IV.

Results: No significant difference was found in the brain volume of anatomic structures in those with mild TBI as compared to those without. However, significant differences were found for DTI tracts measured with MD, RD and AD in the hippocampus-accumbens tract as well the accumbens-amygdala tracts. In PTSD, no significant difference in DTI tracts was shown, but a significant difference in amygdala volume ($p < 0.02$) was present.

Conclusion: Once the distinct radiographic and anatomic manifestation of PTSD and TBI can be identified, medical and psychological therapy can be better tailored to help these patients. We plan on further augmenting our study with Neuropsychological data we have collected.

939. Bridging the Gender Gap: Pharmacokinetic Differences Underlying Thrombolysis by Aptamer Inhibition of Von Willebrand Factor

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Introduction: Stroke remains a major cause of morbidity and mortality. While recombinant tissue plasminogen activator (rTPA) has been the mainstay of ischemic stroke treatment, few patients are eligible for treatment, and recanalization is only seen in 25-50%. Furthermore, females have been shown to suffer more severe strokes with decreased responsiveness to rTPA compared to males. Aptamers are a class of RNA molecules that bind and inhibit proteins. An aptamer binding von Willebrand factor (VWF) was recently developed, preventing platelet adhesion and aggregation.

Methods: Male and female adult wild-type (C57BL/6J) mice were anesthetized, and the right carotid artery was exposed. Baseline carotid flow was recorded (Doppler flow probe, Transonic) and occlusion was induced with a 10% ferric chloride patch. After 20-minute clot stabilization, mice were administered intravenous vehicle (n , male=12, female=8), rTPA (10 mg/kg; n , male=7, female=6), or VWF aptamer (n , male=7, female=15). Aptamer efficacy was assessed using bolus (0.5 mg/kg, 5 min) and continuous infusion (0.05 mg/kg, 2ul/min, 45 min). Statistical analysis was performed using a two-way ANOVA with multiple comparisons.

Results: In males, VWF aptamer successfully restored carotid blood flow 45 minutes following carotid occlusion compared to vehicle ($p<0.01$) and rTPA ($p<0.05$) when given as a bolus. In the female cohort, VWF aptamer restored carotid blood flow after 53 minutes when given as a continuous infusion compared to vehicle ($p<0.01$) and rTPA ($p<0.05$). There was no significant reperfusion in males treated with continuous infusion or in females treated with bolus administration.

Conclusion: Aptamer inhibition of VWF is a potent thrombolytic agent with greater efficacy compared to rTPA in both males and females. While underlying mechanisms behind the gender difference in efficacy based on aptamer administration has not yet been explored in this murine model, these results may yield an important consideration for the clinical treatment of stroke.

940. Angiographic Flow Index on DSA Correlates with Cerebral Flow Measured by Quantitative MRA

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Introduction: Digital subtraction angiography (DSA) has traditionally been used to provide high-resolution anatomical imaging but is not readily used to assess cerebral hemodynamics. Here we examine the relationship between time density transit time (TT) on DSA, vessel cross-sectional area and flow obtained from QMRA of the same artery.

Methods: Patients seen at our institution between 2009 and 2015 who had concomitant DSA and Quantitative MRA prior to any treatment for a vascular lesion were retrospectively reviewed. Transit time (TT) on DSA was defined as time needed for contrast to change image intensity from 25%-25%. Flow volume rate (mL/min) and vessel cross-sectional area were measured using QMRA. Angio flow index (FI) = [Cross sectional area/TT25-25%] was calculated and analyzed relative to flow.

Results: 48 patients (mean age was 51 years) were included. There was a significant correlation (Spearman's) between the MCA and ACA flows and the angio flow index ($P<0.001$, $\rho=0.66$). The same positive correlation was present for the individual MCA flows ($P<0.001$, $\rho=0.81$) and ACA flows ($P<0.001$, $\rho=0.52$) and the angio flow index.

Conclusion: Angio flow index correlated significantly with intracranial flows measured by QMRA, and so angio flow index may be used as an indirect tool for assessment of cerebral flow during interventional procedures.

941. Trigeminal Nerve Stimulation as a Novel Resuscitation Therapy for Polytrauma Model of Traumatic Brain Injury Complicated by Hemorrhage Shock

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Introduction: Traumatic brain injury (TBI) and hemorrhagic shock (HS) often occur concomitantly, leading to increased morbidity and mortality. Hypotension in particular has been linked with increased mortality after severe TBI. Trigeminal nerve stimulation (TNS) has been shown to increase blood pressure systemically as well as cerebral blood flow selectively, which confers protection from hypoxic-ischemic condition to vital organs. In this study, for the first time, we have investigated the effect of electrical TNS in a TBI model compounded by HS.

Methods: A controlled cortical impact (CCI) model was used to create severe TBI in male Sprague-Dawley rats. Immediately after CCI, 30% of the total blood volume was removed over 20 minutes. Electrical stimulation of both trigeminal nerves was performed by introducing two needles (26G) subcutaneously bilaterally in the V1 distribution. Rectangular cathodal pulses (0.5 ms) were delivered by electrical stimulator at 25 Hz, 5V continuously for 60 minutes. Animals were randomized to one of three study groups ($n=6-8$ /group): (1) sham animals; (2) polytrauma (TBI+HS) animals; (3) polytrauma animals with immediate TNS. Brain edema (wet-dry-weight method) and lesion volumes (cresyl violet staining) were measured at 24 hour after TBI.

Results: TBI complicated by HS produced brain lesions (sham vs.

polytrauma: 0 vs. 12.57 ± 1.52 mm³; $n=6$, $p<0.05$) that were accompanied by brain edema (brain water content in sham vs. polytrauma: $77.4\pm0.5\%$ vs. $83.2\pm0.7\%$; $n=8$, $p<0.05$). In the TNS treatment group, there was a significant decrease in brain edema ($80.5\pm0.5\%$ vs. $83.2\pm0.7\%$; $n=8$, $p<0.05$) and lesion volumes (7.3 ± 1.06 vs. 12.57 ± 1.52 mm³; $n=6$, $p<0.05$).

Conclusion: This study demonstrates that by decreasing brain edema and lesion volumes, early electrical TNS may be beneficial in attenuating the consequences of TBI complicated by HS. The results of our study will have application in the management of isolated neurotrauma as well as polytrauma patients.

942. Role of brain hemostatic system in cerebrospinal fluid abnormalities following subarachnoid hemorrhage

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Introduction: In 95% of cases subarachnoid hemorrhage (SAH) results in long-term disabilities due to brain morphological changes, the pathogenesis of which remain uncertain. Hindrance of cerebrospinal fluid (CSF) circulation is a possible mechanism interrupting drainage of subarachnoid space and parenchyma of damaging substances. We explored changes in CSF circulation at different time following SAH and a possible role of brain tissue factor (TF, Factor III) in these changes.

Methods: Perforation of circle of Willis was used as a model of SAH in mice. Fluorescent solute (Alexa 594) and 0.02 μ m fluorescent microspheres injected into cisterna magna were used to trace CSF flow. Distribution of fluorophores and SAH were scored. Activity of brain tissue factor was blocked by intracerebroventricular administration of specific antibodies. Distribution of TF and fibrin deposition were analyzed using immunohistochemistry.

Results: In sham/naive animals, fluorescent solute and microspheres injected into cisterna magna reached olfactory bulbs within 15-20 min along the paravascular route. SAH blocked spread of fluorophores at the rostral pons border and interrupted CSF flow for up to 30 days when no blood in the subarachnoid space was visible any longer. Block of CSF flow did not correlate with the size of hemorrhage. Following the SAH, fibrin was observed on the brain surface including areas without visible presence of blood. Block of astroglia-associated TF not only increased size of hemorrhage by 50% but also facilitated spread of fluorophores in sham/naive animals by $243\pm37.6\%$.

Conclusion: SAH induces long-lasting block of CSF flow. Brain TF plays an important role in localization of hemorrhage. TF also regulates CSF flow under normal conditions. Targeting of the TF system will allow developing of new therapeutic approaches to the treatment of SAH consequences and pathologies related to CSF flow such as hydrocephalus.

943. Cross-Cultural Efficacy of Interactive Educational Interventions in the NeuroTrauma Setting

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Introduction: Neurological surgeons are oftentimes faced with the challenge of educating patients and their families on medical conditions and surgical treatment options. Time constraints, linguistic barriers, and varied educational backgrounds can limit the amount of information that can be disbursed, which may lead to suboptimal patient education. This study aims to assess the cross-cultural validity of interactive educational interventions in non-English speaking traumatic brain injury and concussion patients. We hypothesize that interactive presentation of information will improve patient comprehension and optimize the patient-physician interaction.

Methods: Following IRB approval and informed consent, non-English speaking neurotrauma patients completed a pre-survey (5-point scale), (2) viewed an interactive iBook loaded on an iPad on either concussion or TBI in their native language (limited to Korean, Vietnamese, or Spanish), and (3) completed a post-survey. The surveys assessed knowledge, communication, and comfort constructs, and included an internal measure of validity and reliability.

Results: When pre- and post-survey results were averaged ($n = 238$), preliminary data shows all subjects significantly improved (95% confidence paired T-test, $p < 0.01$) post-survey scores (average pre-iBook score: 2.714 vs. post-iBook score: 4.152). The tested constructs showed inter-construct reliability (Cronbach's $\alpha > 0.70$). Furthermore, subject responses showed significant improvement regardless of native language, cultural/educational background, or age, although Vietnamese-speaking patients scored significantly lower (95% confidence unpaired T-test, $p < 0.01$) than combination of all languages on the post-survey despite similar pre-survey scores. Spanish-speaking patients scored similar to the combination of all languages despite significantly lower pre-survey scores (95% confidence unpaired T-test, $p < 0.01$).

Conclusion: Interactive iBook-based educational interventions on concussion and TBI enhanced (1) patient comprehension, (2) comfort with their medical condition and follow-up care, and (3) improved communication between the patient and the physician. Furthermore, these findings are cross-culturally valid and irrespective of the patients' native language and cultural/educational background.

944. Short-Term Outcomes in Head-Trauma Patients with Associated Skull Fractures

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Introduction: Although traumatic brain-injury has been widely studied, less attention has been devoted to skull fractures (SF) occurring in association with head-trauma.

Methods: Using ICD-9 codes, we identified all trauma-related SF in the 2001-2010 Nationwide Inpatient Sample and assessed trends/outcomes. Weighted data to average the US population were analyzed.

Results: In total, 701,950 head-trauma patients with SF diagnosis were identified. The mean age of patients was 36.7 years (SD $\pm$ 24.9). SF was categorized as closed-SF (91.1%) or as open-SF (8.9%), occurring in the following anatomical sites: skull-base (67.2%), bones of the cranial-vault (22.6%), multiple sites (9.1%), and other unmentioned sites (1.1%), ($p < 0.001$). There were associated facial bone fractures (34.0%). Generally SF was more common among males (71.1%), who compared to females were more likely to have open-SF (10.0% vs. 6.1%, $p < 0.001$). Injury mechanisms implicated were: falls (26.9%), motor-vehicle accidents (14.5%), and struck-by/hit (9.8%), $p < 0.001$; however, motor-vehicle accidents versus falls were more likely to result in open-SF (12.6% vs. 7.3%, $p < 0.001$). Significant intracranial hemorrhage (ICH) was more common in basal-SF (28.5%, $p < 0.001$), and similar to open-SF, more likely to undergo craniotomy/cranioplasty ($p < 0.01$). Mortality was higher in open-SF versus closed-SF (22.3% vs. 7.7%, $p < 0.001$) and in ICH, ($p < 0.001$). The occurrence of post-traumatic bacterial meningitis was 0.2%, more common in open versus closed-SF (0.5% vs. 0.2%, $p < 0.001$). Overall mean hospital stay and individual charges were increased in open versus closed-SF [(10 vs. 7 days, $p < 0.001$) and (\$87,138.39 vs. \$63,763.49, $p < 0.001$)] respectively.

Conclusion: Skull fractures associated with head-trauma result in significant morbidity/mortality. Patients with open-SF experience worse short-term outcomes.

945. Angiogenesis plays a critical role in Group 3 medulloblastoma pathogenesis

Columbia Softball Charity Award

Eric M. Thompson, MD; Stephen Keir; Talaingair Venkatraman, PhD; Christopher Lascola, MD, PhD; Kristen Yeom, MD; Andrew Nixon, PhD; Yingmiao Liu, PhD; Daniel Picard; Marc Remke; Vijay Ramaswamy, MD, PhD; Michael Taylor, MD, PhD (Durham, NC)

Introduction: Of the four medulloblastoma subgroups, Group 3 is the most aggressive but the importance of angiogenesis is unknown. This study sought to determine the role of angiogenesis and identify clinically relevant

biomarkers of tumor vascularity and survival in Group 3 medulloblastoma.

Methods: VEGFA mRNA expression from 546 patient samples identified significant elevation in Group 3. Group 3 xenografts were implanted intracranially in nude rats. Dynamic susceptibility weighted (DSC) MRI and susceptibility weighted imaging (SWI) MRI were obtained. To quantify tumor vascularity, DSC MRI was used to calculate relative cerebral blood volume (rCBV) and flow (rCBF). Tumor vessel density and rat VEGFA expression were determined.

Results: Xenografts D283, D341, and D425 were identified as Group 3 by RNA hierarchical clustering and MYC amplification. The D283 group had the lowest rCBV and rCBF, followed by D341, and D425 ($P < 0.05$). These values corresponded to relative histological vessel density ($P < 0.05$), rat VEGFA expression ($P < 0.05$), and survival ($P = 0.002$). Gene set enrichment analysis identified five putative genes with expression profiles corresponding with DSC MRI and protein expression values: RNH1, SCG2, VEGFA, AGGF1, and PROK2. SWI analysis blinded to xenograft type identified three novel classes of intratumoral vascular architecture with significantly distinct survival ($P = 0.004$): organized, diffuse microvascular, and heterogeneous.

Conclusion: Angiogenesis plays a critical role in overall survival in Group 3 medulloblastoma. DSC MRI and SWI MRI are both valid, clinically relevant biomarkers that accurately reflect tumor vascularity, predict overall survival, and can be used to direct the use of anti-vascular therapies for patients with Group 3 medulloblastoma.

946. Single-neuron correlates of error and conflict monitoring in the human medial frontal cortex

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Introduction: Human executive function relies on the ability to detect and compensate for errors. The error-related negativity (ERN) is an electrophysiological correlate of this process that has been localized to the anterior cingulate cortex by EEG source localization. However, how ERN and the error-monitoring mechanism it represents are reflected in the activity of single neurons remains unknown.

Methods: We used intracranial electroencephalography (iEEG) and single unit recordings to investigate error monitoring in human subjects. 24 epilepsy surgery candidates with implanted intracranial depth electrodes performed 71 sessions of a speeded version of a color-word Stroop task.

Results: Subjects showed robust Stroop interference effect (231.5 ± 22.7 ms, $F(1,76) = 103.6$, $p < 10^{-10}$, mixed-effect one-way ANOVA model with sessions as random effect). We isolated 290 neurons in the dorsal anterior cingulate cortex (dACC) and 323 in pre-supplementary motor area (pre-SMA). 27% of all dACC neurons and 40% of all pre-SMA neurons changed their firing rate immediately after subjects made an error, but before feedback was presented. The neuronal error signal in pre-SMA preceded that in dACC by 172ms. We also simultaneously recorded iEEG from macro electrodes. We identified robust intracranial error-related evoked potentials in both areas. These error-related potentials had a negative component with waveform and latency similar to classical studies of the ERN. Theta power of iEEG increased significantly more in error trials than in correct trials. Here we again found that iERN peaks in pre-SMA preceded those in dACC by 38ms.

Conclusion: The temporal patterns of the ERN and error-related neuronal activity, together with trial-by-trial correlations between ERN amplitude and firing rates in both dACC and pre-SMA, suggested that we have identified a single-neuron correlate of the well-known ERN. Our findings provided the first potential circuit-level mechanism for error monitoring and post-error adjustment in dACC and pre-SMA.

947. Folate Receptor Overexpression Can Be Visualized in Real Time During Pituitary Adenoma Endoscopic Transsphenoidal Surgery

Synthes Skull Base Award

John Y.K. Lee, MD, FAANS; Steve Cho; Ryan Zeh; John Pierce; Nithin Adappa; James Palmer; Kim Learned; Caitlin White; Julia Kharlip; Peter Snyder; Sunil Singhal, MD; Sean Grady (Philadelphia, PA)

Introduction: Transsphenoidal resection remains the primary treatment for many pituitary adenomas. Despite advances in endoscopy visualization, tumor recurrence is seen in up to 20% of surgeries. Because some pituitary adenomas overexpress folate receptor alpha (FRalpha), we hypothesized that a folate analog conjugated to a near infrared (NIR) fluorescent dye could provide increased optical contrast for margin detection. We present preliminary results of this novel clinical trial.

Methods: Nineteen adult patients with pituitary adenoma were enrolled in this pilot study and infused with OTL38 (On Target Laboratories, Indiana) prior to surgery. A VisionSense IridiumTM 4mm endoscope with visible light and NIR light sensor overlay was used to visualize neoplasm in real time. Signal-to-background-ratio (SBR) was calculated for all specimens at different endoscope-to-tissue distances. Immunohistochemistry allowed FRalpha quantification in the specimens.

Results: Data from 15 patients were analyzed for this preliminary analysis. Four patients were excluded for technical considerations. One patient was excluded from video analysis due to concurrent meningioma that interfered with accurate NIR measurement. Patients with strong FR overexpression (n=3) had OTL38 SBR=3.0±0.29 versus SBR=1.6±0.43 for low FR expressing tumors (n=11). The endoscope distance critically affects SBR, demonstrating the need to keep the endoscope at an appropriate distance from the sella. In the three patients with FR overexpression, NIR imaging demonstrated perfect classification of tumor with 100% sensitivity and specificity.

Conclusion: Pituitary adenomas and margins can be visualized real time inside the operating room with preoperative injection of OTL38, a folate analog conjugated to NIR dye. Optical contrast is stronger for FRalpha overexpressing tumors, primarily seen in non-secretory adenomas. Intraoperative quantification of SBR can predict FRalpha overexpression if the endoscope is held at an appropriate distance. Fluorescent-guided pituitary adenoma surgery using folate targeting is promising but remains investigational. Future work will focus on non-functional adenomas and optimization of imaging parameters.

948. Neuronal mechanisms of cognitive control in human prefrontal cortex

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Introduction: Our daily lives require monitoring our environment, attending to relevant information, ignoring irrelevant information, and optimizing future behavior based on previous outcomes. These cognitive control processes arise from prefrontal cortical areas including dorsal anterior cingulate cortex (dACC) and dorsolateral prefrontal cortex (dlPFC).

Methods: We recorded single neuron activity and local field potentials from neurosurgical patients (DBS, N=8; epilepsy, N=7). Patients performed a Stroop-like cognitive interference task with varying levels of difficulty across trials. We used a general linear model to classify neuronal firing, conditional mutual information (CMI) techniques to study information transfer between dACC and dlPFC, and spike-field coherence to understand interactions between single neuron and population activity.

Results: We recorded 138 neurons in dACC and 366 neurons in dlPFC. We identified firing rate coding of task difficulty in both dACC (10% of neurons) and dlPFC (11%). CMI analysis showed direction-specific information

transfer from dACC to dlPFC using theta (4-7Hz) range oscillations. dlPFC neurons also showed temporal coding of task difficulty (not seen in dACC), as measured by phase coherence between spike timing and theta oscillations. Mutual information analysis of <100 simultaneously recorded neuron pairs showed increased spike timing coincidence with task difficulty.

Conclusion: Conversion of rate encoding (dACC) to temporal encoding (dlPFC), not previously seen in humans, is an attractive mechanism for information distribution. These results support a model in which dACC generates a control signal indicating the need for cognitive resources that passes to dlPFC, which allocates resources and regulates downstream behavior.

949. Genetic Abnormalities Correlate with Histological Subtypes of Medulloblastoma – Searching for Therapeutic Targets and Predicting Metastatic Potential

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Introduction: Medulloblastoma (MB) is the most common primary pediatric malignant brain tumor, which presents with profound molecular heterogeneity. Genetic classification and distinct histologic subtypes defines MB into 4 groups: classic (WNT), sonic hedgehog (Shh), group 3 and group 4. Here, we defined specific immunohistological markers, their correlation with the amplification of the oncogene MYC and abnormalities in tumor suppressor gene p53, and their association with metastatic potential.

Methods: IRB approved MB tumors (n=41) were used to evaluate the expression of glioma transcription factor 1 (GLI-1), Grb2-associated binding protein 1 (GAB-1), natriuretic peptide receptor (NPR), voltage-gated potassium channel (KV1), and mutant p53. FISH analysis was done to determine MYC amplification or iso-P53. p53-mutant MB cell line was used to investigate the signaling pathway leading to proliferation, migration, and drug resistance using HDAC (LBH-589) and PI3K/mTOR (BKM-120/rapamycin) inhibitors.

Results: GAB-1 was highly expressed in the Shh group (82%) and KV1 expression was evenly distributed in all subtypes. No obvious correlation with expression of GLI-1, GAB-1, NPR and KV1 with metastasis was found. Analysis of loss of p53 expression and overexpression of MYC varied in each histological subtype. MB cells were resistant to BKM-120 treatment, while LBH-589 caused massive apoptosis. Combined treatment with LBH-589 and BKM-120 reduced cell proliferation, migration, S-phase entry, and tumor formation.

Conclusion: The expression of GLI-1, GAB-1, NPR, KV1 and p53 was important in defining the histological subgroups of MB, however their expression did not correlate with metastatic potential. Cotreatment of MB cells with HDAC inhibitor LBH-589 and PI3K inhibitor BKM-120 synergistically resulted in reduced cell proliferation, cell cycle entry, migration, and tumor formation.

950. DBS of the Bed Nucleus of Stria Terminalis (BNST) for Major Depression

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Introduction: Deep brain stimulation (DBS) is sometimes used to treat depression, however the optimal target and long term outcomes are unclear. We evaluated intraoperative responses and long-term outcomes following DBS of the bed nucleus of stria terminalis (BNST) for treatment-resistant major depression.

Methods: Five females (age 27-60 yrs) with intractable major depression of at least several years duration underwent surgery.

Approval was obtained from the Victorian Psychosurgery Review Board and our Institutional Ethics Committee. Medtronic 3389 electrodes were

implanted bilaterally in the BNST under local anaesthesia. Intraoperative stimulation responses were recorded. Mean follow up was 23 months (12-36 months).

Results: Positive and negative mood effects could be induced intra-operatively. There was a trend for more beneficial DBS-related effects at the more proximal electrodes, and more negative effects with distal stimulation. The pattern varied markedly between patients. Outcomes: At follow up, 2 patients (40%) were in remission, one had a $\geq 50\%$ response, and two had a $< 50\%$ response. Mean reduction in Hamilton Depression Rating Scale-17 was 64% (range 22-97%). Mean improvement in quality of life (Quality of Life Enjoyment and Satisfaction Questionnaire Short Form) was 73% (range 25-110%).

Conclusion: BNST DBS can induce acute intraoperative mood changes and long term clinical improvements in medically refractory major depression. The BNST appears to be a promising DBS target for treatment-resistant depression, and warrants further investigation.

951. Development of Augmented Reality-Based Neuro-Navigation System for use in External Ventricular Drain Placement

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Introduction: Augmented Reality (AR) enhances our reality with the use of computer generated overlays on our physical surroundings. We developed a system that utilizes AR to assist with placement of external ventricular drains (EVD) through interactive 3-dimensional (3D) holograms. The system builds a hologram of the ventricles, displays it on the patient, and provides navigational aids for placing the catheter. The overlay is presented through AR glasses, giving the user the ability to virtually navigate in real-time.

Methods: Software was developed using Unity Technologies' Unity 3D Engine for use on the Microsoft HoloLens.

Results: The software utilizes a head CT scan to generate a 3D hologram of the ventricular system. The hologram and CT scan data can be manipulated without breaking sterility through the use of hand gestures. The software uses fiducials to correctly fuse the hologram to the patient. Once aligned, the user can begin the procedure. The EVD catheter is then detected by the glasses. A hologram of the catheter is generated and aligned to the real catheter. Navigational aids display near the entry site to guide catheter placement. The catheter hologram serves as a visual guide to see in real time the position of the intracranial portion of the catheter.

Conclusion: To our knowledge, this is the first description of the use of Microsoft HoloLens for a neurosurgical procedure. We describe an AR navigation system that has the potential to change the way we perform neurosurgical procedures.

952. Purification and Characterization of Primary Human Glioblastoma Astrocytes

Melanie Hayden Gephart, MD; Ye Zhang; Steven Sloan; Ben Barres (Stanford, CA)

Introduction: Astrocytes play key roles in brain development and disease. The gene expression profile of glioblastoma astrocytes compared to resting, human mature and fetal astrocytes has not been previously ascertained due to challenges in brain cell dissociation, acute purification, and maintenance in chemically defined culture conditions. We developed an immunopanning method to acutely purify astrocytes from primary human glioblastoma and maintain these cells in serum-free cultures. This allowed us to determine the functional and molecular similarities and distinctions between fetal and glioblastoma astrocytes, as well as other brain cell-type (neurons, endothelial, oligodendroglia, microglia/macrophages).

Methods: We acutely purified glioblastoma, matched peritumoral brain, and normal astrocytes using an immunopanning-based technique that utilizes an antibody targeted against HepaCAM (or GlialCAM), and performed transcriptome profiling. Previous cell sorting and culture techniques kill the

primary brain cells quickly, lead to reactive states, are contaminated with other cell types, can only be done on fetal rodent cells, or require serum for in vitro survival. We compared the transcriptome of glioblastoma astrocytes to normal mature and fetal astrocytes, with our user-friendly, searchable, online database (<http://www.brainrnaseq.org>).

Results: Once isolated, we found our astrocytes were minimally reactive, highly pure, and could be maintained in primary cell culture with serum-free media. The RNA sequencing profiles identified novel human-specific glioblastoma astrocyte genes that overlapped with human fetal astrocytes. Our database allows for comparisons of astrocytes that reside within normal fetal and mature brain, within a glioblastoma, and surrounding glioblastoma.

953. Stereotactic Laser Amygdalohippocampotomy for Pharmacoresistant Mesial Temporal Lobe Epilepsy: One-Year Outcomes in a Large Series

Matthew A. Stern, BS; Jon Willie, MD, PhD; Daniel Drane, PhD; Rebecca Fasano, MD; Amit Saindane, MD; Bruno Soares, MD; Robert Gross, MD, PhD; Nigel Pedersen, MBBS (Atlanta, GA)

Introduction: Stereotactic laser amygdalohippocampotomy (SLAH) is a less invasive alternative to open resections for pharmacoresistant mesial temporal lobe epilepsy (MTLE), specifically anterior temporal lobectomy (ATL) and selective amygdalohippocampotomy (SAH). Whereas small series have demonstrated promising short-term outcomes, a large series with 12-month seizure outcomes is required for comparison to open resections, the gold standard of surgical treatment for MTLE. Here we present the largest such series from a single high volume center.

Methods: All MTLE patients (N=47) that underwent SLAH with follow-up of ≥ 12 months were included. 12-month seizure freedom results were retrospectively analyzed as a modified non-inferiority trial comparing SLAH to open procedures. A select subgroup of MTLE patients with mesial temporal sclerosis (MTS) was similarly analyzed.

Results: 44.7% (95% CI $\pm 14.8\%$) of all patients, and 59.3% (95% CI $\pm 19.8\%$) with MTS were seizure free for ≥ 12 months following one ablative procedure. Five of 9 patients not seizure free were determined to have incomplete ablations and underwent repeat ablation yielding 12-month seizure freedom rates of 53.2% (95% CI $\pm 14.8\%$) for all patients and 63.0% (95% CI $\pm 19.4\%$) for MTS patients. These outcomes were superior to the threshold at which SLAH achieves higher quality adjusted life years than ATL (43%), as determined from a recent threshold analysis, and non-inferior to the SAH seizure freedom rate (67%), as determined from a recent meta-analysis. Complications were minimal, with 4 postoperative visual field deficits, one of which was transient, 2 hemorrhages, both without persistent deficit, and 3 cranial nerve palsies, all of which were transient.

Conclusion: Our results demonstrate that SLAH is non-inferior to open resection with respect to 12-month seizure freedom, with greater seizure freedom in the MTS group, consistent with open resection. Thus our results support SLAH as a non-inferior and minimally invasive alternative to open resection for patients with MTLE.

954. The Effects of Age Following Traumatic Brain Injury: Characteristics at Presentation and Risk Factors for Unfavorable Outcome

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Introduction: Age-related differences may complicate the road to recovery following traumatic brain injury (TBI), leading to disparate recovery profiles across subpopulations.

Methods: We utilize the Transforming Research and Clinical Knowledge in Traumatic Brain Injury Pilot (TRACK-TBI Pilot) study to characterize young-adults (18-40), middle-aged (41-64) and elderly (≥ 65 -years) following acute TBI. Multivariable multinomial regression was performed for

patients completing 3-month Glasgow Outcome Scale Extended (GOSE), a measure of global functional outcome, to determine predictors of severe disability/death (GOSE 1-4), moderate disability (5-6) and good recovery (7-8). Odds ratios (OR) and 95% confidence intervals are reported.

Results: In 422 patients, (young-adult=47.8%, middle-aged=41.7%, elderly=10.5%), falls predominated middle-aged and elderly injuries (50.3%/69.2%-vs.-36.6%; $p<0.001$). The elderly showed decreased propensity for loss of consciousness (LOC; 36.9%-vs.-54.0%/56.7%; $p=0.003$) and post-traumatic amnesia (PTA; 30.7%-vs.-55.7%/41.1%; $p=0.008$), and lower incidence of prior TBI (23.1%-vs.-46.4%/54.6%; $p<0.001$). Age associated with intracranial CT pathology (38.1%, 45.4%, 61.5%, $p<0.001$). Elderly patients were more likely to admit to ICU (47.7%-vs.-38.1%/32.5%; $p<0.001$) and less likely to be discharged home (16.9%-vs.-35.1%/25.2%; $p=0.001$). On multivariable regression, middle-age (OR=4.86 [2.52-9.37]), intracranial pathology (OR=2.51 [1.19-5.29]), and psychiatric history (OR=2.27 [1.27-4.12]) predicted moderate disability over good recovery. Middle-age (OR=5.04 [1.61-15.73]) and elderly (OR=5.38 [1.10,26.27]), moderate/severe TBI (OR=13.38 [3.77-47.48]), polytrauma (OR=4.07 [1.49-11.16]) and history of endocrine (OR=5.84 [2.09-16.31]) or ear, nose and throat (OR=3.89 [1.25-12.09]) illnesses predicted severe disability/death over good recovery.

Conclusion: Elderly patients demonstrate lower rates of prior TBI, LOC and PTA, and higher rates of CT pathology and ICU admissions following TBI. At 3-months postinjury, middle-aged and elderly patients experience elevated risk for severe disability and/or death compared to young-adults.

955. Trends in Upper Extremity Nerve Injury using the National Inpatient Sample Database

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Introduction: Peripheral nerve injury can be underappreciated in patients with polytraumatic injuries. We sought to understand trends in upper extremity nerve injuries, treatments and costs.

Methods: Patients with upper extremity (UE) nerve injury from 2001-2002 and 2011-2012 were compared using the National Inpatient Sample. Patients with either brachial plexus or upper extremity nerve injuries were included. Patient demographics, hospital characteristics, associated diagnoses, treatments, and disposition were evaluated and compared between periods.

Results: A total of 5444 and 4572 patients from the early and late years were characterized, respectively, representing a decrease in incidence (356/1,000,000 vs 298/1,000,000 $p<0.001$). Demographically, the later epoch was older (36.9 ± 18.5 vs. 39.9 ± 19.5 , $p<0.001$) years but similar genders (74.2 vs. 73.1% male). Most patients were admitted with trauma designation. 30.3% of patients had damage to a main artery in the UE and 39.5% of patients had an open wound with visible tendon involvement. Treatment of the nerve injury did not statistically differ between epochs for nerve transposition (1.9 vs. 2.6%, $p=0.53$), nerve decompression (3.9 vs. 5.5%, $p=0.24$), nerve suturing (40.3 vs. 35.4%, $p=0.11$), or other neuroplasty (7.9 vs. 6.4%, $p=0.4$). There was a significant increase in nerve grafts (0.7 vs. 5.3%, $p=0.0001$) for later years. Discharge disposition to home or self-care was significantly lower in later years (81.9 vs. 50.1%, $p=0.0001$). Charges were significantly increased in the later epoch (\$26,426 $\pm$ 67,792 vs. \$70,051 $\pm$ 103,480 $p<0.05$).

Conclusion: While the incidence of UE peripheral nerve injury seems to have decreased, the use of nerve graft procedures has increased - suggesting a trend towards higher level reconstructive approaches on a national scale. With majority of cases being referred to large teaching hospitals, peripheral nerve injury should be included within residents' curricula to help improve outcomes via recognition, referral, and primary treatment.

956. Seizure suppression by opto-chemogenetic inhibition in multiple nodes of an epileptic network with chemically-activated luminopsins

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Introduction: Seizure activity can propagate throughout the brain and this distributed nature of pathological brain activity presents a challenge for treatments. Current treatments with either clinical electrical stimulation or experimental optogenetic photostimulation are in principle focal and may not be the most effective. To address this challenge, we have pioneered genetically-encoded opto-chemogenetic probes (luminopsins) that can manipulate neuronal activity in multiple nodes within an epileptic network via a diffusible chemical substrate.

Methods: Rats were bilaterally injected with adeno-associated virus expressing inhibitory luminopsin - ILMO2 - into the dentate gyrus (DG), the anterior nucleus of thalamus (ANT) or both. Seizures were induced by systemic injection of pentylenetetrazol. Seizure duration and intensity were quantified following administration of the ILMO2 activator, coelenterazine (CTZ), or control vehicle.

Results: CTZ administration in rats with ILMO2 in the DG showed a significant decrease only in seizure duration but not in mortality, latency to first twitch or Racine score, whereas rats with ILMO2 in the ANT showed a decrease in mortality, increase in latency to first twitch, and decrease in seizure duration ($*p<0.05$). Interestingly, more robust effects were observed in rats with ILMO2 in both the DG and the ANT, in which there was a significant ($*p<0.03$) decrease in seizure severity (Racine score) in addition to decreases in mortality and duration, and increase in latency.

Conclusion: Simultaneous bilateral opto-chemogenetic inhibition of both the DG and the ANT was more effective at suppressing seizure than inhibition of either structure alone. This work not only elucidates mechanisms of seizure suppression never directly demonstrated before, but also illustrates how multi-focal control of pathological circuits can be advantageous for the treatment of epilepsy, which may also be applicable to the treatment of other neurological disorders involving broad neural circuits.

957. Factors Predicting Inadequate Hematoma Evacuation and Recurrence in Chronic Subdural Hematoma

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Introduction: Chronic subdural hematoma (CSDH) is a disease commonly encountered by neurosurgeons. However, the optimal surgical technique has not been determined. In the current study, we evaluated the prognostic value of preoperative and intraoperative characteristics on CSDH outcome (including incomplete evacuation needing repeat surgery) and recurrence.

Methods: We conducted a retrospective study on 540 CSDH patients admitted to Beth Israel Deaconess Medical Center from 2007 till 2016.

Results: Analysis showed that hematoma density in CT (higher recurrence in mixed hyper and hypodensity), membrane formation, loculation, midline shift, midline shift to hematoma diameter ratio, percent hematoma change after surgery (post-operative relative to preoperative hematoma maximal diameter) and drain size significantly influenced inadequate evacuation and recurrence (all p values < 0.05), while gender, age, trauma history, comorbidity, anticoagulant use, initial GCS, initial modified Rankin Scale, neurologic deficit, hematoma side, hematoma MRI intensity, hematoma diameter before surgery, hematoma location, presence of considerable air in postoperative, surgical technique (burr craniostomy vs. craniotomy), number of burrs, burr location, and irrigation volume had no effect. Probit analysis showed that 0%, 17%, and 90% decrease in hematoma diameter after surgery are associated with a 62%, 50%, and 10% risk of need for repeat surgery, respectively.

Conclusion: Among many factors, membrane formation, CT density, loculation, midline shift, percent hematoma change, and drain size were the strongest predictors of inadequate evacuation or recurrence needing repeat surgery.

958. Immune Checkpoint Protein PD-L1 Induces Glioma-Associated Regulatory T Cell Expansion

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Introduction: Glioblastoma (GBM) is well equipped to escape immune surveillance through induced suppression of the patient immune response. Several mechanisms are believed to be involved, including the expression of immunosuppressive ligands and the involvement of immunosuppressive regulatory T cells (Tregs). Here, we investigate the role of the immunosuppressive ligand, PD-L1, in expanding the Treg subset.

Methods: RNAseq mRNA expression data for GBM patients was extracted from The Cancer Genome Atlas (TCGA) database and evaluated for a relationship of CD274 (PD-L1) with independent Treg markers (CD25, FOXP3). Healthy control lymphocytes were separated from peripheral blood mononuclear cells and activated with an anti-CD23/CD28 tetrameric complex. Cells were incubated for 3 days, with and without co-stimulation with recombinant human PD-L1 (rhPD-L1). On day 3, the lymphocytic phenotype and Treg fraction (CD4+CD25+FoxP3+), as well as the expression of cell surface immune-checkpoint proteins, were analyzed by flow cytometry.

Results: PD-L1 mRNA expression from TCGA tumor samples (n=166) positively correlated with expression of CD25 and FoxP3 ($P=0.0003$ and $P=0.0079$, respectively). Activation of healthy control lymphocytes and co-stimulation with 100ng/mL rhPD-L1 led to expansion of the Treg subset compared to activation alone (38.8% vs. 12.0%, $P=0.002$) or anti-IgG control (38.8% vs. 17.3%, $P=0.023$). Evaluation of immune checkpoint proteins demonstrated upregulation of PD-1 on Tregs with rhPD-L1 stimulation compared to activation alone (58.2% vs. 30.4%, $P=0.004$).

Conclusion: PD-L1 has been well documented for its role in glioma-associated immunosuppression, capable of inducing apoptosis of PD-1-expressing, tumor-directed cytotoxic T cells. We demonstrate, however, that PD-L1 has the potential to also expand the Treg subset. Along with the finding that PD-L1 expression correlates with expression of Treg markers in GBM, this data suggests a paradoxically stimulatory effect of PD-L1 on immunosuppressive T cells. Therefore, for GBM patients with an elevated peripheral or intratumoral Treg fraction, PD-L1 blockade may provide a survival benefit.

959. Pathologic Organization of Laminin in Regeneration after Human Peripheral Nerve Injury

Michael Karsy, MD, PhD; Cheryl Palmer, MD; Mark Mahan, MD (Salt Lake City, UT)

Introduction: Laminins are a family of extracellular matrix proteins which participate in the formation of endoneurial tubes and are important in regeneration and repair of nerves. They act as scaffolds to guide nerves to distal targets, and play a key role in neurite outgrowth. There is evidence that laminin architecture affects nerve regeneration, and we sought to examine the pattern of laminin structure in clinical samples from nerve injury patients.

Methods: A retrospective review of 8 nerve injury cases was performed evaluating neuroma histology in relationship to clinical history and injury type. Immunohistochemical delineation of laminin structure in relationship to neuromas was performed.

Results: Five cases of upper trunk injuries, four from childbirth injury and one from a motorcycle accident were examined. Avulsed nerves demonstrated no neuroma formation with linear laminin architecture, fibrotic deposition and regular Schwann cell arrangement. In regenerative neuromas, laminin immunohistochemistry demonstrated a double lumen laminin tubule, with encapsulation of Schwann cells and axonal processes.

Neonatal stretch injuries displayed significantly greater disorganized regeneration compared to adult stretch injuries. Similarly, three cases of nerve laceration, including two iatrogenic and one occupational injury, demonstrated similar double-lumen laminin tubule, but less severe fibrosis.

Conclusions: In nerve injuries with regenerative capacity, basal lamina tubes become pathologically disorganized. A double-lumen laminin tubule develops, which may be related frustrated regeneration. The appearance of the abnormal channels suggests paired pathology between axon migration and Schwann cell remodeling of fiber architecture. Further exploration of this feature may aid in the generation of novel modes of treatment.

960. Role of hippocampus in human memory redefined: Evidence from stereotactic laser amygdalohippocampotomy

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Introduction: Stereotactic laser amygdalohippocampotomy (SLAH) is a novel highly selective ablative neurosurgical procedure for mesial temporal lobe epilepsy. While significant memory declines occur in epilepsy patients undergoing open temporal lobe resection, we predicted better memory outcome with SLAH, which preserves more neural networks while still ablating the presumed epileptogenic zone.

Methods: We compared verbal and visual memory changes in 30 temporal lobe epilepsy patients after antero-medial temporal lobectomy with 30 analogous patients after SLAH.

Results: Language dominant hemisphere lobectomy was more associated with verbal memory decline versus SLAH [13/16 (81.3%) vs. 5/16 (31.3%), respectively; $p<0.05$, Fisher's exact test]. Verbal and visual memory were more likely to improve after SLAH independent of hemisphere. Verbal memory was more likely to decline in SLAH patients only when additional temporal lobe pathology was already present (e.g. ipsilateral dual pathology). Significant verbal memory decline occurred in lobectomy patients with mesial temporal sclerosis, but rarely occurred in analogous SLAH patients unless additional extrahippocampal temporal lobe pathology was evident. There was a trend for a greater decline in visual memory in open resection patients than in those receiving SLAH [15/30 (50.0%) vs. 9/30 (30.0%), n.s., Fisher's exact test]. Visual memory declined regardless of side of surgery, but was more common when the unoperated hippocampus was abnormal by neuroimaging regardless of surgical approach.

Conclusion: These findings suggest the hippocampus to be less essential for effective verbal memory processing than for visual memory processing, with the latter function represented bilaterally. Laser ablation results in better memory outcome by reducing collateral extrahippocampal surgical damage.

961. Vitamin D Status and Three-Month Glasgow Outcome Scale Scores in Neurocritical Care Patients: A Prospective Analysis of 497 Patients

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Introduction: Vitamin D deficiency has been associated with a variety of negative outcomes in critically ill patients, but there remains little focused study on the effects of hypovitaminosis D in the neurocritical care population. The authors examined the impact of vitamin D deficiency on 3-month outcomes after discharge from the neurocritical care unit.

Methods: The authors prospectively collected 25-hydroxy vitamin D levels on patients admitted to the neurocritical care unit (NCCU) of a quaternary-care center over a 6-month period. Glasgow Outcome Scale (GOS) scores were used to evaluate 3-month outcomes, with univariate and multivariate logistic regression used to evaluate the effects of vitamin D deficiency.

Results: Four hundred ninety-seven patients met the inclusion criteria. In the binomial logistic regression model, patients without vitamin D deficiency (<20 ng/dl) were significantly more likely to have a 3-month GOS of 4 or 5 compared with those who were deficient (OR 1.768, 95% CI 1.095-2.852). Patients with higher Simplified Acute Physiology Scores (SAPS II) (OR 9.25, 95% CI 0.910-0.940) and those admitted for stroke (OR 0.409, 95% CI 0.209-0.803) or "other" diagnoses (OR 0.409, 95% CI 0.217-0.772) were significantly more likely to have a 3-month GOS of 3 or less.

Conclusion: Vitamin D deficiency is associated with worse 3-month post discharge GOS scores in patients admitted to the NCCU. Further study is indicated to determine the role of vitamin D supplementation in the NCCU population.

962. Targeted Sequencing Reveals Clinically-Actionably Mutations in Skull Base Meningiomas

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Introduction: Recently discovered non-NF2 oncogenic drivers, such as SMO and AKT1 activating mutations, may be the key to targeted therapies for skull base meningiomas (SBM). Vismodegib and afuresertib inhibit SMO and AKT1, respectively, and are currently under evaluation in a national Phase II study of progressive or recurrent meningiomas (NCT02523014). In this study, we sought to analyze the frequency, clinical characteristics, and outcomes associated with SMO and AKT1 mutations in posterior SBM.

Methods: We performed targeted sequencing of 160 known cancer drivers in a cohort of 75 WHO grade I and II posterior SBM to better define the frequency of SMO, AKT, and other clinically actionable mutations in these tumors, which we correlated with clinical and survival data.

Results: We confirmed a high prevalence of NF2 mutations, which were present in 40% of our cohort. Moreover, 8% had AKT1 E17K mutations. In these mutant tumors, no statistically significant changes in overall survival or progression-free survival were observed. Notably, there were no posterior SBM with oncogenic SMO mutations that have been described in anterior SBM. Additional known cancer-associated genes including CREBBP, PTEN, PIK3K, and MTOR.

Conclusion: Meningiomas with clinically-actionable AKT1 mutations comprise a significant portion of posterior SBM. In addition, other known cancer associated genes are also clearly implicated in their etiology, and inhibitors in these pathways also exist. Interestingly, no posterior skull base tumors had SMO mutations, which strengthens the theory that SMO mutations are confined to the anterior skull base. This highlights the role of SMO in craniofacial patterning, as part of the SHH pathway. Overall, the identification of AKT1 and other targetable mutations in meningiomas of this surgically challenging area of the skull base will be the first step in developing early treatment with AKT1-inhibitors and provide options for patients who fail standard therapy.

963. Anti-Apoptotic Effect of G-CSF on Spinal α -motoneurons after Traumatic Nerve Lesion

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Introduction: Granulocyte-colony stimulating growth factor (G-CSF) has been observed to have direct protective effects on neurons after stroke in experimental models and in humans. In this study, possible anti-apoptotic effects of G-CSF on α -motoneurons were evaluated after traumatic nerve lesion of the sciatic nerve in a rat model.

Methods: The right sciatic nerve in 48 rats was lesioned. Twenty-four animals were treated with G-CSF and 24 animals were treated with intravenous glucose 5%-solution serving as control group. Lumbar spinal cord sections of 6 animals of each group were removed at day 1, 4, 7

and 14. α -motoneurons of both sides were investigated for expression of Choline-Acetyltransferase (ChAT), G-CSF receptor (G-CSFR), and Bcl-2 and Bax. To proof evidence of anti-apoptotic effects within α -motoneurons, fluorescence double-staining was performed for ChAT/Bcl-2, ChAT/Bax and ChAT/G-CSFR.

Results: Counting of α -motoneurons revealed a significantly smaller number of ChAT-stained motoneurons on the lesioned side only in animals of the control group from day 1 to day 14 ($p < 0.05$). Numbers of α -motoneurons in G-CSF-treated rats were equal. Bcl-2 and G-CSFR-expression on the lesioned side of the control group was significantly less ($p < 0.05$) whereas Bax-expression was significantly higher ($p < 0.05$). Double-staining in motoneurons was positive for ChAT/Bcl-2, ChAT/Bax and for ChAT/G-CSFR.

Conclusion: The application of G-CSF after traumatic nerve lesion seems to have a strong neuroprotective effect in α -motoneurons. The number of motoneurons in animals of the control group was decreased whereas no difference was observed in animals treated with G-CSF. Concordantly, apoptotic effects were shown by decreased Bcl-2 expression and an increased Bax-expression in motoneurons of animals treated with G-CSF-solution instead of G-CSF. These results indicate that the application of G-CSF contributes to anti-apoptotic effects after peripheral traumatic nerve lesion.

964. A Novel Technique to Optimize Microelectrode Recording Accuracy in DBS Surgery using Intraoperative CT

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Introduction: Microelectrode recording (MER) is used to evaluate electrophysiological signals within the intended anatomic target during deep brain stimulation (DBS) surgery. We have described a novel technique called intraoperative CT-guided extrapolation (iCTE) which aims to improve MER targeting accuracy. We now investigate whether this technique can reduce the number of MER tracks, increase the length of recorded STN, and reduce operative time.

Methods: Prior to dural opening, a guide tube was inserted through the headstage and rested on dura. Intraoperative CT (iCT) was obtained, and a trajectory was created along the path of the guide tube using targeting software. The trajectory was extrapolated to target depth and the coordinates recorded and compared to the initial plan targeting the dorsolateral subthalamic nucleus (STN). If needed, adjustments were made using the head stage to correct for error. The guide tube was then inserted and MER ensued. At target, iCT was performed and microelectrode tip coordinates were compared with the planned/adjusted track coordinates. Radial error between MER track and planned/adjusted track was then calculated. We compared cases before and after implementation of iCTE to determine the impact of this technique on operative time, number of MER tracks and length of recorded STN.

Results: Thirty-nine patients with Parkinson's disease who underwent STN DBS prior to iCTE were retrospectively reviewed and compared to 33 STN DBS surgeries in which iCTE was utilized. The iCTE technique significantly ($p < 0.001$) reduced average radial MER track error from 1.90 ± 0.12 mm ($n=54$) to 0.84 ± 0.09 mm ($n=49$) while also significantly ($p < 0.001$) reducing operative time for bilateral lead placement from 272 ± 9 min ($n=30$) to 233 ± 10 min ($n=24$). The average number of MER tracks per hemisphere was also significantly ($p < 0.001$) reduced from 2.24 ± 0.13 mm ($n=66$) to 1.75 ± 0.09 mm ($n=63$) while average length of recorded STN was significantly ($p < 0.05$) increased from 4.01 ± 0.3 mm ($n=64$) to 4.75 ± 0.28 mm ($n=56$).

Conclusion: The iCTE technique improves MER targeting accuracy thus improving the efficiency and quality of MER-based DBS surgery through a reduction of operative time and MER tracks while increasing the length of recorded STN.

965. CSF Cytokine Profile of Patients with Post-Traumatic Hydrocephalus Following Severe Traumatic Brain Injury

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Introduction: Post-traumatic hydrocephalus (PTH) is an important cause of morbidity following severe traumatic brain injury (sTBI). Early diagnosis and treatment of PTH is critical to maximizing neurological outcomes and reducing hospitalizations. We hypothesized that inflammation following TBI may contribute to the pathogenesis of PTH and thus aid in identifying patients at risk.

Methods: Twenty-five sTBI patients with PTH were matched by age, sex and GCS with twenty-five patients without PTH. All patients suffered a sTBI and were treated with continuous CSF drainage via an EVD in the ICU. CSF cultures, cell count, glucose and protein were monitored daily. CSF was banked at post trauma days 1, 3 and 5 for analysis via Luminex Array scanner. CSF concentration of 36 inflammatory markers were determined at each time point.

Results: No significant difference in age, sex, GCS, CSF RBC, WBC or protein was found between groups. Across all time points IL-15 ($p=0.007$), IL-5 ($p=0.038$) and CX3CL1 ($p=0.031$) were significantly lower in PTH patients. CCL4 was significantly higher in the PTH group ($p=0.029$). IL-2 levels increased at a significantly slower rate in patients with PTH ($p=0.037$). No other statistically significant differences were found.

Conclusions: Lower levels of IL-15 and IL-5 suggest a decrease in the recruitment and proliferation of both NK and T cells as well as B-cells and eosinophils in PTH. High levels of CCL4 in PTH patients may indicate a more macrophage rich environment. A slower increase in IL-2 may be indicative of a global impairment of immune function including T cell function and differentiation. Overall, our data suggests that immune dysfunction in patients who develop PTH may impede clearing of debris following sTBI. Further study will require a larger cohort and correlation with CSF immune cell populations as well as establishing normative values for CSF cytokines in the general population.

966. Downregulation of sphingosine-1-phosphate receptor type 1 mediates T-cell sequestration in bone marrow amidst glioblastoma

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Introduction: Glioblastoma (GBM) proves one of the most immunosuppressive solid tumors, limiting efficacy for immune-based interventions. We have previously described lymphopenia, systemic T-cell dysfunction, and lymphoid organ retraction in treatment-naïve patients with GBM. Furthermore, we have demonstrated that missing T-cells are sequestered in large numbers in the bone marrow (BM) in both patients and mice. Here we investigate the role of the sphingosine-1-phosphate receptor type 1 (S1P1) in mediating BM T-cell sequestration. S1P1 normally permits T-cell exit from spleen, thymus, and lymph node, but can control egress from BM in alymphoplastic mice lacking these lymphoid organs, as seen with GBM.

Methods: Wildtype and S1P1 knocked-in murine models of intracranial and subcutaneous tumors were established. T-cells from lymphoid organs were harvested, labeled with relevant antibodies, and analyzed by flow cytometry. For adoptive transfer studies, T-cells from donors were labeled with CFSE and injected intravenously.

Results: BM-sequestered T-cells showed decreased surface S1P1 expression in GBM (4.38%) compared to controls (19.66%) ($p<0.0001$). Interestingly, sequestration characterized not only GBM, but various other malignancies (lung, melanoma, and breast), although only when tumors were situated intracranially. A strong inverse relationship was observed between T-cell S1P1 levels and T-cell counts in BM across all tumor models ($r=-0.65$; $p<0.0001$). Forced S1P1 loss on T-cells was sufficient to elicit their rapid sequestration in GBM-bearing mice, while mice knocked-in for stabilized T-cell S1P1 demonstrated abrogated sequestration. Reversing

sequestration alone elicited increased numbers of activated tumor-infiltrating lymphocytes and a long-term survival rate of 15%, with long-term survivors universally rejecting intracranial re-challenge with tumor.

Conclusion: Our findings suggest the existence of brain-specific mechanisms for down-regulating S1P1 and preventing T-cell entry into the CNS, mechanisms that are usurped by tumors of the intracranial compartment to maintain T-cell sequestration and ignorance. Reversal of such sequestration is anticipated as a promising immunotherapeutic adjunct.

967. First Human Experience with Autologous Schwann Cells to Supplement Sciatic Nerve Repair: Long-term Follow-up in Two Cases

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Introduction: Long-segment injuries to large peripheral nerves present a challenge to surgeons as insufficient donor tissue limits repair. Multiple supplemental approaches have been investigated including the use of Schwann Cells (SCs). We present the first two cases using autologous SCs to supplement a peripheral nerve graft in humans with long-term follow up data.

Methods: Two patients selected with long-segment injury to sciatic nerve (Sunderland Grade V). One from propeller injury (A) and another a bullet wound (B). FDA approval attained using expanded access. SCs obtained from sural nerve and damaged sciatic nerve stump. SCs expanded and purified in culture using heregulin $\beta 1$ and forskolin. Repair carried out with sural nerve grafts, SCs in suspension, and a Duragen graft to house the construct. Follow-up was 12 and 36 months for patients A and B, respectively.

Results: Patient A had a boat propeller injury with complete transection of both sciatic divisions at mid-thigh. Graft length was approximately 7.5 cm. In the postoperative period the patient regained motor (4+/5) function in the tibial distribution with partial function in peroneal distribution (2/5 on dorsiflexion). Partial return of sensory function was also achieved.

Neuropathic pain was completely resolved. Patient B sustained a gunshot wound to the leg with complete disruption of the tibial division of sciatic nerve at the mid-thigh. Graft length was 4 cm. Postoperatively the patient regained complete motor function of the tibial nerve with partial return of sensation. Neuropathic pain was manageable. MR and ultrasound demonstrating continuity and absence of tumor. **Conclusion:** Presented here are the first two cases using autologous SCs to supplement human peripheral nerve repair in long-segment injury. Both patients had significant improvement in both motor and sensory function with correlative imaging. This study demonstrates safety and efficacy of SC transplantation for peripheral nerve repair.

968. Persistent Neuronal Activity in Medial Temporal Lobe and Medial Frontal Cortex Supports Short-Term Memory

Jan Kaminski; Shannon Sullivan; Jeffrey Chung; Ian Ross; Adam Mamelak; Ueli Rutishauser (Los Angeles, CA)

Introduction: The predominant models of short-term memory (STM) postulate that in the absence of external stimuli, memoranda are maintained by persistent neuronal activity. Theoretical work, animal experiments and non-invasive imaging in humans supports this model but so far no neuronal recordings in humans exist to support this hypothesis.

Methods: 13 Patients with drug-resistant epilepsy were implanted with depth electrodes targeting the medial temporal lobe (MTL) and the medial frontal cortex (MFC). Using microwires, we recorded single-unit activity while patients performed a STM (Stenberg) task with pictures as a study material. In each patient, we used a screening task to select the images for which neurons responded strongest and most selective. We then used these images as study material in the task.

Results: In the hippocampus and amygdala, we found 83 neurons (12.3%) neurons during the screening task that responded selectively only for one of the images used. During the STM task, such concept cells were persistently active during the delay period if the patient held in memory the image to which this cell responded. Analysis of the dynamics of activity of these neurons showed that during maintenance of information they formed stable attractors. We observed a second class of persistently active cells in the MFC. In contrast to the MTL, this persistent activity was not stimulus specific but was instead modulated by memory load and task set.

Conclusion: Together this shows, for the first time in humans, that STM is supported by a distributed network of persistently active neurons in the MTL and MFC.

969. Triage Patterns of Traumatic Subarachnoid Hemorrhage: Is Referral to a Tertiary Care Center Necessary?

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Introduction: Isolated traumatic subarachnoid hemorrhage in mild head injuries has growing evidence that triage to a tertiary care facility, ICU admission, and repeat imaging is not warranted. However, many patients are elderly and on antiplatelet or anticoagulation agents which increases concern for clinical deterioration. The authors try to identify certain factors that predict radiographic and clinical progression in hopes of preventing avoidable cost that occur with transfer and subsequent management.

Methods: A retrospective analysis identified 67 patients transferred between January 2010 and December 2014 who met inclusion criteria. Primary outcomes assessed were neurosurgical intervention, radiographic and clinical progression. Secondary outcomes included any operative intervention, length of stay, standardized hospital costs, disposition at discharge, and 30-day mortality.

Results: The mean age of the cohort was 67.7 +/- 16.4 with the majority (82.1%) having a Glasgow coma score (GCS) of 15. Warfarin was used in 10 patients (14.9%), although 55.2% were on an antiplatelet or anticoagulation agent. No patient required neurosurgical intervention. Only one patient, on Plavix and Warfarin, neurologically declined with radiographic progression. Older age seem to correlate with radiographic progression (mean age of 74 versus 62, Unit OR 1.00-1.69, p = 0.05). Dementia (6.7, 1.1-38.8, p = 0.05) as well as Warfarin use (p = 0.06) correlated with clinical progression. Cost in patients without other injuries was associated with Warfarin (p = 0.0002), injury severity scores (ISS) (p = 0.01) and initial GCS (p = 0.0003) on multivariate analysis.

Conclusion: In this small series of patients with mild TBI, the rate of neurologic deterioration due to expansion of iTSAH in patients is low, regardless of the use of antiplatelets/anticoagulants. Triage to a tertiary care facility generally is not warranted and can prove costly to patients with iTSAH without other injuries. However, certain patients (i.e. on anticoagulation, older age) may need some form of neurosurgical consultation before disposition can be determined.

970. Host Lymphopenia Enhances the Abundance, Activation Status, and Antitumor Efficacy of Tumor-specific T Cells Delivered Directly into the Brain

Carter Suryadevara; Pakawat Chongsathidkiet, MD; Rupen Desai, MD; Melissa Abel; Aladine Elsamacic; Karolina Woroniecka; David Snyder; Qi-Jing Li, PhD; Peter Fecci, MD, PhD; Luis Sanchez-Perez, PhD; John Sampson, MD, PhD (Durham, NC)

Introduction: Glioblastoma (GBM) remains uniformly lethal and novel therapies are urgently needed. Adoptive transfer of T cells expressing tumor-specific chimeric antigen receptors (CARs) represents a promising strategy to safely and efficiently target tumor cells within the central nervous system. We explored the loco-regional delivery of EGFRvIII-specific CARs in the brain as immunotherapy against murine GBM.

Methods: CARs were evaluated against two stringent models of syngeneic GBM (14-day established KR158B-Luc-EGFRvIII and 7-day established CT2A-EGFRvIII). For radiation experiments, 5Gy total body irradiation (TBI) was administered to mice immediately prior to CAR infusion. For temozolomide (TMZ) experiments, mice were administered 400 mg/kg by intraperitoneal injection 24 hours before CAR infusion.

Results: CARs prolonged survival at modest doses, but they were hampered by a poor expansion profile and displayed classical markers of T-cell exhaustion. To circumvent these factors, we explored whether lymphodepleting preconditioning would enhance efficacy by reducing competition for homeostatic cytokines and by depleting immunoinhibitory cells in the brain. Mice were subjected to 5Gy TBI followed by immediate intracranial infusion of CARs. In both tumor models, lymphodepletion significantly improved the abundance, activation status, and antitumor efficacy of CARs, leading to a 100% cure rate. Interestingly, CARs ultimately leaked into systemic circulation through the cervical lymphatics and expanded dramatically within peripheral lymphoid organs. In order to determine whether enhanced efficacy was dependent on CAR leakage into the periphery, we blocked CNS exit/re-entry using a blocking antibody against VLA-4. Antitumor efficacy remained unperturbed, suggesting that lymphopenia enhances CAR efficacy through a local mechanism within the brain. Importantly, we found that the lymphodepleting side effects of TMZ can be leveraged to sufficiently precondition hosts for loco-regional CAR therapy, supporting the translatability of these observations for patients with GBM.

Conclusion: Standard of care TMZ can be leveraged to enhance loco-regional T-cell immunotherapy in the brain.

971. Electrical Stimulation of the spinal cord as a Therapeutic Modality to treat Amyotrophic Lateral Sclerosis

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Introduction: Amyotrophic lateral sclerosis is an adult-onset neurodegenerative disease affecting both upper and lower motor neurons. The gene encoding superoxide dismutase (SOD1) has been shown to be a prominent cause of inherited ALS, no effective intervention has been developed. This study aims to determine if spinal cord electrical stimulation delays disease onset manifestations and preserves hind limb muscle mass in SOD1-G93 rats.

Methods: Thin-film wireless stimulators were utilized to electrically activate lumbar spinal cord in 30 week SOD1-G93 rats following onset. Three experimental groups were evaluated: no stimulation (control), stimulation on Day 1, and stimulation on Day 1-7. Animals underwent weekly evaluation of weight, grip strength, behavioral evaluation (Neuroscore), and motor evoked potential. The double blind study included 9 low SOD1 rats that were gender and litter matched.

Results: Significant differences were observed in the survival of control and experimental groups. Control animals (no stimulation) expired 1.5 weeks post-operatively. Animals receiving 1 hour of electrical stimulation on Day 1 and Day 1-7 survived 8 and 8.5 weeks post-operatively, respectively. Animals in the control group presented symptoms of ALS significantly earlier than the experimental groups. The control group presented 1 week post-operatively, while animals receiving electrical stimulation on Day 1 and Day 1-7 presented 6 weeks and 7 weeks post-operatively, respectively. No difference was observed in maintaining weight or slowing the progression of weight loss between the control or treatment groups. After onset, all the animals lost approximately 37-46% of their original body weight.

Conclusion: Preliminary results suggest that electrical stimulation of the lumbar spinal cord may delay onset and prolong survival of ALS-like symptoms in a rodent model. These results support further investigation into the use of direct spinal cord stimulation as a neuroprotective strategy.

972. Surgical Management of Intractable Epilepsy: Nationwide Rates, Causes, Risk Factors, and Outcomes Associated With 30-day and 90-day Readmission

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Introduction: The reduction of readmission rates, which is known to improve patient outcomes and save money, is a major goal of the U.S. healthcare system. However, the etiology of readmissions for specific surgery types is lacking. The national rates, causes, risk factors, and outcomes associated with readmission following surgery for intractable epilepsy have not been previously reported.

Methods: We queried the 2013 Nationwide Readmissions Database longitudinally from January to September using ICD-9-CM diagnosis codes to identify patients with intractable epilepsy 345.x.1, exclude 345.2, 345.3, 345.61, 345.71). Next, we searched ICD-9-CM procedural fields for patients who underwent hemispherectomy (01.52), temporal lobectomy (01.53), and amygdalohippocampectomy or partial excision of brain (01.59). A readmission was defined as the first hospitalization following the elective surgical visit. Predictor variables included demographics, comorbidities, epilepsy diagnosis, procedures, complications, and adverse discharge disposition (not routine). Univariate and multivariable analysis were employed to identify predictors of readmission.

Results: In 1,587 patients, the 30-day and 90-day readmission rates were 11.5% and 16.8% and the most common reasons for readmission were persistent epilepsy, V-EEG monitoring, postoperative infection, and postoperative CNS complication. In multivariable analysis, significant predictors of 30-day readmission were Medicare payer (OR: 3.7, 95% CI: 1.4-9.4) and medical complication occurrence (OR: 4.1, 95% CI: 1.6-10.6). Predictors of 90-day readmission were Medicare payer (OR: 2.6, 95% CI: 1.3-5.4), hemispherectomy (OR: 4.5, 95% CI: 1.5-13.1), and medical complication occurrence (OR: 3.6, 95% CI: 1.6-8.0). Readmission visits within 30-days were associated with longer length of stays (6.8 vs. 5.8 days), greater costs (\$18,660 vs. \$15,515), and increased percentage of adverse discharges (26.4% vs. 21.8%) than readmissions within 90-days.

Conclusion: The majority of readmissions occur within 30-days and are associated with poorer discharge outcomes. Our results indicate that medical, not surgical complications, are independently associated with readmission.

973. Plasticity of motor representations in patients with brain lesions: a navigated TMS study

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Introduction: The present study investigates the spatial distributions of motor representations in terms of tumor-induced brain plasticity by analyzing navigated transcranial magnetic stimulation (nTMS) motor maps derived from 100 patients with motor eloquently located brain tumors in or adjacent to the precentral gyrus (PrG).

Methods: 8,774 motor evoked potentials (MEPs) were elicited in 6 muscles of the upper and lower extremity by stimulating four gyri (superior frontal gyrus=SFG, middle frontal gyrus=MFG, PrG, and postcentral gyrus=PoG) in patients with five possible tumor locations (frontal tumor: n=24, Rolandic tumor: n=35, postcentral tumor: n=17, temporal tumor: n=5, and parietal tumor: n=19). Regarding the MEP frequency of each muscle-gyrus subdivision per patient, the expected frequency was 3.53 (8,774 divided by 100 patients, further divided by 6 muscles and 4 gyri). Accordingly, the patient ratio for each subdivision was calculated by defining the per-patient minimum data points as 3.

Results: 60.71% of the MEPs were elicited in the PrG. The overall and tumor-location specific patient ratios were rather high (APB-in-PrG: 93.00%) and balanced, indicating robust motor representations in the PrG. Regarding the motor representations in SFG and MFG, the overall patient ratios were much lower (APB-in-SFG: 16.00%, APB-in-MFG: 36.00%). The tumor-location specific patient ratios were higher for frontal tumors in both gyri (ADM-in-SFG 29.17%, ADM-in-MFG 50.00%) than for other tumor locations. This suggests that the finger representation reorganization in these frontal gyri, which corresponds to location of dorsal premotor areas, might be due to within-premotor reorganization rather than relocation of motor function from PrG into premotor areas one might expect from the Rolandic tumors.

Conclusions: Reorganization of the finger motor representations might be limited along the middle-to-dorsal dimension of the dorsal premotor areas (posterior MFG and SFG) and might not cross rostrally from the primary motor cortex (PrG) to the dorsal premotor cortex.

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