Oral Presentations
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Best International Abstract Award

600 5-Aminolevulinic acid fluorescence exceeds Gd-DTPA enhanced intraoperative MRI in tumor detection at the border of glioblastoma multiforme: A prospective study based on a histopathological assessment.

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Introduction: Glioblastoma multiforme (GBM) shows an invasive growth pattern extending into neural tissue beyond margins of contrast enhancement in MRI. Aim of the present study is to evaluate whether 5 aminolevulinic-acid fluorescence (5-ALA) provides an additional benefit to detect invasive tumor compared to intraoperative MRI (iMRI).

Methods: We prospectively enrolled 34 patients harboring a GBM with intended gross total resection. All patients had surgery using iMRI and 5-ALA guided resection following a specific protocol: First a white-light tumor resection was performed. Then, spatial location of residual fluorescence was subsequently marked. After that, an iMRI was performed and residual uptake of contrast was marked. Navigated biopsies were taken from these areas and from additional sites according to surgeons judgment. Cross tables and ROC-curves were calculated assessing performance of the imaging methods for tumor detection alone and for combined detection including infiltration zone (pathological tissue). Correlations of histopathological findings with imaging results were tested using Spearman's rho.

Results: 114 histopathological samples were harvested. Sensitivity for tumor detection was significantly higher ($p < 0.001$) in 5-ALA (0.85) than in iMRI (0.41). Specificity was significantly ($p < 0.001$) lower in 5-ALA (0.43) as in iMRI (0.70). For detection of pathological tissue 5-ALA exceeded iMRI in specificity (0.80 vs. 0.60) and sensitivity (0.91 vs. 0.66) significantly ($p < 0.001$). Imaging results of iMRI and 5-ALA did not correlate significantly. Only 5-ALA showed a significant correlation with final histopathological diagnosis of specimen and with typical histopathological features of GMS.

Conclusions: Imaging results of 5-ALA and iMRI are significantly different at the border zone of GBMs. 5-ALA has a higher sensitivity and a lower specificity for tumor detection than Gd-DTPA-enhanced iMRI. For detection of infiltrating tumor 5-ALA is superior to Gd-DTPA-enhanced iMRI concerning both sensitivity and specificity. Thus, additional use of 5-ALA to iMRI might be beneficial to maximize extend of resection.

601 Prospective, Multicenter Assessment of Acute Neurologic Complications following Complex Adult Spinal Deformity Surgery: The Scol-RISK-1 Study

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Introduction: The neurologic complication rate following complex adult spinal deformity surgery (ASD) has not been ascertained in any prospective, multicenter, observational study. Here, we compare preoperative lower extremity motor scores (LEMS) to 6 month postoperative scores.

Methods: 276 complex ASD patients from 15 sites worldwide were enrolled in this prospective, multicenter observational study. Diagnoses included primary coronal and/or sagittal deformity $< 80^\circ$ ($n=78$), congenital deformity ($n=13$), revision deformity requiring osteotomy ($n=107$) and/or patients undergoing a 3-column osteotomy (3-CO) ($n=202/276$, 73% all patients). There were 186 females (67%) and 90 males (33%) with a mean age of 57.7 years (range, 18-85). The patients had ASIA neurologic exams preoperatively, at discharge (D/C), and 6 weeks and 6 months postoperatively.

Results: 207/276 (75.0%) patients had normal LEMS preoperatively (Preop NML group) while 69 (25.0%) had some motor weakness (Preop ABNML group, mean 43.8 ± 7.6). At hospital D/C, 6 weeks and 6 months postoperatively, there were statistically significant declines in LEMS in the Preop NML group (48.91 ± 3.51 , $p < 0.05$; 49.03 ± 3.29 , $p < 0.05$; 49.36 ± 2.84 , $p < 0.05$), while there was no LEMS change in the ABNML group at hospital D/C (43.67 ± 8.33 , $p=0.977$), 6 weeks postoperatively (44.98 ± 8.05 , $p=0.182$), but an improvement at 6 months postoperatively (47.02 ± 6.28 , $p < 0.05$). Overall, 23.1% of patients experienced worsening of their LEMS at hospital D/C, 17.8% at 6 weeks postoperatively, and 10.7% at 6 months postoperatively. Older age at time of surgery was a risk factor for deterioration in LEMS postoperatively (mean, 56.8 without vs. 61.7 with decline, $p=0.0057$).

Conclusions: The Scol-RISK-1 Trial documented the acute lower extremity motor weakness complication rate of 23.1% at hospital D/C, 17.8% at 6 weeks postoperatively, and 10.7% at 6 months postoperatively following complex ASD surgery. This neurologic complication rate should be considered the Gold Standard in complex ASD procedures due to the prospective, multicenter nature and strict protocols followed.

602 A Novel Phase 1/2A Study of Intraparenchymal Transplantation of Human Modified Bone Marrow Derived Cells in Patients with Stable Ischemic Stroke

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Introduction: No treatment exists to restore lost brain function after stroke. Animal studies demonstrate that brain transplantation of SB623, a human modified bone marrow derived stromal cell, after experimental stroke can improve neurologic outcome. This clinical study is the first North American trial of intraparenchymal transplantation of bone marrow derived cell therapy for chronic stroke patients.

Methods: This is a two center open-label safety, dose escalation feasibility study. Stereotactic transplantation targets the subcortical peri-infarct area. Inclusion criteria include 18–75 yo, 6–60 mos post subcortical MCA ischemic stroke, mRS 3–4 and NIHSS < 7. Safety endpoints include WHO toxicity scale, MRIs and clinical follow-up to 2 years. The primary efficacy endpoint is European Stroke Scale (ESS) at 6 mos; secondary efficacy measures are ESS, NIHSS, Fugl-Meyer, mRS, cognitive scores and FDG-PET.

Results: Eighteen patients were treated (6 each with 2.5M, 5M and 10M cells. Follow-up is < 6 mos in 16 pts and < 12 mos in 12 pts. There were 3 serious adverse events (SAEs) related to the surgery, but not to the cells (seizure, subdural hematoma, pneumonia) and 2 SAEs unrelated to either surgery or cells (UTI, delayed new neurologic symptoms). Cytokine levels, HLA antibody levels, and PBMC function were unchanged. NIHSS, ESS, Fugl-Meyer all show a significant benefit in neurologic outcomes. Two patients showed remarkable improvement in their motor function within 24h of surgery, effects which have been sustained during follow-up (20 and 5 mos). These were the only 2 patients with new FLAIR lesions (DWI neg) in the motor cortex that resolved at 2 mos.

Conclusions: This open-label clinical study indicates that intraparenchymal transplantation of human modified bone marrow derived stromal cells in chronic stroke patients is safe, feasible and results in improved neurologic function. Larger studies will be initiated to further assess clinical efficacy.

Stryker Neuro-Oncology and Young Neurosurgeons Abstract Award

603 Mesenchymal stem cell exosomes enhance glioma stem cell viability and stemness via delivery of microRNA

Javier Figueroa (Richmond, TX); Tal Shahrar, MD; Anwar Hossain, PhD; Lang Frederick, MD (Houston, TX)

Introduction: Although recent evidence indicates that human cancers are maintained by a population of cells with stem-like properties called cancer stem cells (CSCs), the influence of the surrounding stromal cells on the behavior of the CSCs remains poorly understood. We have recently shown that the micro-environment of human gliomas contains both glioma stem cells (GSCs) and cells that resemble human bone marrow mesenchymal stem cells (BM-hMSCs), called Glioma

Associated-MSCs (GA-MSCs). We have also shown that these GA-MSCs enhance the growth of Glioma Stem Cells (GSCs). However, the mechanism underlying the communication between GA-MSCs and GSCs has not been established. Recent studies have suggested that nano-vesicles, called exosomes, may contribute to cellular communication within the tumor niche. Therefore, we hypothesized that exosomes released by GA-MSCs may promote the growth of GSCs.

Methods: GA-MSC exosomes were harvested by ultracentrifugation and sucrose cushion, and analyzed by both CD63 western blot and immuno-gold electron microscopy. Both GA-MSCs and GSCs were isolated from patient tumor samples.

Results: Here we show for the first time that in vitro delivery of exosomes isolated from GA-MSCs significantly increased both the viability and clonogenicity of GSCs. Furthermore, in vivo xenograft implantation of GSCs, pre-treated with GA-MSC exosomes, into the brains of nude mice resulted in a greater tumor burden and a significant decrease in animal survival compared with untreated controls. These exosomes were also found to contain a wide variety of miRNA, including many which are associated with glioma. Treatment of GSCs with GA-MSC exosomes, was enough to alter the miRNA profile of GSCs, increasing the amount of these oncogenic miRNAs intracellularly.

Conclusions: We conclude that exosomes released by GA-MSCs represent a novel and alternative intra-tumoral communication mechanism for the exchange of miRNA, which significantly impacts the tumor microenvironment and enhances the aggressive nature of gliomas.

Synthes Skull Base Award

604 Incidence of headache as a presenting complaint in over 1000 patients with sellar lesions and factors predicting postoperative improvement

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Introduction: Because of the high incidence of headaches and pituitary tumors, neurosurgeons are often asked to evaluate patients with benign-appearing sellar lesions and headaches without insight into whether the headache is attributable to the lesion. We sought to evaluate the incidence of headache as a presenting complaint in over 1000 patients with sellar lesions of variable pathology and to identify factors predicting postoperative improvement.

Methods: We conducted a five-year retrospective review of our first 1015 transsphenoidal surgeries since establishing a pituitary center of expertise.

Results: Of 1015 patients with sellar lesions, 340 presented with headache. Of patients with headache, 30% presented with headache as their only symptom. Patients with Rathke's cleft cysts (RCCs) had the highest percentage of headache at 60%, followed by craniopharyngioma (46%) and apoplexy (44%), while endocrine inactive and active adenomas had lower rates of headache (28–29%). Multivariate analyses revealed diagnosis ($P=0.01$), younger age ($P=0.001$), female gender ($P=0.002$), and recurrent lesions ($P=0.04$) to be associated with headache, with lesion size, suprasellar extension, and hypopituitarism not associated. Of patients presenting with headaches, 36% reported improvement of headaches at 6-week follow-up and 47% had improved at the 6-month follow-up. Multivariate analyses including associated symptoms, duration and location of headache, age, gender, lesion

size, and extent of resection revealed only gross total resection (GTR; $P=0.04$) and younger age ($P=0.03$) to be associated with improvement.

Conclusions: In analyzing over 1000 consecutive patients undergoing surgery for sellar lesions, younger patients, females, and patients with RCCs were more likely to present with headache. Younger patients and patients undergoing GTR were more likely to experience headache improvement. This information can be used to counsel patients presenting with these common lesions and this common complaint.

National Brain Tumor Society Mahaley Award

605 Tetanus toxoid conditioning enhances migration and efficacy of dendritic cell vaccines in patients with glioblastoma

Kristen Batich; John H. Sampson, MD, PhD, FAANS; Elizabeth Reap, PhD; Luis Sanchez-Perez, PhD; Gary Archer, PhD; David Snyder, MS; Smita Nair, PhD; Michael Gunn, MD (Durham, NC); Duane Mitchell, MD, PhD (Gainesville, FL)

Introduction: Dendritic cell (DC) vaccine efficacy is limited by suboptimal migration to vaccine site-draining lymph nodes (VDLNs). We assessed the impact of DC migration on clinical outcomes by randomizing patients with newly-diagnosed glioblastoma (GBM) to one of two conditioning strategies, unpulsed DCs or tetanus-diphtheria (Td) toxoid prior to DC vaccination.

Methods: We compared effects of vaccine site conditioning on migration of ^{111}In -labeled DCs using SPECT/CT imaging and evaluated clinical outcomes with progression-free and overall survival (OS). Transgenic mouse models were used to determine if increased DC migration induced greater antitumor responses.

Results: Td-conditioned patients showed increased DC migration ($p=0.04$) and significantly improved OS ($p=0.013$). Td-conditioned mice demonstrated increased DC migration to VDLNs ($p=0.0001$) and suppressed tumor growth ($p=0.0001$). Adoptive transfer of Td-activated CD4⁺ T cells increased DC migration in naïve mice ($p=0.01$), and CD4⁺ depletion in Td-conditioned mice abrogated increased DC migration ($p=0.005$). Td administration induced a significant increase in serum CCL3 levels ($p=0.028$). In vitro, we observed increased chemotaxis of mature human and murine DCs towards serum from Td-conditioned hosts, which was abrogated with CCL3 blockade ($p=0.02$). In vivo, DCs migrated to VDLNs in a CCL3-dependent manner ($p=0.003$). Td-conditioned CCL3 knockout mice demonstrated accelerated growth comparable to that of controls, owing to the importance of this chemokine in driving the trafficking of DC vaccines to VDLNs ($p=0.01$).

Conclusions: Td administration increased DC migration and tumor responses in a preclinical model corroborating effects of Td conditioning on DC migration observed within our phase I/II clinical trial.

Springer Journal of Neuro-Oncology Award

606 Replicating retrovirus Toca-511 delivered using convection-enhanced real-time MRI guidance for recurrent glioblastoma

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Introduction: Glioblastoma gene therapy has been limited by suboptimal intratumoral spatial distribution of virus. A Phase I trial is being conducted in patients with recurrent glioblastoma with a replicating retrovirus Toca 511, in which a cytosine deaminase (CD) transgene converts prodrug 5-fluorocytosine (5-FC) to anti-cancer drug 5-fluorouracil.

Methods: Toca 511 was injected intratumorally using a brain biopsy needle (BBN) or with real-time MRI-guided convection-enhanced delivery (CED). Four weeks later, patients received 5-FC every 4 weeks along with serial MRIs until progression. Some patients who progressed underwent post-treatment resection.

Results: Five Toca 511 doses, escalated by half logs, were injected via BBN in 22 patients. Analysis of post-5-FC resected tumors in some patients showed viral protein, DNA, and RNA including CD, but with viral genes only detected in limited amounts and not in all samples (up to 2000 DNA copies/ μg tissue). MRI immediately after injecting Toca 511 plus gadolinium showed imprecise delivery. Therefore, real-time MRI-guided CED was implemented. In 7 patients at a single center (average tumor volume = 10.5 cm³, range=2.6-25.0 cm³) 12-70% of tumor volume (mean=45%) was infused. A 14-gauge cannula allowed flow rates up to 50 $\mu\text{L}/\text{min}$ without reflux, and 3.1 mL was delivered to 1-3 targets with improved spatial distribution revealed by Vd (volume distribution)/Vi (volume infusion) ratios averaging 1.6 (range=1-3.5). Resection from one patient two months post-CED and one course of Toca FC (extended-release 5-FC) revealed <90,000 viral DNA copies/ μg tissue in the infusion location. Histologic necrosis and radiographic regression was also observed post-Toca FC dosing.

Conclusions: Real-time MRI-guided CED of Toca 511 was well tolerated and led to 45-fold more viral DNA detected at subsequent resection than BBN injection and associated tumor response.

607 Administration of Toca 511 to Subjects with Recurrent HGG Undergoing Repeat Resection- A Ph1 Study

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Introduction: High-Grade Glioma (HGG) remains one of the most debilitating and deadly cancers. Gene transfer using Toca 511, a tumor-selective retroviral replicating vector has the

advantage of targeting residual tumor not removed at the time of resection. Toca 511 expresses the transgene cytosine deaminase (CD) in infected tumor cells, and subsequent oral administration of extended-release 5-FC (Toca FC) results in formation of 5-FU in tumor cells expressing CD. The primary purpose of this study is to identify the highest safe and well-tolerated dose of Toca 511 administered to subjects undergoing resection for rHGG.

Methods: This is a Phase 1 clinical trial (NCT01470794) utilizing a standard 3+3 dose escalation design. Toca 511 doses are escalated at half-log intervals starting at 1.4×10^7 TU and current patients receive 1.5×10^9 TU. Following tumor resection, multiple injections of vector are administered into the walls of the resection cavity. Starting approximately 6 weeks after surgery oral Toca FC is administered in cycles.

Results: 26 patients have been enrolled to date across 5 protocol-defined dose groups; the combination treatment has been safe and well tolerated and the MTD has not been reached. Subsequent resection of tumor from subjects who previously received Toca 511 confirmed virus can selectively infect residual tumor cells. Some subjects experienced clinical and radiographic improvement.

Conclusions: Administration of Toca 511 at the time of tumor resection and followed by cyclic administration of Toca 511 has been safe and well tolerated. Further dose escalation is warranted.

608 Delayed contrast MRI – a novel tool for decision making in neuro-oncology

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Introduction: Conventional MRI is unable to differentiate tumor from non-tumoral enhancing tissues on conventional T1-MRI (such as radionecrosis). We have applied delayed contrast MRI for calculating high resolution maps clearly differentiating tumor/non-tumoral tissues.

Methods: 485 maps were calculated for 144 patients with primary/metastatic brain tumors post treatment recruited to the study and followed using the maps. The maps were validated by comparing pre-surgical maps of patients undergoing surgery during the study with histology.

Results: 52 stereotactic tissue samples and 32 resected lesions acquired from 48 patients with primary/metastatic brain tumors were histologically examined showing near complete agreement with the pre-surgical maps. This validation confirms that blue regions in the maps (efficient clearance of the contrast agent <1hr post contrast injection) represent morphologically active tumor while red regions (contrast accumulation) represent non-tumor tissues. In addition, the maps were used for making 219 decisions. In 61 cases the decision was to continue follow-up (no treatment change); In 158 cases the decision was to change treatment (including surgery, chemoRT, RT, Avastin, SRS etc).

Conclusions: Delayed MRI enables complete separation between tumor (negative signal) and treatment effects (positive signal) with no overlap. In addition it enables using robust MR sequences resulting in high resolution maps clearly depicting tumor/non-tumor tissues. The maps are being used for routine neuro-oncological clinical decisions in Israel (5 major hospitals). Histological validation together with extending to 3D maps of 1mm3 resolution, suggests that the maps may be also applied for planning high precision procedures such as biopsies, resections, SRS, FSR and more.

609 Inducing Brain Function Plasticity by High Frequency Cortical Stimulation Permits to Increase the Extent of Resection in WHO Grade 2 and 3 Gliomas. A Pilot Study In 5 Cases

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Introduction: Extent of resection is the most relevant factor in prognosis of gliomas. This is limited by the presence of eloquent areas close to or within the tumors. Topographic plasticity has been shown associated to slowly growing gliomas. Enhancing plasticity artificially could increase the extent of resections.

Methods: We present 5 cases of gliomas located at eloquent areas: an anaplastic astrocytoma at Broca's area, a large left frontal oligodendroglioma, a left temporoparietal anaplastic oligodendroglioma at Wernicke's area, an anaplastic astrocytoma at the left primary motor area and a large left frontal astrocytoma covering motor movement and language areas. These patients were operated awake and the tumors could not be resected according to established cortical stimulation standards. A cortical grid of electrodes was placed over the functional areas and the remaining tumor. Inhibitory continuous stimulation (130 Hz, 60 us) was continuously applied to the grid's functional contacts. The current intensity was set daily to the threshold of inducing a mild functional deficit, while the patient performed an intensive rehabilitation of the disturbed function. The intensity threshold to produce a mild deficit increased steadily. When an intensity of 10 mA was reached in all contacts producing none or mild deficit (usually after 3 weeks), the patients were reoperated awake.

Results: Cortical stimulation demonstrated absence of function at the previously eloquent points. This permitted extended resection and a complete or subtotal resection of the tumors. Functional studies showed a displacement of the functions to other locations in neighboring areas or at the contralateral hemisphere.

Conclusions: We present evidence of artificial enhancement of plasticity by high frequency cortical stimulation in tumors containing eloquent cortex, thus permitting an extended resection of grades 2 and 3 gliomas. This approach permits to improve the prognosis of these lesions while preserving eloquent brain function.

610. BRAFV600E mutated melanoma patients may have an increased rate of metastatic brain disease when compared to wild-type BRAF melanoma

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Introduction: BRAF mutations in melanoma confer a worse prognosis with CNS diseases often serving as a terminal event. In this study we: 1] Compared the incidence of metastatic disease to the brain and the time to development of CNS metastases in patients with BRAFV600E mutations vs. wtBRAF, 2] Attempted to determine differences in outcome between patients with surgery and/or radiation therapy, and 3] assessed the effect of BRAF inhibitor therapy on the incidence of brain metastases.

Methods: Retrospective review of all melanoma patients who underwent BRAF mutation testing at The University of Colorado Hospital between 2002-2012. 107 patients were identified, 18 patients were excluded because of loss to follow-up. Of the remaining 89 patients: 48 patients had BRAF mutations and 27 patients had wtBRAF.

Results: 24 of 48 (50%) patients with BRAF melanoma developed brain metastases at a mean of 4.5 months. 15 of 41 (36%) patients

with wtBRAF developed brain metastases at an average of 9 months. Relative risk of developing brain metastases with mutated BRAF was 2.37 comparatively. Earlier development of CNS involvement was associated with a lower overall survival in patients with BRAF mutations.

Conclusions: BRAF inhibitors do not appear to have an impact on CNS disease. Patients with BRAFV600E are at a higher relative risk for the development of brain metastasis and have a worse prognosis. Patients with BRAFV600E melanoma should be subject to careful CNS disease monitoring as early neurosurgical involvement may increase prognosis.

611. Multifunctional Bioconjugated Magnetic Nanoparticles for Radiosensitivity Enhancement of Glioblastoma

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Introduction: Multifunctional magnetic iron-oxide nanoparticles (IONPs) can be sensitively imaged by MRI and can provide targeted therapy of glioblastoma (GBM) in preclinical models. The goal of this study is to investigate whether an EGFR- and EGFRvIII-specific antibody bioconjugated to IONPs can also permit the radiosensitivity enhancement of GBM.

Methods: IONPs bioconjugated to the monoclonal EGFR antibody, cetuximab, were used for therapeutic targeting of experimental GBM in combination with single or multiple fractions of ionizing radiation (IR). Human GBM cells overexpressing EGFRvIII or wt EGFR and normal human astrocytes were treated with control (PBS), free IONPs, cetuximab, cetuximab-IONPs and subsequent fractionated irradiation (10 Gy x 2) in vitro. Four different groups of athymic nude mice were intracranially implanted with EGFRvIII-expressing GBM cells and underwent treatment 5 days later with convection-enhanced delivery (CED) of control (PBS), free IONPs, cetuximab, cetuximab-IONPs and subsequent fractionated IR (10 Gy x 2), 24 and 72 h after CED. MRIs were performed on mice to confirm intracranial xenograft formation.

Results: A significant GBM antitumor effect of cetuximab-IONPs was found in vitro and significantly prolonged survival of athymic nude mice implanted with GBM xenografts after CED of cetuximab-IONPs and subsequent IR was observed in vivo (median OS of 16 days for control, 42 days for cetuximab, 77 days for cetuximab-IONPs). No significant toxicity was found with normal human astrocytes.

Conclusions: Use of cetuximab-IONPs may permit the advancement in the treatment of GBM due to the combination of their sensitive imaging qualities on MRI, therapeutic effect, and radiosensitivity enhancement.

612. In vivo Multiplexed Interrogation of Amplified Genes in Cancer

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Introduction: Large scale genomic characterization of cancers has uncovered many alterations that underlie tumor development.

However, the identities of the true driver genes within the somatically altered genomic landscape often remains undefined. Therefore, we have developed and implemented a multiplexed in vivo transformation assay to identify genes recurrently amplified in high-grade ovarian cancers that suffice to induce tumorigenic growth of immortalized human cells.

Methods: We queried The Cancer Genome Atlas (TCGA) and identified recurrently amplified genes, created a lentivirally delivered collection of open reading frames (ORFs), and then screen for genes that induced tumorigenicity in an immortalized human cell background using a multiplexed in vivo transformation assay. Tumors that developed were interrogated using next generation sequencing to identify the transforming ORFs.

Results: We successfully developed a pooled in vivo approach to oncogene discovery. Using a collection of nearly 500 ORFs, we identified the signaling adaptor GAB2 as a recurrently amplified gene that potentially transforms immortalized ovarian and fallopian tube secretory epithelial cells. In addition, we identified 25 additional potential oncogenes that drove tumor formation. Cancer cell lines overexpressing GAB2 require GAB2 for survival and show evidence of PI3K pathway activation, which was required for GAB2-induced transformation. Cell lines overexpressing GAB2 were as sensitive to PI3K inhibition as cell lines harboring mutant PIK3CA.

Conclusions: These observations credential GAB2 as a potent human cancer oncogene and also describe a generalizable, scalable multiplexed in vivo oncogene discovery methodology applicable to the functional phenotypic interrogation of somatically altered cancer genomes across all cancer types.

613. Nanoparticle conjugated IL-12 RNA therapy targeting of Glioblastoma Multiforme microenvironment by Convection Enhanced Delivery mediates increased T cells at tumor site in an adoptive transfer T cell model

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Introduction: Glioblastoma Multiforme (GBM) despite aggressive treatment is inevitably fatal. Hence, new treatments such as Active Immunotherapy are necessary. However, one of its main challenges is limited trafficking and accessing of the tumor by T cells. Herein, we describe convection enhanced delivery (CED) of RNA therapy of IL-12 to reverse local immunosuppression by GBM and increased adoptively transferred T cells at the tumor site.

Methods: IL-12 or GFP RNA was conjugated at a ratio of 2µg RNA to 15µl DOTAP and loaded to osmotic pumps connected to brain infusion kits stereotactically inserted into tumor site at day 14. After which, Luciferase transduced T cells were intravenously delivered to the animals and were monitored using bioluminescence imaging while the pumps functioned over 7 days.

Results: The radiance of tumor site was measured over a month. In the CED IL-12 RNA group, mean radiance was 3.11 x10⁶, 3.55 x10⁶, 4.57 x10⁶, 3.73 x10⁶ and 7.48 x10⁶ p/s/c/sr for Day 1, 2, 3, 14, 24 respectively. In GFP control, means were 1.27 x10⁶, 1.65 x10⁶, 1.46 x10⁶, 1.67 x10⁶ and 2.92 x10⁶ p/s/c/sr for the same time points. Other than Day 1, CED infused IL-12 RNA was statistically significantly higher. In the spleen, IL-12 RNA group had means of 6.88x10⁷, 8.62 x10⁷, 6.23 x10⁷, 3.09 x10⁶, 1.93 x10⁶ p/s/c/sr compared with the GFP control group : 2.80 x10⁶, 3.46 x10⁶, 1.84 x10⁶, 1.56 x10⁶, 1.32x10⁶ p/s/c/sr. Other than day 3 and 14, both groups were not significantly different from each other.

Conclusions: Novel therapeutic modality of Convection Enhanced Delivery of IL-12 RNA protected by DOTAP is able to increase the bioluminescence signal of adoptively transferred T cells at the site of Glioblastoma Multiforme without long-term systemic proliferation of T cells. This is potentially mediated by reversing the immunosuppressive microenvironment of the tumor and encouraging T cell chemotaxis and proliferation.

614 Enhancing Nanoparticle Immunotherapeutic Treatments for Glioblastoma Utilizing Histotripsy Ultrasound Radiotherapy

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Introduction: Glioblastoma multiforme remains the most lethal form of primary brain cancer, despite optimal tumor resection and adjuvant therapy. It is hypothesized that delivering loaded nanoparticles with doxorubicin, as well as modified leukocyte receptor cells found in excised tumor tissue can elucidate an anti-tumor response. Histotripsy ultrasound, a novel non-invasive radiotherapy, may significantly enhance brain blood barrier penetration of these promising treatment delivery vehicles.

Methods: In this radiotherapy method, an array transducer applies high intensity ultrasound pulses which evoke pressure changes, forming micro-bubbles within gas nuclei of mammalian tissue. The high energy micro-bubbles fragment instantaneously, temporarily subdividing tissue on a nanoscale. Moreover, this novel micro-bubble heating technique allows low frequency histotripsy ultrasound to achieve a high aperture on a relatively small focal zone. This makes the BBB readily targetable within its 220-700 kHz reported disruption zone.

Results: The method of histotripsy ultrasound on the brain utilizes the ability to cross the disruption zone with ultrasound operating near 700 kHz. All subjects demonstrated brain blood barrier disruption in serial imaging at 0.29-0.57 MPa. This range is supported by an extensive finite difference time domain (FDTD) 3-D computer simulation study, using a 0.27-1.2 MPa range ($P < 0.05$).

Conclusions: Our data suggests that histotripsy ultrasound, administered at low frequency, shows promise to optimize nanoparticle and leukocyte receptor cell immunotherapies. Specifically, the heat-derived creation of nanoscale micro-bubbles can significantly enhance the bioavailability of these delivery vehicles.

615 Does time until recurrence predict effect of repeat surgery in GBM patients?

Paul Andre Ronning, MD; Einar Vik-Mo, MD, PhD; Eirik Helseth, MD, PhD; Torstein Meling, MD, PhD (Oslo, Norway)

Introduction: Patients with glioblastoma (GBM) usually undergo initial treatment with surgery, radiotherapy and chemotherapy. At the time of recurrence, patients are often referred for repeat surgery. The time until recurrence has often been cited as a proxy for the biological aggressiveness of the tumor. However, the documentation on this topic is conflicting. Hence, our aim was to investigate the influence of time until recurrence on survival in patients undergoing repeat GBM surgery.

Methods: A prospective tumor database was searched for all

histologically verified GBM operations between Jan-1-2003 and Dec-31-2012. Patients undergoing more than one reoperation were excluded. Patients were divided into one-time-surgery (OTS) and two-time-surgery (TTS) groups. In the TTS group we excluded the censored patients and modeled the time from repeat surgery to death as a linear function of time until recurrence after checking pertinent assumptions.

Results: We identified 1079 GBM operations in 984 different patients, hence 9.7% (95) of all GBM patients underwent repeat surgery. The median age at primary surgery was 63.3 (Interquartile range (IQR) 54.6-71.3) and 57.0 years (IQR 46.7-64.0) and the median time from primary surgery to death was 9.1 (95% CI 8.4-10.0) and 17.3 (95%CI 16.0-21.8) months in the OTS and TTS groups, respectively. The median time from repeat surgery to death was 5.5 months (95% CI 4.6-7.1). The time until recurrence was not associated with survival after repeat surgery ($\beta = -0.1$, 95% CI -0.2, 0.1, $p = 0.5$).

Conclusions: The time until recurrence for GBM patients does not predict survival after repeat surgery.

616 Prognostic value of radiosurgery prescription dose on the local control of small (less than 2 cm) brain metastases

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Introduction: Radiosurgery is used widely for the treatment of brain metastases (BM). The recommended prescription dose (PD) for BMs smaller than 2cm, based upon RTOG 90-05, is 24Gy. Some clinicians believe that the 24Gy dose is associated with an unnecessarily high risk of radiation necrosis. There is a lack of high quality evidence regarding the relationship between PD for small BM and local control versus radiation necrosis.

Methods: We retrospectively reviewed 896 patients with BM less than 2cm (3034 tumors) treated with Gamma Knife radiosurgery between 2000 and 2012. Local progression or radiation necrosis were study endpoints. Each tumor was followed from the day of radiosurgery until reaching one of the endpoints or last MRI follow up. Median radiographic follow up per lesion was 6.2 months.

Results: Median tumor volume and largest dimension were 0.16cc and 0.8cm, respectively. PDs for 216 tumors were 15-18Gy, for 408 tumors 19-23Gy, and for 2410 tumors 24Gy. 87 patients (10%) had local progression of 104 tumors (3%) and 148 patients (17%) had radiation necrosis of 199 tumors (7%). Univariate and multivariate analysis were performed for local progression and radiation necrosis. For local progression, tumors less than 1cm ($p < 0.001$), PD of 24Gy ($p = 0.01$), and additional WBRT ($p = 0.001$) were positive prognostic factors. For radiation necrosis, significant predictors included size greater than 1cm ($p < 0.001$), location in corpus callosum ($p < 0.001$) and uncommon pathologies ($p = 0.05$).

Conclusions: A PD of 24Gy results in significantly better local control than lower doses. Tumor size is an independent prognostic factor for both local progression and radiation necrosis.

617 Therapeutic vaccination against autologous cancer stem cells with mRNA transfected dendritic cells in patients with glioblastoma

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Introduction: Glioblastoma, the most common primary brain tumor, is invariably fatal, with a median survival of approximately one year. The growth and recurrence of glioblastoma is suggested to be driven by a population of cancer stem cells (CSCs). Although experimental data have suggested the importance of CSCs, little data exist regarding the potential relevance and importance of these cells in a clinical setting.

Methods: We here present data from an ongoing phase I/II trial using a dendritic cell (DC)-based vaccine targeting CSCs. Brain tumor biopsies are dissociated into single-cell suspensions, and autologous CSCs are expanded in vitro as tumorspheres. From these, CSC-mRNA was amplified and transfected into monocyte-derived autologous DCs. The DCs were aliquoted to 9-18 vaccines containing 107 cells each. These vaccines were injected intradermally at specified intervals after the patients had received a standard six-week course of postoperative radio-chemotherapy.

Results: Autologous CSC cultures were established in seventeen patients. High-quality RNA was isolated, and mRNA was amplified in all cases. Twelve patients able to be weaned from corticosteroids after radiotherapy received DC immunotherapy. An immune response induced by vaccination was identified in a high frequency of patients evaluated by T-cell proliferation in vitro. No patients developed adverse autoimmune events or other side effects. So far the median overall survival is 25.3 months. Data on progression-free and overall survival, compared to a historical matched control population, will be presented.

Conclusions: These preliminary findings suggest that vaccination against glioblastoma stem cells is safe, well tolerated, and support establishment of a randomized phase II trial.

618 Contemporary Analysis of the Risk of Neurosurgical and Anesthetic Complications Following Procedures Performed in the Sitting Position

Benjamin T. Himes, MD; Grant Mallory, MD; Jeffrey Pasternak, MD; Jamie Van Gompel, MD (Rochester, MN)

Introduction: The use of the sitting position has become the subject of debate due to a perceived high risk of complications compared to other operative positions in neurosurgery. The present study sought to analyze the complication risk of sitting neurosurgical procedures in a contemporary series.

Methods: A prospectively maintained operative case log and morbidity and mortality database was reviewed for patients undergoing neurosurgical procedures at Mayo Clinic Rochester in the sitting position from January 2000 through September 2013. Patients undergoing cervical spine procedures, occipital or suboccipital craniotomies, or deep brain stimulator implantation were included in the analysis. Patients undergoing percutaneous procedures or refusing consent for research were excluded. Operative reports, electronic medical records, and morbidity mortality logs were reviewed for venous air embolus (VAE), subdural hematomas, tension pneumocephalus, and positioning palsies. The overall incidence of complications as well as

individual complication rates were analyzed. Further subset analysis was performed according to procedure type. Odds ratios was used to compare the incidence of overall complication rate and incidence of venous air embolism between suboccipital craniotomy/craniectomy, deep brain stimulation, and posterior cervical procedures.

Results: A total of 1636 procedures were included. The overall complication rate was 1.77% (29 procedures). The incidence of clinically significant VAE, tension pneumocephalus, and subdural hematoma were 1.41%, 0.24%, and 0.12% respectively. Overall complications (OR= 5.4, 95% CI-2.1-14.9, p less than 0.001) and VAE (OR= 5.3, 95% CI-2.0-13.7, p less than 0.001) were higher in patients undergoing sitting suboccipital procedures.

Conclusions: Despite perceived risks of the sitting position in neurosurgery, we conclude that the overall complication rate is low. Suboccipital craniotomy/craniectomy procedures have the highest incidence.

619. Time to Surgery Does Not Impact Outcomes in Cauda Equina Syndrome: Analysis of 48 Cases

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Introduction: Our goal was to study time to surgery as a continuous variable in order to determine its effect on outcomes in cauda equine syndrome (CES).

Methods: We retrospectively reviewed 48 patients who presented to our institution and underwent surgery for CES. Only patients with MRI-proven discogenic CES and records that allowed precise calculation of time to surgery were included. Time to surgery was analyzed as a continuous variable using linear regression, as an ordinal variable using Spearman's rank correlation, and as a discrete variable by comparing patients treated before and after set thresholds. A Bonferroni correction of 10 was used due to the number of tests performed.

Results: Ordinal analysis of time revealed no benefit in outcome for early treatment. Comparing patients treated before and after distinct thresholds found no significant differences using p

Conclusions: We present one of the largest single-center series of CES patients and the first analysis of time as a continuous variable to determine its impact in a clinically relevant manner. We found that time to surgery does not have a continuous relationship with outcomes of CES.

620. Incremental Cost-Effectiveness of Adult Spinal Deformity Surgery: Observed QALYs with Surgery Compared to Predicted QALYs without Surgery

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Introduction: The incremental cost-effectiveness ratio (ICER) of surgery for adult spinal deformity (ASD) has eluded the literature due in-part to inherent self-selection into surgical treatment. This study builds a statistical model to predict hypothetical QALYs without surgical treatment. The analysis compares predicted

QALYs to observed post-operative QALYs and forms the resulting ICER.

Methods: Single-center, retrospective analysis of consecutive patients undergoing primary surgery for ASD. Payments (expressed in 2010 dollars) to the hospital were collected from administrative data and QALYs calculated from the SF-6D, each discounted at 3.5% per year. Regression analysis was used to predict hypothetical QALYs without surgery based on pre-operative longitudinal data for 141 crossover surgical patients with similar diagnosis, baseline HRQOL, age, and gender compared to the study cohort.

Results: 239 patients evaluated at 3yrs, predominantly female (n=203, 85%) with average age of 49 (range 18-82). With discounting, total payments to the hospital averaged \$211,529, including readmissions, with average QALYs of 1.9 at three-year follow-up. Average QALYs without surgery were predicted to be 1.5 after 3yrs. At three and five-year follow-up, the ICER was \$570,000 and \$278,000, respectively. Projecting through 10-year follow-up, the ICER was \$105,600.

Conclusions: Based on the World Health Organization's (WHO) suggested upper threshold for cost-effectiveness (3 times per capita GDP, or \$140,000 in 2010 dollars), the analysis reveals that surgical treatment for ASD is cost-effective after a 10-year period. At earlier follow-up intervals, the ICER well exceeds the WHO threshold, highlighting the importance of extended follow-up in the appropriate economic evaluation of surgical treatment for ASD.

621. Utility of routine biopsy at vertebroplasty in the management of vertebral compression fractures

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Introduction: The role of routine biopsy at vertebroplasty for vertebral compression fracture (VCF) has not been established. We aimed to determine the utility of routine biopsy in the early detection of malignancy in presumed benign VCF.

Methods: A prospective observational study was conducted on 147 consecutive patients who underwent vertebroplasty over a 5-year period at a single institution. Of these, 135 had routine intraoperative biopsy at every level of VCF. Pain visual analogue scale (VAS) and Oswestry Disability Index (ODI) scores, and complications were recorded.

Results: Analysis of routine vertebral biopsies in 135 patients revealed that in 86 patients with presumed osteoporosis and no prior cancer diagnosis, 4 (4.7%) had a malignant VCF. In 20 known cancer patients presumed to be in remission, 2 (10%) had a malignant VCF. Routine vertebral biopsy returned an overall cancer diagnosis rate of 5.7% (6/106) when combining the two groups of unsuspected patients. In these 6 patients, history, examination, laboratory tests and pre-procedure imaging all failed to suggest malignancy diagnosed at routine biopsy. A sustained reduction in pain VAS and ODI scores were observed at 1 year postoperatively. The complication rate was 6% (9/147) with zero surgery-related mortality.

Conclusions: Routine biopsy performed at vertebroplasty may demonstrate cancer in unsuspected patients or active malignancy in patients previously thought to be in remission. This will expedite patients' subsequent cancer management. Routine biopsy did not add morbidity to the procedure. We advocate biopsy at each level of VCF to maximise diagnostic yield and avoid missing a malignancy at a single level.

622. Anterior Shift of the Lumbar Plexus within the Surgical Corridor in Scoliotic Spines: Considerations during the Transpsoas Approach

Ashish Patel, MD; Dante Leven, DO; Robert Pivec; Qais Naziri; Jason Oh, MD; Srinivas Kolla, MD; Carl Paulino; Nicholas Post, MD (Brooklyn, NY)

Introduction: Indications for the transpsoas approach to the lumbar spine have expanded to include patients with spinal deformities. Approaching the deformity from the curve concavity affords the surgeon the ability to modify the concave intervertebral height thereby correcting a coronal curvature. However, modifications in lumbar plexus (LP) anatomy may occur in deformity patients. This study sought to investigate differences in concave-convex lumbar plexus anatomy as it relates to the transpsoas approach.

Methods: Lumbo-sacral MRI scans (L1-S1) from right-convex thoracic adolescent idiopathic scoliosis (AIS) patients were analyzed. The anterior vertebral body axis was used to provide a reference line. Parameters evaluated at each intervertebral level included; Vertebral Rotation (VR), Psoas depth (PD) and Psoas height (PH), Lumbar Plexus depth (LPD), and Vascular Encroachment (VE). Paired t-test analyses were used to describe concave-convex differences.

Results: 50 AIS patients (17M, 33F) with a mean 49.8 deg (13-91) thoracic Cobb and 42.3 deg (8-75) lumbar Cobb were included for analysis. VR significantly increased from distal to proximal in the lumbar spine (L5-S1=1.3, L4-5=2.8, L3-4=4.6, L2-3=6.7, L1-2=5.3, degrees all p <0.05), except between L2-3 and L1-2 (p=0.39). Significant differences (all p <0.5) were found between concave-convex LPD at each level (L5-S1=2.2mm, L4-5=2.2mm, L3-4=3.5mm, L2-3=4.7mm, L1-2=4.5mm), except L4-5 (p=0.07). A significant correlation was found between increasing vertebral rotation and concave-convex lumbar plexus depth difference (r=0.56).

Conclusions: Care must be taken during the transpsoas approach to the lumbar spine in patients with rotational spinal deformities. This study demonstrates a significant anterior shift in the concave lumbar plexus with increasing vertebral body rotation toward the curve convexity. A modification in the formal lateral decubitus position may be helpful to avoid lumbar plexus injury.

623. Outcome Comparison Between Decompression Alone Versus Decompression with Fusion in Managing Adjacent Segment Disease

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Introduction: Adjacent segment disease (ASD) is characterized by symptomatic degenerative changes at a segment adjacent to a previous spinal fusion. Surgical treatment involves decompression with or without extending the fusion. Here we present a retrospective analysis comparing treatment outcomes between these two treatment options.

Methods: A retrospective analysis of patients who underwent decompression with or without fusion at a level adjacent to a previous fusion in the past 10 years was performed. Data was acquired on patient demographics, comorbidities, perioperative data, and motor scores. Patients completed pre- and postoperative visual analog scale (VAS) and Oswestry Disability Index (ODI) surveys. Bivariate analysis was performed comparing decompression alone versus decompression with fusion with respect to rate of reoperation, and change in VAS and ODI.

Results: 170 patients (83 males, 87 females, mean age 57.8) who underwent surgery for ASD were identified. Decompression with extension of fusion was performed in 115 cases (68%) and decompression without fusion in the remaining 55 (32%). 9.9% of patients undergoing fusion required a subsequent operation compared with 26.3% of patients undergoing decompression alone ($p=.004$). 53% of the patients requiring a subsequent operation in the decompression group required fusion at the previously decompressed level. 82% of patients in the fusion group with preoperative motor weakness improved, compared to 61% in the decompression group ($p=.03$). Postoperative reductions in VAS and ODI scores did not differ significantly between the two groups.

Conclusions: Decompression with fusion is associated with fewer subsequent surgeries than decompression alone in the management of adjacent segment disease.

624. Negative Pressure Wound Therapy Reduces Incidence of Wound Infection and Dehiscence After Long-Segment Thoracolumbar Fusion

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Introduction: Wound dehiscence and SSI's can have a profound impact on patients. Negative Pressure Wound Therapy (NPWT) exposes the wound site to negative pressure, resulting in the improvement of blood supply, removal of excess fluid and stimulation of cellular proliferation of granulation tissue. The primary aim of this study was to assess the incidence of wound infection and dehiscence in deformity patients undergoing thoracolumbar fusion before and after the routine use of NPWT.

Methods: The study included all adult patients undergoing thoracolumbar fusion for spinal deformity over six years at Duke University Medical Center by the senior author (C.B.). In 2012, a categorical change was made by the senior author (C.B.) that included the post-operative routine use of NPWT after primary wound closure in all long-segment spine fusions. Prior to 2012, NPWT was not utilized. We retrospectively reviewed the first 46 cases with NPWT and compared them with the immediately preceding 114 cases to assess incidence of wound infection and dehiscence.

Results: 160 (NPWT:46, non-NPWT:114) thoracolumbar spine fusions were performed for deformity correction. Baseline demographics and comorbidities were similar between cohorts. Compared to the non-NPWT cohort, a 50% decrease in the incidence of wound dehiscence was observed in the NPWT cohort (NPWT:6.38% vs. non-NPWT:12.28%, $p=0.02$). Similarly, compared to the non-NPWT cohort, the incidence of post-operative SSIs was lower in the NPWT cohort (NPWT:10.63% vs. non-NPWT:14.91%, $p=0.04$).

Conclusions: For patients undergoing long-segment thoracolumbar fusion, negative pressure wound therapy was associated with a reduction in the incidence of post-operative wound infection and dehiscence.

625. To Operate or Not?: A Meta-Analysis of Surgical Outcomes in 95 Patients with Parkinson's Disease Following Spinal Fusion

Christopher Ashot Sarkiss, MD; John Caridi, MD (New York, NY)

Introduction: Degenerative spondylosis and kyphoscoliosis are increasingly recognized entities in patients with Parkinson's disease. Surgical treatment with spinal fusion can be complicated due to poor bone quality and muscular dysfunction in this patient population.

Methods: We performed a meta-analysis using the PubMed and Google Scholar search engines investigating Parkinson's disease and spinal fusion surgery from the period of 2000-2013. A total of 95 patients with Parkinson's disease who underwent spinal fusion surgery were reviewed.

Results: 47 out of 95 patients (49%) were judged to have satisfactory outcomes. Poor outcomes were noted in the remaining 51% and included but were not limited to pseudoarthrosis, hardware failure/pullout, development of adjacent level disease, persistent kyphosis or sagittal imbalance, and no improvement or worsening in their postoperative visual analog pain scale. Out of this subset of unsatisfactory outcomes, 32 out of 95 patients (34%) required revisions.

Conclusions: It remains unclear whether Parkinson's patients benefit from spinal fusion surgery to correct their spinal deformities. Further prospective research is warranted to investigate surgical outcomes in this subset of patients.

626. Combined Neonatal Enzyme Replacement Therapy and Simvastatin for Treatment of Cervical Spine Intervertebral Disc Disease in Mucopolysaccharidosis I Dogs

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Introduction: Mucopolysaccharidosis I (MPS I) is a genetic disorder affecting children, characterized by accumulation of poorly degraded glycosaminoglycans, and is associated with significant cervical spine disease, leading to cord compression and kypho-scoliosis. The effect of enzyme replacement therapy (ERT), currently used clinically for MPS I patients, on spine disease is as yet unclear, as many patients commence treatment after spine disease is established. The objective of this study was to determine whether initiation of ERT in the neonatal period alone or in combination with oral simvastatin (ERT+S) could attenuate intervertebral disc disease in MPS I, using the naturally occurring canine model.

Methods: Four groups were studied (all $n=5$): normal controls; MPS I untreated; MPS I ERT (0.58mg/kg IV IDUA, weekly) treated; and MPS I ERT+S (2mg/kg, daily) treated. Treatments commenced at 1 week-of-age, and all animals were euthanized at 12-months-of-age. Semi-quantitative grading schemes were used to evaluate disc condition and spinal cord compression from MRIs, and disc height index (DHI) was determined from x-rays.

Results: DHI was significantly lower, and disc grade and cord compression severity were all significantly higher for untreated compared to normal. ERT and ERT+S resulted in significant improvements in all parameters. For both disc grade and spinal cord compression severity, ERT+S was modestly, but not significantly, improved relative to ERT alone.

Conclusions: These results demonstrate that ERT commenced from a very early age partially attenuates cervical spine intervertebral disc disease in MPS I, in agreement with previous

findings. Our findings here also suggest that supplementation with simvastatin provided some additional benefit over ERT alone.

627. Electrophysiologic Monitoring as Diagnostic and Therapeutic Tools in Spinal Surgery

Curtis J. Rozzelle, MD, FAANS; Beverly Walters, MD, MSC; Mark Hadley, MD (Birmingham, AL)

Introduction: Electrophysiological monitoring techniques allow assessment of somatosensory evoked potentials (SEP), motor evoked potentials (MEP), and electromyography (EMG). Theoretically, alterations in recordings during spinal cord/spinal column surgery implicate an impending spinal cord injury that may be prevented to allow better outcome following surgery. This review examines the medical evidence on this important topic.

Methods: A National Library of Medicine computerized literature search from 1966 to 2013 was undertaken to identify English language clinical reports of intraoperative monitoring (IOM) for spinal surgery. Titles and abstracts were reviewed and relevant articles were selected for analysis. Additional citations were extracted from the reference lists of the remaining papers, resulting in 59 manuscripts which form the foundation for this review. Clinical studies were categorized as evaluating IOM as a diagnostic modality or a therapeutic intervention.

Results: Eleven studies offer Class I medical evidence that multi-modality IOM is a reliable diagnostic tool to describe spinal cord integrity and that MEP is superior to SSEP. Nineteen studies offer Class III medical evidence that multi-modality IOM may improve neurological outcome. No Class I or II evidence exists to establish a therapeutic relationship between IOM and spinal surgery neurological outcome.

Conclusions: Multi-modal IOM is a valid diagnostic adjunct to describe spinal cord integrity during spinal cord/column surgery and is recommended if used for this purpose. While IOM may detect neurological injury during spinal surgery its use has not been shown to result in improved neurologic outcomes and it cannot be supported as a standard of care or Class I recommendation.

628. Indirect foraminal decompression following anterior lumbar interbody fusion (ALIF): a prospective study using a new Pedicle to pedicle (P-P) technique

Prashanth J Rao (Mascot, Australia); Monish Maharaj, MBBS; Manil Abeygunasekera, MBBS; Ralph Mobbs, MD (Sydney, Australia)

Introduction: To measure indirect neural foraminal decompression in surgically operated patients following anterior lumbar interbody fusion using radiographic measurement. Introduction A frequently quoted advantage for ALIF is indirect foraminal decompression although there are very few studies substantiating this statement. Also there are no clinical studies employing a standardized method to measure the foraminal area and correlating with disc height (DH) parameters. This study is proposed to measure the degree of indirect foraminal decompression radiologically using a standardized method and correlate with intervertebral disc parameters.

Methods: This is an analysis of a prospectively maintained database of patients undergoing an ALIF from 2010 to 2013. Pre-and postoperative CT scans were employed to obtain a standardized foramen snapshot using the pedicle to pedicle (P-P) technique and measurements obtained using image j software. Radiological parameters such as disc height, local disc angle(LDA)

and lumbar lordosis (LL) were measured using radiographs and Surgimap software.

Results: 140 patients with 184 levels were operated. ALIF resulted in a statistically significant ($p < 0.01$) improvement in foraminal dimensions (area= 67%, height=21% and width=38%). Other parameters also significantly improved including ADH (90%), PDH (77%), LDA and, LL (6%). PDH change correlated significantly with foraminal height improvement only. Statistically the P-P technique presented with here has intra- and interclass observer reliability.

Conclusion: ALIF results in significant indirect foraminal decompression based on a new P-P technique. Restoration of posterior disc height is a key factor in reestablishment of the foraminal height.

629. Does Minimally Invasive Posterior Instrumentation (PPI) Prevent Proximal Junctional Kyphosis (PJK) in Adult Spinal Deformity (ASD) surgery? A Prospectively Acquired Propensity Matched Cohort Analysis

Kai-Ming Fu, MD, PhD (New York, NY); Praveen Mummaneni (San Francisco); Wang Michael (Miami); Virginie LaFage (New York); David Okonkwo (Pittsburgh); Juan Uribe (Tampa); Neel Anand (Los Angeles); Shay Bess (Denver); Adam Kanter (Pittsburgh); Christopher Shaffrey (Charlottesville)

Introduction: Proximal junctional kyphosis (PJK) is an unwanted complication of ASD surgery. Multiple theories exist why PJK occurs. One potential contributor is damage to the paraspinal musculature and intervertebral stabilizers frequently disrupted during exposure and screw placement. This study aims to investigate the effect of PPI vs. Open screw placement on PJK development.

Methods: 280 pts in 2 prospective databases (MIS n=85; OPEN n=195) were retrospectively reviewed, divided in 2 separate approaches and propensity matched for pelvic incidence – lumbar lordosis (PI-LL) and change of LL. Inclusion criteria: age <45, Cobb <20°, min 1 yr follow up. Groups defined as: 1)cMIS-lateral interbody fusion (LIF) with PPI (n= 31) and 2)Hybrid (HYB)- LIF followed by open posterior instrumentation (n=31). PJK was defined as Proximal junctional angle (PJA) <10° and change post op <10°.

Results: A mean of 4.1 levels were fused (range 2-6). The mean age was 64 years and mean BMI was 26.1. Mean follow-up was 27.5 months. There was no preop difference between groups for LL-PI or SVA. Both groups showed significant improvement in LL (cMIS: 33°-41°; HYB: 35°-44°; $p < 0.001$) and PI-LL (cMIS:19.7°-12.4°; HYB: 19.6°-7.4°) and significant difference in PT. SVA remained physiologic for cMIS (29-26mm) and improved in HYB (54-31 mm; $p=0.024$). The cMIS group had a smaller change in PJA (+1.3°) than HYB (+6°) ($p=0.005$). PJK developed in 19.4% of HYB patients and 0% in cMIS ($p < 0.01$). Both groups saw significant improvement in ODI (cMIS 39 to 20.1; HYB 46.7 to 30; $p < 0.001$).

Conclusions: The addition of PPI seems to have a protective effect on the development of PJK. The analysis controlled for preoperative sagittal alignment as well as for correction of PI-LL. HYB was effective in restoring sagittal global alignment and cMIS in maintaining it.

Philip L. Gildenberg Resident Award

630. Striatal Stimulation for Enhancement of Recovery in a Rodent Traumatic Brain Injury Model

Joshua Paul Aronson, MD; Husam Katnani, PhD; Jimmy Yang, BA; Matthew Thombs, BA; Ryan Margolin; Emad Eskandar, MD (Boston, MA)

Introduction: Behavioral and physical therapy after traumatic brain injury (TBI) to rehabilitate cognitive and motor function is limited by lack of information optimizing neural recovery at the cellular and systems level. The striatum plays a critical role in learning and motivation, key aspects of recovery from TBI. We hypothesized that intermittent stimulation of the ventral striatum could enhance behavioral performance in a rodent TBI model.

Methods: Forty-eight C57BL/6 mice were used. Thirty-two mice underwent right parietal craniotomy and controlled cortical impact over the right parietal cortex and hippocampus. Sixteen mice underwent craniotomy but not cortical impact (Control Group). Seven days later, electrodes were implanted in all mice ipsilateral to the TBI, with the contact in the nucleus accumbens (NAcc). Mice were tested in the Morris Water Maze for five consecutive days. Sixteen mice received 5 seconds of 50 μ A biphasic stimulation (Stimulation group) upon finding the platform (130 Hz, 160 μ s pulse width) and fifteen did not receive any stimulation (Sham group).

Results: All mice demonstrated decreased escape latency over a 5-day testing period. Mean latencies at days 3-5 was significantly improved in the stimulation group compared with the sham group ($p < 0.01$). Percentage improvement from days 1 to 5 was $63.5 \pm 4.4\%$ ($\pm$ SE) in the control group, $46.1 \pm 3.2\%$ in the stimulation group, and $27 \pm 4.2\%$ in the sham group.

Conclusions: Intermittent stimulation of the NAcc can enhance behavioral performance in a rodent model of TBI, with a significant improvement in performance compared to non-stimulated TBI control mice.

631. Functional subpopulations of neurons within the human dorsal anterior cingulate cortex

Sameer A. Sheth, MD PhD (New York, NY); Emad Eskandar, MD (Boston, MA); Guillermo Horga, PhD (New York)

Introduction: The medial prefrontal cortex, especially the dorsal anterior cingulate cortex (dACC), plays an important role in decision-making in the setting of conflicting choices. Previous human fMRI studies and monkey single neuronal recordings have arrived at opposing conclusions regarding the specific role of the dACC. We sought to resolve this longstanding discrepancy using human dACC single neuronal recordings.

Methods: Six subjects underwent dorsal anterior cingulotomy for severe, treatment-refractory obsessive-compulsive disorder. We recorded single neuronal firing rates during microelectrode recordings in the dACC while subjects performed a Stroop-like decision-making task. We analyzed firing patterns using a general linear model to test for neuronal selectivity for relevant behavioral events, including 1) the amount of cue-related conflict; and 2) response choice.

Results: We isolated 59 individual neurons, with a mean firing rate of 5.7 Hz. Seventeen neurons (29%) significantly modulated their firing rate according to the amount of conflict present in the cue. Fifteen neurons (25%) modulated their firing based on the preferred response choice. Only four neurons (7%) encoded

both effects, and zero showed a significant interaction term. A timecourse plot of the model regressor coefficients demonstrated a peak in the conflict effect soon after cue presentation, and a smaller peak in the response effect after the choice.

Conclusions: This study is the first to demonstrate functional neuronal subpopulations within the human dACC. One subpopulation of dACC neurons encodes perceived conflict within the environmental context, and the other encodes preferred response choices. These data suggest a functional segregation between sensory and motor aspects of decision-making, and resolve previous discrepancies about the role of the dACC in this cognitive process.

632. Intralaminar Thalamic Deep Brain Stimulation Ameliorates the Memory Deficit and the dendritic regression in β -Amyloid infusion Rats

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Introduction: Intralaminar thalamic deep brain stimulation (ILN-DBS) has been shown to improve cognition and spatial memory acquisition through neuronal activation and structural plasticity of brain. Here, we explored whether ILN-DBS attenuates the dementia-associated alterations in β -amyloid infusion rats.

Methods: Intraventricular β -amyloid protein infusion in rats were used as the dementia model. The spatial memory acquisition of the rats was evaluated with Morris water maze task (WMT). Expressions of the glutamatergic post-synaptic density protein 95 (PSD95) in the medial prefrontal cortex (mPF) and CA1 hippocampus was examined to assess excitatory connectivities. Morphologically, the dendritic arbors and spines of the pyramidal neurons in the studied areas were revealed with intra-cellular dye injection and analyzed accordingly as well.

Results: ILN-DBS significantly improved the escape latency in WMT of amyloid-infusion rats to a level comparable to that of the normal control rats. In addition, ILN-DBS reversed the reductions of PSD95 in the mPF and CA1 hippocampus seen in β -amyloid infusion rats to levels comparable to those of the normal controls. Morphologically, ILN-DBS restored the densities of dendritic spines on the pyramidal neurons in mPF and CA1 hippocampus of the β -amyloid infusion rats to levels comparable to those of the normal controls as well.

Conclusions: ILN-DBS effectively reversed the deterioration in cognition and the loss of dendritic spines and glutamatergic synapses in the mPF and hippocampus, hallmarks of dementia, resulted from β -amyloid toxicity. This translational study supports the application of DBS to ILN on dementia and neurodegenerative diseases that cause severe cognitive dysfunction.

633. Sensing-enabled hippocampal deep brain stimulation in idiopathic nonhuman primate epilepsy

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Introduction: Epilepsy is a debilitating condition affecting 1% of the population worldwide. Medications fail to control seizures in at least 30% of patients and deep brain stimulation (DBS) is a promising alternative treatment. A modified clinical DBS hardware platform was recently described (PC+S) that

allows long-term recording of electrical brain activity such that the acute and chronic effects of DBS on neural networks can be examined. In this study, idiopathic epilepsy was characterized for the first time in a nonhuman primate (NHP) implanted with the PC+S device, and the effect of DBS on local field potential (LFP) activity was examined.

Methods: Clinical DBS electrodes were implanted in the hippocampus bilaterally in an NHP with idiopathic epilepsy. Baseline LFP recordings were collected for seizure characterization using the PC+S device. The effects of variable DBS stimulation paradigms delivered acutely under ketamine anesthesia were examined, in order to establish settings for subsequent chronic testing in the awake, normally behaving state.

Results: Real-time automatic detection of ictal events was demonstrated using the PC+S device and validated by concurrent visual observation of seizure behavior. Seizures consisted of large-amplitude 8-25Hz oscillations originating from the right hemisphere and quickly generalizing, with an average duration of 49 ± 7 seconds and occurrence of 8.5/week. Variable stimulation parameters resulted in either suppression of local neural activity or seizure induction, during stimulation under ketamine anesthesia. Chronic stimulation in the awake animal was studied to evaluate the effects of predicted therapeutic stimulation configurations on seizure activity.

Conclusions: This is the first electrophysiological characterization of idiopathic epilepsy using a next-generation clinical DBS system that offers the ability to record and analyze neural signals from the stimulating electrode. These results will inform further development of this technology and should ultimately provide insight into therapeutic mechanisms of DBS for epilepsy.

634. Deep Brain Stimulation (DBS) in Tourette Syndrome (TS)

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Introduction: Tourette Syndrome (TS) now recognized affecting 1% of the worldwide population. Symptomatology is complex and variable including motor, sound tics and in majority of the cases psychopathologies (mostly OCD/OCB, depression, anxiety, NOSI, SIB), responsible of variable degree of Social Impairment. In patients with severe disease and who are drugs treatment-refractory DBS has been applied.

Methods: Since November 2004 in the Functional Neurosurgery Unit at Galeazzi Hospital, Milan, 50 patients (age min/max 16-58; 35male/15female) have been treated with DBS. Four different target have been used: Vo-CM/Pf, NA-ALIC, antero-medial and posteroventral Gpi. The targets were chosen according to the symptoms presented by the subjects.

Results: Long term follow-up (2-9 years) showed significant reduction in tic severity ($p < 0.001$), and improvement in obsessive compulsive behaviours ($p = 0.003$), anxiety ($p < 0.001$) and depression ($p < 0.001$). Social Impairment resulted significantly reduced (YGTSS, Y-BOCS, DCI, PUTS, GTS-QOL). In almost 40% of the patients the medication was reduced or stopped after DBS. Overall positive results has been 52% on tics and 60% on OCB. The long term patients self assessment versus medical scales evaluation showed a significant unexpected differences. No major clinical side effects were recorded. No intracranial hematoma has been reported. In 8 patients DBS electrodes/IPG have been removed due to erosion/infection (2 patients) and later replaced, while in 1 patient the complication was hardware related.

Conclusions: At long term follow-up DBS was successful in terms of significant improvement in tics, in behavior and could be

proposed as specific treatment in drug refractory TS patients. The Quality of the Life improved as well as the Social Impairment. The importance of patient selection and choice of target is discussed in details on the light of the positive results.

635. Clinical outcomes after anterior thalamic stimulation for medically refractory epilepsy

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Introduction: The SANTE trial demonstrated the effectiveness of anterior thalamic nucleus (AN) stimulation for treatment of medically refractory epilepsy. This procedure is currently under regulatory review by the Food and Drug Administration for approval as a standard treatment for these patients. Long-term outcomes after stimulation are desirable to demonstrate the durability of this procedure.

Methods: Consecutive patients who underwent AN DBS implantation by the senior author were identified in our surgical database. Standardized data abstraction sheet were developed to accurately obtain information of interest. Besides the demographic variables data regarding the seizure frequency, medication usage (total number and changes in dosage) and stimulation parameters were abstracted. The Engle classification was used to classify post-operative outcomes.

Results: Seventeen patients (8 females and 9 males) underwent DBS implantation between 1997-2013. The mean age of the cohort was 32 ± 9 year with a mean follow-up of 5.1 years (6 months-16 years). Majority of patients had focal onset seizures with a mean seizure frequency of 47 seizures per month (range 3-225 seizures per month). Patients were, on an average, taking more than three antiepileptic medications preoperatively and tried more than 6 meds on an average in the past. At the last follow-up, the stimulation was 'on' in 12 patients. Among these 7 patients had significant seizure reduction from stimulation (29-91% decrease from baseline), three patients had worsening of seizure frequency (25-33% increase from baseline) and two patients had stable seizure frequency. Overall 10 (58.9%) patients had Engle 2 or 3 outcome while 7 patients had Engle 4 outcome.

Conclusions: Chronic AN stimulation is an effective and durable treatment option for patients with medically refractory epilepsy who are not candidates for surgical resection.

636. Comparative study of efficacy and safety between radiosurgical callosotomy and open callosotomy in a third-level neurological center

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Introduction: Radiosurgical corpus callosotomy is a new non-invasive, apparently safe and successful option to achieve control in drug-resistant severe epilepsy that involves drop attacks. There are no studies that compare efficacy and safety of this technique compared to surgical corpus callosotomy. This study objective is to describe and compare the clinical variables, safety and efficacy of both techniques

Methods: Retrospective analysis (2004-2011) of patients who underwent either radiosurgical corpus callosotomy (RC) or surgical corpus callosotomy (SC) was performed. Clinical, neurophysiological, neuroimaging and follow up variants were

obtained and analyzed using descriptive statistics (means and standard deviations) as well as Fisher's exact test for paired groups.

Results: 18 subjects were included 9 [7 males] in SC and 9 [3 males] in RC. The average age at time of surgery was 21.3 ± 9.08 years in RC and 25.5 ± 7.97 in SC. Average time to diagnosis was 2.04 ± 2.30 y in RC and 3.14 ± 2.92 y in SC. 17 out of 18 subjects (94%) were diagnosed with cryptogenic Lennox-Gastaut Syndrome and multi-focal epileptic activity. To perform the surgery in the RC group a mean dose of 40.88Gy (± 2.66) were used. Follow-up was performed at 10.3 (± 6.4) months. There was a decline in monthly seizure frequency for RC (-66.6%) as well as for SC (-71.1%) with no significant difference between them ($p=0.064$). Tonic and Atonic seizures were the most reduced in both groups. In RC 3 subjects presented with complications; There were no complications reported on SC.

Conclusions: Radiosurgical corpus callosotomy shows similar efficacy compared with surgical corpus callosotomy in reducing crisis frequency in subjects with drug-resistant epilepsy that involves drop-attacks. Even though there is a major incidence of complications in the RC group. More prospective alleatory studies with a larger study population are required to confirm this finding.

637. Scanning Electron Microscopy of Chronically Implanted Silicon-Based Intracortical Microelectrode Arrays in Non-Human Primates

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Introduction: Signal attenuation is a major problem facing intracortical microelectrode arrays (MEA) used for chronic neuroprosthetic applications. Studies suggest that failure is due to gliosis around the electrode tips, however material failures are often overlooked. We examined a series of chronically implanted MEAs using scanning electron microscopy (SEM) after explantation from non-human primates in order to identify failure modes.

Methods: Eight silicon MEAs were implanted into five Rhesus Macaques. MEAs remained in-situ for 37, 554, 554, 639, 994, 994, and 1051 days. MEAs were explanted and placed in NaCacodylate fixative, then ethanol. They were dried using a liquid CO₂ critical point dryer, sputter-coated with 30nm of Au/Pd, then imaged. Three control MEAs were also imaged.

Results: SEM showed progressive tissue encapsulation on all arrays over time. Cells were rarely seen near the tips. Many cells were found along the base. Early implants had macrophages, but later implants had considerably more fibroblasts. Large collagen fibers were often suspended between electrodes. Parylene cracks became more frequent over time and delamination from the platinum tips was common. Later implants showed tissue ingrowth. Delamination at the silicone-parylene border was seen in some arrays. Later arrays showed possible platinum degradation and erosion of underlying silicon.

Conclusions: Intracortical MEAs are exposed to an aggressive foreign body reaction and materials clearly degrade over time. The reactive oxidative chemicals released by immune cells may play a role in this interaction. Future work should look to quantify how cellular reactions affect these materials in-situ.

638. Convection Enhanced Delivery Enhances the MRI Visualization of Basal Ganglia for Stereotactic Surgery

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Introduction: Stereotactic surgery depends upon precision. Traditionally, treatments are confirmed with awake intraoperative clinical and electrophysiologic verification; but image-guided surgery has more recently been proposed as CT and MRI systems become available in the operating room. We are developing a new method which uses convection enhanced delivery (CED) to manipulate the extracellular space, thus enhancing the MR imaging of deep, subcortical structures. This technique could greatly improve the accuracy and success of stereotactic surgery, and could eliminate the reliance on awake surgery.

Methods: An FDA-approved, EvitarTM intracerebral catheter was stereotactically inserted into basal ganglia in ten swine, so that various infusates could be convected with concurrent MRI at a flow rate of $<5\mu\text{L}/\text{min}$. The infusions were monitored every 15 minutes with T2 weighted images. The swine were then clinically observed and sacrificed for histological analysis.

Results: Infusion highlights the distinction between white and gray matter – thus enhancing the visualization of deep brain nuclei and anatomy. As the volume of distribution increased, the basal ganglia nuclei and deep brain anatomy became well defined. Histological analysis demonstrated no damage to neurons when the correct infusate is chosen.

Conclusions: This work provides the initial foundation of a novel approach for higher precision visualization of the deep brain structures during stereotactic procedures. Convective infusion alters the extracellular water content of brain for improved MR imaging. Preclinical safety testing in a large brain, animal model is now complete, and a clinical trial is being designed to assess the feasibility in patients with movement disorders.

639. Brain Computer Interface Technology for Patients Suffering Disorder of Consciousness

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Introduction: Patients with disorders of consciousness (DOC) usually stay in rehabilitation institutions several months before they are released to professional home-care or to their homes. For that it would be advantageous to have a system that can assess cognitive functions and potentially allows patients to communicate. The aim of this study was to test if locked-in syndrome (LIS) patients and healthy controls could use a vibrotactile brain-computer interface (BCI) system to establish communication.

Methods: We designed an EEG-based system by using (i) auditory evoked potentials (AEP), (ii) vibrotactile (VT) evoked potentials and (iii) motor imagery (MI) experimental protocols. Auditory and vibrotactile experiments were designed to elicit P300 responses whereas the motor imagery experiment allowed to analyze event-related desynchronization/synchronization (ERD/ERS) driven by motor imagination. Six LIS patients and ten controls performed an experimental oddball task to elicit a P300 response by mentally counting deviant stimuli. Then, they had to answer five questions by counting the vibrations on the right wrist for 'yes' or the left wrist for 'no'.

Results: All participants were able to elicit a P300 response using the vibrotactile paradigm. In the counting task, four patients

and all controls achieved an accuracy of 100 % and in the question task, one patient and five controls reached 100 % accuracy.

Conclusion: This study shows the feasibility of a vibro-tactile based BCI system for communication in healthy subjects and LIS patients. The combination of P300 and MI based paradigms forms a testing battery that can be used for the detection of consciousness in non-communicating patients.

640. Potentiating Cortico-Cortical Connectivity Between Distant Cortical Locations with Activity Dependent Stimulation in the Rat

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Introduction: Facilitating recovery following CNS trauma remains an ongoing challenge. Electrophysiological techniques that promote recovery, such as transcranial magnetic, direct-current and epidural stimulation, have met with some success (Edwardson 2013). Recently, encouraging results have been achieved (Guggenmos 2012, Jackson 2006) using activity-dependent stimulation (ADS), founded upon Hebbian plasticity. Our study expands upon this by potentiating connectivity using ADS in the anesthetized rat within a single four-hour session.

Methods: Rostral forelimb area (RFA), barrel field (BF) and forelimb somatosensory (S1) were identified in sixteen healthy, ketamine-sedated Long-Evans rats. In each, RFA neuronal activity was recorded using a sixteen-contact intracortical microelectrode (NeuroNexus), and stimulation was applied to either S1 or BF using either ADS or random stimulation. For ADS, RFA action potentials triggered stimulation following 10 ms delays, whereas random stimulation was delivered at 10 Hz.

Results: BF-RFA ADS facilitated more stimulus-triggered spikes per stimulus (0.11 ± 0.13) than random stimulation (0.06 ± 0.09 , Mann-Whitney $p = 0.016$), suggesting greater cortico-cortical facilitation, and BF-RFA ADS trigger channel activity (0.271 ± 0.187) was greater than non-trigger channel activity (0.0978 ± 0.123 , Mann-Whitney $p = 0.026$), demonstrating cortico-cortical potentiation via synchronous firing specificity. Finally, ADS facilitated inhibitory S1-RFA connectivity and excitatory BF-RFA connectivity.

Conclusions: Our results reveal ADS can induce significant connectivity modification between both BF-RFA and S1-RFA within a single recording session, suggesting Hebbian influence on the circuitry. Facilitating connectivity using this paradigm provides the foundation for assessing optimal stimulus parameters for implementing ADS, and may in the future aid in directly facilitating cortico-cortical entrainment.

641. Ten Year Hearing Outcomes Following Gamma Knife Radiosurgery for Acoustic Neuromas

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Introduction: Treatment paradigms and research into acoustic neuromas emphasize minimizing adverse events and preserving neurological function, particularly hearing in patients with serviceable hearing. Few studies have analyzed hearing preservation at ten years after stereotactic radiosurgery (SRS).

Methods: A retrospective analysis of 69 patients who underwent Gamma Knife SRS patients between 1996-2003 was performed. All patients had Gardner Robertson grade I or II hearing. Primary

end points were a ten year audiogram documenting preserved hearing or an audiogram showing loss of serviceable hearing prior to ten years.

Results: Sixteen patients, (23%) had documented grade I or II hearing at ten years. Grade 3 hearing was found in 40, grade 4 hearing was found in 11, and 2 patients were deaf. There was no significant difference in age, sex, tumor volume or tumor margin dose between those who retained hearing and those with reduced or absent hearing. Two patients required surgical removal for progressive disease, five patients developed trigeminal sensory dysfunction and 97% retained normal HB Grade 1 function

Conclusions: In this experience Gamma Knife SRS achieved long term tumor control in 97% of acoustic neuromas and preserves Grade 1 or 2 hearing in 23% of patients. Hearing preservation at levels greater than grade 5 were found in 97% patients. Those who maintained serviceable hearing tended to have higher SDS and lower PTA preoperatively. Additional analysis of margin dose, volume, timing of SRS, cochlear dose may increase the number of future patients with high level long term hearing.

642. Random Waveform Brain Stimulation for Seizure Control

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Introduction: Brain stimulation has been investigated for the control of epilepsy but the technology has developed from cardiac stimulation devices and therefore utilizes a charge-balanced pulse stimulation waveform. Unlike the heart, the brain demonstrates non-linear waveform activity under normal conditions and loses its non-linearity when seizures occur. This study was designed to determine if random waveform stimulation or simultaneous stimulation through multiple electrodes would control seizures better than pulse waveforms in an animal model.

Methods: Sixteen Sprague-Dawley rats had eight cortical electrodes surgically implanted in the right frontal lobe, were injected with intra-cortical kainic acid after one week of recovery, and developed baseline seizures. By random selection each rat received one of five conditions; no stimulation, pulse stimulation through one or eight electrodes, or random stimulation through one or eight electrodes. The stimulation was performed at a previously determined voltage that was sub-threshold for motor signs. The rats had a 10-minute baseline period of seizures followed by 30 minutes of stimulation then 10 minutes of observation following stimulation. Clonic jerks were counted as a measure of seizure duration.

Results: During stimulation there was a reduction in seizure activity compared to baseline using the random waveform (1 electrode 53%, 8 electrodes 41%) and an increase in seizure activity compared to baseline using the pulse waveform (1 electrode 150%, 8 electrodes 154%) but neither reached statistical significance.

Conclusions: Random-waveform brain stimulation may prove more effective in seizure control than standard pulse-waveform brain stimulation.

643. Impact of Microelectrode Recording on Health Outcomes following Deep Brain Stimulation Surgery for Parkinson's Disease

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Introduction: Currently, single-neuron microelectrode recording (MER) is widely used to improve anatomic accuracy of deep brain stimulation (DBS) lead placement for the treatment of Parkinson's Disease (PD). With increasing accuracy of MRI/CT-only-based targeting, controversy still exists over the relative merits of MER, given the increased operative time and need for monitored awake surgery.

Methods: We designed a retrospective cohort analysis using the Thompson Reuter's MarketScan database. Patients selected were over age 18 and underwent DBS between the years 2000 and 2009 for PD. Patients were then separated into two cohorts based on whether or not they received intraoperative MER. Rates of post-operative complications, lead revision, annual healthcare cost, and reprogramming time were examined.

Results: Of the 1,265 patients that met our inclusion criteria, 1,181 (93.7%) underwent DBS-surgery with MER and 80 (6.3%) without MER. Post-operative results showed no significant differences in hemorrhagic rate (MER: 2.54% vs. non-MER: 2.50%, $p=0.984$), lead revision rate (MER: 12.53% vs. non-MER: 11.25%, $p=0.728$) and annual healthcare cost (MER: \$159K/yr vs. non-MER: \$129K/yr, $p=0.227$) over the study period. However, non-MER patients, on average, required less post-operative programming time (mean: 4.2hours vs. 5.5hours for MER, $p=0.035$).

Conclusions: There does not seem to be a difference in lead revision rate, hemorrhage rate or overall healthcare cost. As imaging technology continues to improve, the ability to provide non-MER-based DBS targeting to select patients along with an understanding of its relative risk and impact on health outcomes will be essential.

644. Assessing memory lateralization using resting state functional connectivity MRI in pediatric epilepsy surgery patients

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Introduction: Memory mapping is an integral part of the presurgical workup for epilepsy patients. Functional MRI (fMRI) has been best established for mapping motor and sensory cortex but has also been useful for language and memory mapping. However, fMRI can be technically challenging, especially in the pediatric population, because it requires that patients cooperate with tasks needed to elicit activation. Resting state functional connectivity MRI (fcMRI), which does not require such cooperation, has shown promise as a tool for assessing eloquent cortex. We sought to compare memory fMRI with resting state fcMRI in the assessment of memory lateralization in pediatric patients.

Methods: We performed a retrospective review of 19 patients who had memory fMRI and resting state fcMRI at Seattle Children's Hospital from 2010 to 2013. For fcMRI, we computed a region of interest (ROI) analysis using the Retrosplenium and the Posterior Cingulate Cortex (PCC) as seeds. Lateralization index (LI) scores were calculated from memory fMRI and fcMRI data

for masks covering the hippocampus and the parahippocampal gyrus.

Results: LI scores calculated from the activation of the posterior hippocampus and parahippocampal gyrus during memory fMRI correlated with LI scores from resting state fcMRI using the Retrosplenial seed with a correlation coefficient (r) of 0.5 ($p<0.03$). We did not find a statistically significant correlation using the PCC seed.

Conclusions: Using the Retrosplenium as a seed, resting state fcMRI could potentially be used to assess memory lateralization during epilepsy surgery workups. This would be particularly beneficial for patients who have difficulty participating in task-based fMRI.

645. Postnatal erythropoietin mitigates impaired cerebral cortical development following subplate loss from prenatal hypoxia-ischemia

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Introduction: Premature birth causes debilitating cognitive and behavioral abnormalities resulting from impaired cortical circuit function. Transient subplate neurons facilitate thalamocortical connections, refine axonal pathways, and promote essential inhibitory circuit formation. We hypothesized that subplate neuronal loss from very preterm birth disrupts cortical inhibitory circuit formation in developing brain by limiting postnatal cortical KCC2 oligomer upregulation and GABAAR subunit maturation.

Methods: On embryonic day 18, transient systemic hypoxia-ischemia (TSHI) was induced via uterine artery occlusion. Pups were given either intraperitoneal vehicle (saline) or erythropoietin (2000U/kg/day) on postnatal days 1-5. Neuronal loss, protein expression and motor function was assayed ($n=6$ or more/group for all) using stereological, Western blotting, slice culture, and motorized treadmill techniques. Statistical analysis was performed with two-way ANOVA with p less than 0.05 significant.

Results: Prenatal TSHI induced a 45percent loss of subplate P2 Nurr1+ immunolabeling compared to shams ($p=0.038$), along with increased subplate NeuN/TUNEL double labeling, indicative of subplate neuronal apoptosis. At P11, in vivo cortical layer IV GABAAR subunit maturation is impaired with lower GABAAR α 2 levels ($p=0.002$), together with a 33percent reduction in cortical layer IV KCC2 oligomers ($p=0.001$). At P28, layer IV KCC2 loss is sustained, and motor deficits observed ($p=0.001$). Postnatal EPO treatment attenuated KCC2 and GABAAR subunit loss, and restored motor function.

Conclusions: Impaired inhibitory circuit formation is implicated in developmental cognitive delay from prematurity. EPO treatment after injury restores KCC2 levels and GABAAR subunit maturation, and may provide a clinically viable intervention for diseases with sustained KCC2 loss, including encephalopathy of prematurity, chronic pain and neurodegenerative disorders.

646. Finite Element Analysis of the Pediatric Occipitotlantoaxial Complex

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Introduction: The biomechanics of the pediatric occipitotlantoaxial complex (Oc-C1-C2) are poorly understood, mostly due to lack of pediatric spinal cadaveric tissue available

for laboratory analysis. Finite element (FE) models can provide biomechanical data, but ultimately these models need to be validated with experimental testing. We describe our method of developing a FE model of the pediatric Oc-C1-C2 complex, using an established adult FE model for comparison and cross-validation.

Methods: Segmentation of volumetric CT data from a normal pediatric spine was performed using Amira software. Polygonal surfaces were generated from the bones, cartilage, and ligaments of the Oc-C1-C2 complex. The surfaces were imported into TrueGrid software for three-dimensional hexahedral meshing. Solid and shell elements were added to represent ligamentous structures. FEBio software was used for model generation and execution of subsequent FE analyses.

Results: The model was validated by assigning adult material properties to anatomical structures and comparing the torque/rotation response of the model to adult experimental data. Parameter studies were performed to establish the decrease in ligament and cartilage material properties that are probable for the pediatric Oc-C1-C2 complex.

Conclusions: We report the development of a FE model of the pediatric Oc-C1-C2 complex based on an open-source framework. Both the results from this research and the models created will be disseminated for use by other institutions.

647. Risk factors for traumatic carotid injury diagnosed by CT Angiography in the pediatric population

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Introduction: CTA is frequently performed in children after cranial trauma to evaluate for cerebrovascular injury, but patients are exposed to high doses of radiation and the at-risk population is poorly defined. We sought to determine the incidence of carotid injury following cranial trauma and identify children at high risk.

Methods: Patients who underwent CTA during evaluation for traumatic cranial injury between 2003 and 2013 were retrospectively reviewed. Demographic, clinical and radiographic data were collected. The primary outcome was carotid injury on CTA.

Results: We identified 235 patients (mean age 8.3 years, range 0.04 - 17); 150 (64%) were male, 24 (10%) had a focal neurological deficit, and 154 (66%) had intracranial hemorrhage on head CT. The average radiation DLP was 648mGy-cm. ICA abnormalities were reported in 33 (14%) patients; these patients had three-fold higher mortality. There were 16 (6.8%) deaths. A Rotterdam score of 4-6 was significantly associated with ICA injury. Multivariate regression analysis identified several independent risk factors for carotid injury, including fracture through the carotid canal (OR 5.6 [CI 2.1, 14.8]), temporal bone fracture (OR 10.1 [24, 42.9]), GCS less than 9 (OR 3.1 [1.2, 7.9]), focal neurological deficit (OR 5.0 [1.7, 14.8]), and stroke on initial CT (OR 7.0 [1.8, 27.5]). Area under the curve for the model was 0.84, indicating a high degree of accuracy.

Conclusions: In pediatric cranial trauma, CTA is indicated in the context of a fracture through the temporal bone or carotid canal, focal neurological deficit, stroke, or GCS less than 9.

648. Volumetric Analysis of MRI-guided Laser Ablation for Pediatric Brain Tumors

Margaret Riordan, MD (Syracuse, NY); Gentian Toshkezi, MD; Zulma Tovar-Spinoza, MD (Syracuse)

Introduction: Treatment deep intracranial lesions pose a challenge to neurosurgeons. Recent literature showing promising results in adults describes MRI guided laser induced thermal therapy as a way to treat these lesions, but there is no reported data in the pediatric population.

Methods: This is a case series of 5 pediatric patients with a total of 6 intracranial tumors that were treated with MRI laser ablation. Pathology results, initial clinical presentation, post-operative length of stay, and clinical outcome were recorded. Additionally, tumor volume based on MRI imaging preoperatively, post operatively, and in follow up at 3 month intervals with one year follow up was calculated and compared to initial tumor size.

Results: All patients presented with headaches or seizures. Pathology results were midbrain pilocytic astrocytomas in two patients, thalamic ependymoma, bilateral choroid plexus xanthrogranuloma, and one SEGA. The median LOS was two days. Post-operatively, the tumor volume in two patients increased by 2.5 times in the pilocytic astrocytoma patients, 6 times in the ependymoma, 1.5 times in the SEGA; however, the tumor volume of the xanthrogranulomas decreased by half. At longest follow up, all tumors except for the SEGA significantly decreased in size from the initial volume.

Conclusions: In this case series, although there is an initial increase in tumor volume due to post-operative tissue swelling, MRI guided laser ablation effectively decreases the tumor volume in different pediatric brain tumors over time. Additional data is needed to determine the effect on a greater population size with different tumor pathologies.

649. Comparing outcomes of sagittal synostosis using three different techniques: Open strip craniectomy, total cranial vault reconstruction, and endoscopic strip craniectomy: A retrospective study including cost analysis.

Sarah Tamara Garber, MD; Jay Riva-Cambrin, MD (Salt Lake City, UT)

Introduction: Neurosurgical techniques for repair of sagittal synostosis include total cranial vault reconstruction (TCV), open sagittal strip craniectomy (SS), and endoscopic strip craniectomy (ES). Previous studies looking at outcomes are few and have never included a detailed cost analysis.

Methods: A retrospective chart review was performed to find consecutive patients with sagittal synostosis who underwent surgical correction between January 1, 1993 and June 30, 2013. Clinical, operative, and process of care variables were analyzed along with overall cost.

Results: We found 328 patients who underwent surgical correction for sagittal synostosis: 88 with TCV, 133 with SS, and 107 with ES. When comparing the ES and SS cohorts, ES patients had more preoperative CT scans (66% versus 35.6%, $p < 0.001$), longer operative times (67.9 minutes versus 56.6 minutes, $p = 0.003$), but required less revision procedures (2% versus 17%, $p = 0.003$). The endoscopic procedure cost \$21,503 versus the open procedure which cost \$18,094. When comparing the ES and TCV cohorts, ES patients had fewer transfusions (21.4% versus 94.4%, $p < 0.001$), ICU days (0.25 versus 1.2, $p < 0.001$) and overall length of hospital stay (1.8 days versus 4.2 days, $p < 0.001$), and required fewer revisions (2% versus 8.9%, $p < 0.03$). The

endoscopic procedure cost \$21,503 versus the TCV which cost \$40,808.

Conclusions: The ES procedure for sagittal synostosis appears to have superior outcomes and cost savings to the TCV; where it appears to be slightly more expensive but have significantly less revisions than SS.

650. Low Threshold Monopolar Motor Mapping for Resection of Motor-eloquent Brain Lesions in Children and Adolescents

Philippe Schucht, MD (Bern, Switzerland); Michael Murek, MD (Berne, Switzerland); Lennart Stieglitz, MD (Zürich); Natalie Urwyler, MD; Roland Wiest, MD; Maja Steinlin, MD; Kurt Leibundgut, MD; Andreas Raabe, MD; Jürgen Beck, MD (Berne)

Introduction: Lesion resection in proximity to the primary motor cortex (M1) and the corticospinal tract (CST) is regarded as high-risk due to rates of post-operative deficits of up to 50%. Our objective was to determine the feasibility and safety of low-threshold motor mapping and its efficacy for increasing the extent-of-resection in the proximity of M1 and the CST in children and adolescents.

Methods: We analyzed eight consecutive pediatric patients who received nine resections for motor eloquent lesions (≤ 10 mm to M1 and/or the CST). Monopolar high-frequency (HF) motor mapping with train-of-5 (TOF) stimuli (pulse duration 500 microseconds; inter-stimulus interval 4.0 msec; frequency 250 Hz) was used. The motor threshold was defined as the minimal stimulation intensity that elicited motor evoked potentials (MEPs) from target muscles (amplitude < 30 mV). Resection was performed towards M1 and the CST at sites negative to 1-3 mA HF-TOF stimulation.

Results: M1 was identified through HF-TOF via application of varying low intensities. The lowest motor thresholds during resection ranged from 1-9 mA in eight cases, and up to 18 mA in one case, indicating close proximity to motor neurons. EEG documented absence of seizures during all surgeries. Two transient and no permanent neurologic deficits were observed. Post-operative imaging revealed complete resection in eight patients and minimal resect (< 0.175 cc) in one patient.

Conclusions: HF-TOF with a minimal threshold of 1-3 mA is feasible and safe for resections in the proximity of M1 and CST and might thus be used as a functional navigation tool to expand the safety envelope for safe resection in pediatric patients with lesions located within the precentral gyrus and in proximity to the CST. The additional use of continuous MEP monitoring serves as safety feedback for the functional integrity of the CST, especially because the true excitability threshold in children is unknown.

651. Prediction of successful ETV outcome in childhood hydrocephalus: an Artificial Neural Networks analysis

Parisa Azimi, MD (Tehran, Iran (Islamic Republic of)); Hasan Mohammadi, MD (Tehran, Iran (Islamic Republic of))

Introduction: To develop an Artificial neural networks (ANNs) model to predict 6-month success of the endoscopic third ventriculostomy (ETV) and compared it with traditional predictive measures in childhood hydrocephalus.

Methods: An ANN, ETV Success Score (ETVSS), CURE Children's Hospital of Uganda (CCHU) ETV Success Score (CCHU ETV) and a logistic regression (LR) models were applied. The etiology, age, Choroid plexus cauterization (CPC), previous shunt, gender, type of hydrocephalus (TOH), and body weight were considered as input variables for established ANN model. To do so

data from childhood hydrocephalus patients who had ETV surgery were trained. Successful ETV outcome was defined as the absence of ETV failure within 6 months follow-up. Sensitivity analysis was performed for the established ANN model to identify the most important variables that predict outcome. The ROC analysis, accuracy rate, and Hosmer-Lemeshow (H-L) were measured.

Results: In all the data for 168 patients (80 male, mean age 1.4 ± 2.6 years) were analyzed. They were divided into: training group ($n=84$), testing group ($n=42$), and validation group ($n=42$). Successful ETV outcome was 47%. The etiology, age, CPC, TOH, and previous shunt were the most important variables that were indicated by the ANN analysis. Compared to the ETVSS, CCHU ETV, and the LR models, the ANN model showed better **Results:** accuracy rate (95.1%); the H-L statistic (41.2 %); and AUC (0.87 %).

Conclusions: The findings show that ANNs can predict 6-month successful ETV with a high level of accuracy in childhood hydrocephalus diseases. Our results will need to be confirmed with further prospective studies.

652. Cumulative survival analysis of spinal myxopapillary ependymomas in the first 2 decades of life: A systematic review

Sunil Kukreja, MD; Sudheer Ambekar, MD; Anthony Sin, MD; Anil Nanda (Shreveport, LA)

Introduction: Reports of myxopapillary ependymomas (MPEs) of spinal cord in pediatric patients are scarce. The aim of our study is to perform a survival analysis of patients in the first 2 decades of life selected from the published studies and examine the influence of various factors on outcomes.

Methods: Comprehensive English literature search was performed on PubMed. Patients with age ≤ 20 years were included for integrative analysis. Degree of association of the various factors with the survival outcome was calculated by using Kaplan-Meier estimator and Cox's proportional hazard model techniques.

Results: Total 95 patients were included for the analysis. Overall rate of recurrence (RR) was 34.7% ($n=33$) with median time to recurrence of 36 months (range 2-100). Addition of RT following surgical resection significantly improved PFS ($p = 0.008$). Patients who underwent subtotal resection, administering RT (STR+RT) improved outcome with the lowest failure rates (10.3%), superior to patients who underwent gross-total resection (GTR) alone (RR 43.1%; $p = 0.000$). Addition of RT to patients who underwent GTR was not beneficial ($p = 0.628$). High-dose RT (< 50 Gy) did not change PFS ($p = 0.710$).

Conclusions: Complete resection is always the goal of tumor resection, however when complete resection does not seem to be possible in complex lesions; RT should be used as an adjunct in order to avoid aggressive resection and to minimize inadvertent injury to the surrounding neural tissues. High dose RT (< 50 Gy) did not provide additional survival benefits, though this association needs to be evaluated by prospective studies.

653. Pediatric Low Grade ganglioglioma: epidemiology, treatments, and outcome analysis on 331 children from the SEER datasets

Roy William Roland Dudley, MD, PhD, FRCS(C); Michelle Torok, PhD; Danielle Gallegos, BS; Arthur Liu, MD, PhD; Michael Handler, MD; Todd Hankinson, MD (Aurora, CO)

Introduction: The SEER datasets allow statistical analysis of rare tumors, such as low grade ganglioglioma, which account for only 1% of CNS tumors.

Methods: We identified all patients aged 0-19 years with a diagnosis of low grade ganglioglioma (ICD-O-3 9505/1) in the SEER datasets. Using the Kaplan-Meier method and log rank tests, we examined associations between patient/treatment characteristics and survival.

Results: There were 331 children with low grade ganglioglioma diagnosed between 2004 and 2010, with a median follow-up of 37 months. These tumors were more prevalent in males (n=196) than females (n=135) ($p < 0.001$). Sixty-two percent occurred in children < 10 years, while only 3% were found in those < 1 year old. Over 83% were found in Caucasian children, and 60% were located in the temporal/frontal lobes. Surgery was performed on 91.7% of these patients, with gross total resection being achieved in 68.5%, while radiation was used in only 3%. Overall 5-year survival was 96.3%, but in infants (< 1 year) this dropped to 43.2%. There was also a non-significant trend towards shorter overall and tumor specific survival in children of non-white race and those who required radiation (HR 4.70 and 6.16, respectively).

Conclusions: This study confirms the overall good prognosis for pediatric low grade ganglioglioma, but highlights three groups of children that appear to be at increased risk of earlier death: the very young, children of non-white race, and those that require radiotherapy.

654. Comparison of Spinal Deformity in Children with Chiari I Malformation with and without Syringomyelia: Matched Cohort Study

Jakub Godzik (St Louis, MO); Agnes Dardas, BS; Terrence Holekamp, MD, PhD; Lawrence Lenke, MD; Michael Kelly, MD; David Limbrick, MD, PhD (St. Louis, MO)

Introduction: Spinal deformity is frequently diagnosed in Chiari I Malformation, particularly in the setting of syringomyelia. Current theory holds that spinal cord syrinx expansion is the mechanism behind curve development and progression. However, scoliosis has been previously reported in the absence of syringomyelia. In the current study, we sought to compare initial curve patterns and presenting physical symptoms between two groups.

Methods: A retrospective review of medical records from 2000 and 2013 at our institution was performed to identify Chiari I Malformation patients with scoliosis in the absence of syringomyelia. Patients were matched in a 1:1 ratio by age and gender to Chiari I Malformation patients with scoliosis and syringomyelia. Radiographic curve patterns, MR-imaging parameters, and associated physical findings were compared between the two cohorts.

Results: Eighteen patients with Chiari I Malformation associated scoliosis in the absence of syringomyelia were identified. Four (22%) were male with a mean age of 11.5 years. On presentation, patients without syringomyelia demonstrated less severe scoliotic curve (30.2° vs. 50.3° , $p = 0.008$), despite a comparable extent of hyperkyphosis (46° vs. 51° , $p = 0.98$). Two (11%) patients demonstrated left-facing deformities compared to 50% in the syringomyelia cohort ($p = 0.01$). A higher prevalence of neurological deficit was observed in the syringomyelia cohort (33%) than in the group without syringomyelia (0%, $p = 0.007$).

Conclusions: We report the largest series specifically evaluating Chiari Malformation I associated scoliosis patients in the absence of syringomyelia. Compared to CIM with syringomyelia, these patients appear to present less atypically, with less severe scoliotic curves, fewer left-facing curves, and fewer related physical symptoms. Future studies are needed to better understand pathogenesis of spinal deformity in this population.

DePuy Synthes Award

655. Morbidity and Mortality of Endovascularly Treated Intracerebral Aneurysms: Does Specialty Matter?

Vernard S. Fennell, MD; Sheri Palejwala, MD; Nikolay Martirosyan, MD; G Lemole, MD; Travis Dumont, MD (Tucson, AZ)

Introduction: There is a wide variety of clinical background and training of physicians who treat cerebrovascular pathology through endovascular means. The impact of clinical training on patient outcomes is not well documented.

Methods: Retrospective analysis of a national database (University Healthcare Consortium), was queried from, 2009 – 2013. Cases of ruptured and unruptured cerebral aneurysms treated with endovascular obliteration were reviewed. Morbidity and mortality were evaluated by specialty of the treating physician.

Results: Embolization of unruptured aneurysm was primary diagnosis and procedure for 12,400 cases. Patients with at least one complication were reported in 799 cases (6.4%), mortalities in 193 cases (1.6%). Complications and mortalities varied by specialty. The fewest complications were by neurosurgeons (5.4% complications, 1.4% mortality). For neurologists complications were (11.1%) and mortality (3.0%) ($p < 0.0001$ [complications]; $p < 0.0001$ [mortality]) and radiologists 7% ($p = 0.0093$ [complications]). Subarachnoid hemorrhage was the primary diagnosis and procedure for 8,197 cases. At least one complication was reported in 2,385 cases (29%). Mortalities in 983 cases (12%). Complications and mortality were varied between specialty. Again the fewest complications were by neurosurgeons (27% complications, 11.5% mortality), with incidence of complications in cases performed by neurologists at (34% $p < 0.0001$) and mortality at 13.5% ($p = 0.0372$) and radiologists complications (30% $p < 0.0676$) and mortality 12.1% ($p = 0.4884$). There was a decrease in the overall percentage of cases performed by Neurosurgeons, most pronounced in unruptured aneurysms.

Conclusion: Physicians of varying training types employ endovascular treatment of ruptured and unruptured intracerebral aneurysms. The variant incidence of peri-procedural complications and mortality between specialties suggests efforts to homogenize neuroendovascular training may be warranted.

Women in Neurosurgery Louise Eisenhardt Traveling Scholarship

656. Effects of Extracranial Carotid Stenosis on Intracranial Blood Flow

Sophia F. Shakur, MD; Tomas Hrbac, MD, PhD; Ali Alaraj, MD; Xinjian Du, MD; Victor Aletich, MD; Fady Charbel, MD; Sepideh Amin-Hanjani, MD (Chicago, IL)

Introduction: Effects of percentage stenosis, stenosis length, and residual lumen on intracranial blood flow were examined in patients with extracranial carotid stenosis.

Methods: Extracranial carotid stenosis patients at our institution between 2004-2012 with vessel flow rate measurements using quantitative magnetic resonance angiography were retrospectively studied. Anatomic measurements were made from digital subtraction angiography. The impact of percentage stenosis, residual lumen and stenosis length on ipsilateral internal carotid

artery (ICA) flow, and ipsilateral-to-contralateral middle cerebral artery (MCA) flow ratio, was assessed.

Results: 44 patients had anatomic and flow data. Mean age was 67 years, 64% had symptomatic stenosis <50%. Univariate analysis demonstrated that higher percentage stenosis and smaller residual lumen are associated with a significant decrease in ICA flow ($P < 0.001$ and $P = 0.03$, respectively). On multiple regression analysis percentage stenosis remained as the primary predictor of ICA flow ($P < 0.001$). MCA flow ratio was not significantly associated with percentage stenosis, stenosis length, or residual lumen ($P = 0.70$, 0.86 , 0.78 , respectively). However, mean MCA flow ratio was significantly lower in symptomatic compared to asymptomatic patients (0.92 vs. 1.22 , $P = 0.001$). Mean ICA flow ratio was similar in these two groups (0.55 vs. 0.55 , $P = 0.99$).

Conclusions: Percentage stenosis and residual lumen are significantly associated with ICA but not MCA flow, suggesting that local hemodynamic effects of carotid stenosis do not translate directly to distal vasculature, as intracranial flows can be maintained through collaterals. However, mean MCA flow ratio was significantly lower in symptomatic compared to asymptomatic patients, highlighting the potential importance of distal hemodynamics in symptomatic presentation.

657. Development of an Aneurysm Clipping Model using 3D printing

Kaith K. Almefty, MD; Justin Ryan, BA; David Frakes, PhD; Peter Nakaji, MD (Phoenix, AZ)

Introduction: The present healthcare environment has created increased demand for procedural simulators due to duty hour limitations, demand for transparency, outcomes-based reimbursement, and an emphasis on milestone-based training. Aneurysm clipping is a skill that would particularly benefit.

Methods: CTA datasets from 9 patients with cerebral aneurysms at varying locations, were reconstructed with medical image segmentation software (Mimics, Materialise). These computational models were merged onto an idealized cerebrovascular tree with Geomagic engineering software. The augmented vascular tree was further modified for the capability of interchangeable aneurysms. The resulting tree was 3D printed in a rubber-like material. A skull model was printed in a composite material. The brain medium was created in a multi-modality process. The computation model was printed in an ABS fused-deposition modeling printer. The model underwent selective surface dissolution before being used to create a silicone mold. A silicone cast was created from the mold. These components were assembled in to a craniocerebral simulacrum.

Results: A 3D printed aneurysm clipping model incorporating multiple modalities from CTA was successfully developed. The modular feature allowed for inexpensive integration of multiple patient specific datasets with life-size aneurysms.

Conclusions: Simulators are becoming an important tool in surgical training. Aneurysm clipping, due to technical complexity and diminishing volume, will benefit from a useful, realistic simulator. Further studies with this model are designed to examine its utility in training. The modular feature allows for insertion of patient specific aneurysms and may be used as a surgical rehearsal tool.

658. Emergent Revascularization of Carotid Artery Stenosis: Nationwide Analysis of Mortality, Iatrogenic Stroke, and Economic Measures

Amit Singla, MBBS; Mark R Villwock, MS; David Padalino, MD; Eric Deshaies, MD (Syracuse, NY)

Introduction: The factors influencing outcomes following emergent revascularization of carotid artery stenosis with carotid endarterectomy (CEA) or carotid artery stenting (CAS) are yet to be fully elucidated.

Methods: We analyzed non-elective revascularization of carotid artery stenosis using the Nationwide Inpatient Sample (2008-2011). Admission characteristics and economic measures were compared between (1) CEA/CAS, (2) patients with and without cerebral infarction, and (3) early (day of admission)/delayed intervention. In-hospital mortality and iatrogenic stroke were examined in multivariate analysis adjusted for time, intervention, and comorbidity-burden.

Results: 16,744 cases of non-elective carotid artery revascularization were identified (80.2% CEA, 19.8% CAS; 78.0% without infarction, 22.0% with infarction). Healthy male patients treated with CAS were most likely to receive early intervention ($P < .05$). The factors associated with delayed intervention were weekend admission, teaching hospitals, Medicaid payers, and cerebral infarction ($P < .05$). Presenting with infarction at a teaching hospital increased cost and length-of-stay ($P < .05$). Early intervention decreased these economic measures ($P < .05$). CAS decreased length-of-stay but increased cost ($P < .05$). No differences in iatrogenic stroke or mortality between CAS and CEA were observed for patients without infarction on admission. Patients with infarction receiving early revascularization had increased odds of iatrogenic stroke ($OR = 2.119, P = .033$) and death ($OR = 3.597, P < .001$). Patients with infarction receiving CAS experienced increased odds of mortality ($OR = 3.998, P < .001$), but no significant difference in iatrogenic stroke ($OR = 1.600, P = .128$) compared to CEA.

Conclusions: While early intervention after a stroke decreased economic measures, it increased risk of post-operative stroke. Of these patients treated with CAS, the standard dual-antiplatelet regimen may have contributed to catastrophic events causing increased mortality.

659. The risk and treatment of rupture of cerebral arteriovenous malformations during pregnancy and the puerperium

Zhao Jizong; Liu Xingju, MD (Beijing, China)

Introduction: Pregnancy and puerperium may increase risk of intracerebral hemorrhage, but it is not clear whether risk of rupture of arteriovenous malformation (AVM) increased during this period. We sought to analyze the risk of rupture of AVM during pregnancy and puerperium.

Methods: Participants included 979 female patients with intracranial AVM admitted in Beijing Tiantan Hospital between 1960 and 2010. Two neurosurgery residents reviewed medical records for each case. Of them, 393 patients with rupture of AVM between 18 to 40 years of age were used for case-crossover analysis. Number of children born and clinical information during pregnancy and puerperium were retrieved to identify whether rupture of AVM occurred this period.

Results: Of the 979 women, 797 hemorrhages occurred during 25578 patient-years of follow-up, yielding an annual hemorrhage rate of 3.11%. The annual AVM hemorrhage rate in patients aged 18-40 years ($n = 579$) was 2.78%, lower than the rate in

other age groups (OR=0.75, 95% CI, 0.65 to 0.86, $P < 0.05$). Of the 393 patients with rupture of AVM between 18-40, 12 hemorrhages occurred in 12 patients over 452 pregnancies, yielding a hemorrhage rate of 2.65% per pregnancy or 3.32% per year. Among the remaining 381 patients, 441 hemorrhages occurred during 10627 patient-years of follow-up, yielding an annual hemorrhage rate of 4.14%. The odds ratio for rupture of AVM during pregnancy and puerperium, compared to not during this period, was 0.79 (95% CI 0.44 to 1.41; $P=0.43$).

Conclusions: No increased risk of hemorrhage was found in patients with hemorrhagic AVM during pregnancy and the puerperium. There is no need to advise against pregnancy in women with intracranial AVM.

660. Prediction model for three-year rupture risk of unruptured cerebral aneurysms in Japanese cohorts

Akio Morita, MD PhD (Tokyo, Japan); Shinjiro Tominari, MD, MPH (Kyoto, Japan); Toshihiro Ishibashi, MD, PhD (Tokyo, Japan); Tomosato Yamazaki, MD, PhD (Mito, Japan); Office for UCAS Japan Investigators (Tokyo)

Introduction: Whether to treat unruptured cerebral aneurysms has long been a dilemma for both patients and medical staff. The risk of aneurysm rupture is the most important factor in making this decision. However, prediction model which estimates rupture risk in a certain time period does not exist. Our objective is to build a prediction model that estimates the three-year absolute rupture risk of unruptured saccular cerebral aneurysms.

Methods: Four Japanese prospective cohorts were identified which followed unruptured cerebral aneurysms. We performed survival analysis to predict the prognosis of aneurysms with derivation data from largest cohort, using each aneurysm as the unit for analysis. The model was externally validated with combination data of remaining three cohorts and presented in the form of a scoring system.

Results: The analysis includes a total of 6,606 unruptured cerebral aneurysms in 5,601 patients. During the 11,482 aneurysm-year follow up period, 107 ruptures were observed. The predictors chosen for the scoring system were patient age, gender, hypertension, and aneurysm size, location, and the presence of a daughter sac. The three-year risk of rupture ranged from less than 1.0% to over 15% according to the individual characteristics of patients and aneurysms. External validation indicated good discrimination and calibration property.

Conclusions: A simple scoring system which only needs easily available patient and aneurysmal information was constructed. This scoring system can be used in clinical decision making regarding management of unruptured cerebral aneurysms whether preventive intervention should be performed or not.

662. Proton beam stereotactic radiosurgery for pediatric cerebral arteriovenous malformations

Brian P. Walcott, MD (Boston, MA); Jona Hattangadi-Gluth, MD (San Diego, CA); Christopher Stapleton, MD; Paul Chapman, MD; Jay Loeffler, MD (Boston, MA)

Introduction: For cerebral arteriovenous malformations (AVMs) determined to be high risk for surgery or endovascular embolization, stereotactic radiosurgery (SRS) is considered the mainstay of treatment. We sought to determine the outcomes of pediatric patients with AVMs treated with proton SRS.

Methods: We reviewed the records of 44 consecutively treated

pediatric patients (age < 18) who underwent proton SRS at our institution from 1998-2010. The median target volume was 4.45 ± 5.9 mL (range = 0.3-29 mL) and the median maximal diameter was 3.60 ± 1.49 cm (range = 1-6 cm). Radiation was administered with a median prescription dose of 15.50 ± 1.87 CGE to the 90% isodose.

Results: At a median follow-up of 52 ± 25 months, two patients (4.5%) had no response, 24 patients (59.1%) had a partial response, and 18 patients (40.9%) experienced obliteration of their AVM. The median time to obliteration was 49 ± 26 months, inclusive of 17 patients who underwent repeat proton radiosurgery. Four patients (9%) experienced hemorrhage following treatment at a median time of 45 ± 15 months. Univariate analysis identified modified AVM scale score ($p=0.045$), single fraction treatment (0.04), larger prescription dose (0.01), larger maximum dose (<0.001), and larger minimum dose (0.01) to be associated with AVM obliteration.

Conclusions: High-risk AVMs can be safely treated with proton radiosurgery in the pediatric population. Since protons deposit energy more selectively than photons, there is the potential benefit of protons to lower the probability of damage to healthy tissue in the developing brain.

663. Reversal of Vasospasm and Changes in Cerebral Blood Flow and PtiO2 in Patients with severe Vasospasm during continuous intraarterial Application of Nimodipine via Microcatheter

Sylvia Bele, MD; Gerhard Schuierer, MD, PhD; Martin Kieninger, MD; Alexander Brawanski, MD, PhD (Regensburg, Germany)

Introduction: Severe cerebral vasospasm after subarachnoid hemorrhage (sah) remains a challenge for neurointensivists despite a large number of clinical multicenter trials. If conservative treatment strategies fail to improve patient condition, continuous application of nimodipine into the carotid artery via microcatheters could be a promising alternative. We wanted to assess the feasibility of this method as well as the dynamic of changes in cerebral blood flow (CBF) and PtiO2 during this treatment.

Methods: If severe vasospasm was presumed in transcranial doppler and angio CT, multimodal monitoring including CBF (Hemedex), PtiO2 (Raumedic, Licox) and ICP was established to get baseline values before angiography. If angiography revealed severe cerebral vasospasm, microcatheters were placed in one or both carotid arteries. Nimodipine was started at 0.5 mg/h and increased to 1 mg/h if MAP and ICP were stable, treatment was between 24h and 7 days using continuous measurements of MAP, ICP, CBF and PtiO2.

Results: 12 patients were included in this study showing no significant treatment complication. 10 patients showed a significant increase in CBF 5 minutes after starting nimodipine infusion, declining after 1 h CBF but stayed significantly above baseline. All patients showed good clinical results after 4 weeks and were transferred to rehabilitation. 2 patients showed a completely different pattern in CBF and PtiO2 with a non-significant, short lived increase in CBF after nimodipine application followed by a decline under the baseline values. Those patients developed a multi-infarct syndrome.

Conclusions: This preliminary study shows that continuous intraarterial nimodipine application is a safe and effective treatment of severe vasospasm after sah. The Hemedex system as well as PtiO2 (Raumedic) are useful tools to assess effects of nimodipine and to guide therapy in the ICU.

664. The Six Thalamic Regions: Surgical Approaches to Thalamic Cavernous Malformations, Operative Reports, and Clinical Outcome

Leonardo Rangel-Castilla, MD; Robert Spetzler, MD (Phoenix, AZ)

Introduction: The ideal surgical approach to thalamic cavernous malformations (CMs) varies according to their location within the thalamus. To standardize surgical approaches, authors have divided the thalamus into six different regions and matched them with the corresponding surgical approach.

Methods: The regions were defined as Region 1 (anteroinferior), Region 2 (medial), Region 3 (lateral), Region 4 (posterosuperior), Region 5 (lateral posteroinferior), and Region 6 (medial posteroinferior). The senior author's surgical experience with 46 thalamic CMs was reviewed according to this classification. An orbitozygomatic approach was used for Region 1; anterior ipsilateral transcallosal for Region 2; anterior contralateral transcallosal for Region 3; posterior transcallosal for Region 4; parietooccipital transventricular for Region 5; and supracerebellar-infratentorial for Region 6.

Results: Region 3 was the most common location (17, 37%). There were 5 CMs in Region 1(10%), 9 CMs in Region 2(20%), 17 CMs in Region 3(37%), 3 CMs in Region 4(6%), 4 CMs in Region 5(9%), and 8 CMs in Region 6(18%). Complete resection was achieved in all patients except for two, who required a second-stage operation. Mean follow-up period was 1.7 years (range, 6 months – 9 years). At the end of the study, 40(86%) patients had excellent or good outcome (mRS 0-2). Relative to their preoperative condition, 42(91%) patients were unchanged or improved, and 4(8%) were worse.

Conclusions: We have presented the largest series reported to date of surgically treated thalamic CMs achieving excellent results. Conceptually dividing the thalamus into 6 different regions aids in the selection of the ideal surgical approach for a specific region.

665. Surgeon specialty and outcome of carotid endarterectomy

Andreea Seicean (Cleveland Heights, OH); Nima Alan, BS; Sinziana Seicean, MD, PhD; Duncan Neuhauser, PhD; Robert Weil, MD (Cleveland, OH)

Introduction: Neurological, general and vascular surgeons all perform carotid endarterectomy. However, the relationship between primary specialty training and outcome of this surgery is unknown.

Methods: We identified 54,050 patients who underwent carotid endarterectomy, from 2006-2012 in the National Surgical Quality Improvement Program (NSQIP), a prospectively-collected, national clinical database with established reproducibility and validity. Four hundred and forty eight patients were operated on by neurosurgery, n=2,653 by general and n=50,949 by vascular surgery. We compared demographic variables, preoperative laboratory values and comorbidities between patients operated by each surgical specialty before and after 1:1 propensity score matching. We used logistic regression to examine association between surgical specialty and carotid endarterectomy outcome.

Results: In the general cohort, admission from skilled care facility, functionally dependent status, chemoradiotherapy, sepsis and emergency cases were more common in neurosurgical patients than general or vascular patients. In unadjusted analyses, neurosurgical patients were more likely to experience minor complications (Odds ratio 3.2, 95% CI 2.0-5.1), prolonged length

hospitalization (2.4, 2.0-2.9) and be discharged to skilled care facility (2.5, 1.9-3.5). In adjusted analyses, however, outcome of carotid endarterectomy by neurosurgeons was comparable with general and vascular surgeons.

Conclusion: Neurosurgical patients of carotid endarterectomy tend to be less healthy than general or vascular surgery patients, which contributed significantly to more morbid postoperative course. But in equally healthy patients, outcome of carotid endarterectomy does not appear to depend on surgical specialty.

666. Comparing Clinician and Patient Reported Outcome Measures over Time after Hemispherectomy for Ischemic Stroke

Michael Liam Kelly, MD; Benjamin Rosenbaum, MD; Varun Kshetry, MD; Robert Weil, MD (Cleveland, OH)

Introduction: The association between clinician- and patient-reported health status measures (HSM) after hemispherectomy for ischemic stroke is understudied. We compared clinician- and patient-reported HSMs to determine how HSM type and follow-up affect the interpretation of outcomes.

Methods: We identified all patients admitted to the Cleveland Clinic (CC) from 2009-5/2013 who underwent hemispherectomy for ischemic stroke and reported HSMs in the CC Knowledge Program Registry. Outpatient follow-up was divided into 1-5 month and 6-12 month time periods. Clinician-reported HSMs (National Institutes of Health Stroke Scale (NIHSS) and Modified Rankin Scale (mRS)) were compared to patient-reported HSMs (EuroQol quality of life index (EQ-5D), Patient Health Questionnaire-9 (PHQ-9), and the Stroke Impact Scale-16 (SIS-16)).

Results: 11 of 39 patients completed all HSMs at both follow-up periods. Clinician-reported mean NIHSS scores improved from 12.7 to 7.4 over time (p=0.003). Mean mRS scores showed little improvement from 3.9 to 3.4 (p=0.2). Patient-reported mean EQ-5D scores improved from 0.32 to 0.54 (p=0.03). Among mean EQ-5D sub-scores, usual activity improved from 2.8 (extreme problems) to 2.2 (some problems) (p=0.02). Mean PHQ-9 scores improved from 9.7 to 4.7 (p=0.06) as did SIS-16 from 34.1 to 57.0 (p=0.01). On matched pairs analysis, only EQ-5D and mRS score differences between periods were correlated (r=-0.67, p=0.02), and the EQ-5D showed greater improvement than the mRS (p=0.03).

Conclusions: Hemispherectomy for ischemic stroke was associated with improvement across several HSMs over time. Patients-reported EQ-5D showed greater improvement than clinician-reported mRS, suggesting that HSM type influences interpretation of outcome.

667. Embolic Complications Associated with the Solitaire Flow Restoration Device during Thrombectomy for Acute Ischemic Stroke

Craig Kilburg, MD; Marcus Dennis Mazur, MD; Philipp Taussky, MD (Salt Lake City, UT)

Introduction: The use of stent retrievers for restoring flow after acute ischemic stroke is rapidly growing. The risk of embolic complications, however, is not well defined.

Methods: We reviewed the cerebral angiography of all patients with acute ischemic stroke who underwent mechanical thrombectomy using the Solitaire flow restoration device (Covidien/ev3) from 2012 to 2013 at the University of Utah. Intraprocedural images were compared after the microcatheter was positioned distal to the region of occlusion but prior to Solitaire

deployment (pre-Solitaire) and after the mechanical thrombectomy was performed (post-Solitaire). Images were compared for the presence of filling defects located distal to the primary region of thromboembolic occlusion. Distal filling defects present on post-Solitaire imaging but absent on pre-Solitaire imaging were considered to be new emboli associated with Solitaire deployment.

Results: 39 patients underwent mechanical thrombectomy using Solitaire, of whom 37 had successful revascularization (95%). New emboli associated with Solitaire use occurred in 6 patients (16%). Filling defects located distal to the primary thromboembolic occlusion was visualized on pre-Solitaire imaging in 18 patients (47%), of whom 11 (61%) had complete spontaneous resolution of these defects after thrombectomy on post-Solitaire imaging. Emboli into a new vascular territory was seen in 2 patients. Number of Solitaire passes was associated with increased morbidity ($p=0.04$). Post-Solitaire filling defects, Reopro treatment, and the use of a balloon were not associated with poor outcomes.

Conclusions: We report a 16% incidence rate of new emboli associated with use of Solitaire flow restoration device during thrombectomy.

668. FasL modulates disruption of the blood-spinal cord barrier, glial scarring and inflammation after spinal cord injury: Evidence from human tissue and mouse models

Wenru Yu, MD; Michael Fehlings, MD, PhD (Toronto, Canada)

Introduction: Accumulating evidence indicates that the death receptor Fas and its specific ligand (FasL) has gained a wide range of physiological non-apoptotic functions inducing an inflammatory cell migration and cytokine responses, cell survival and migration. We sought here to study the role of Fas ligand mediated BSCB disruption, glial scarring and inflammation following SCI.

Methods: Human postmortem spinal cord tissue from acute, sub-acute and chronic SCI cases was examined for fibronectin and fibrinogen expression and cytokines/chemokines by confocal immunohistochemistry. Complementary studies were conducted using the in vivo Fejota™ clip compression model of SCI in FasL-deficient B6Snn.C3-Tnfsf6gld/J (gld) and wild-type (Wt) mice. We tested FasL-mediated BSCB permeability, scarring formation and inflammatory responses by immunohistochemistry, Western blotting, and ELISA with Mouse 32-plex cytokine/chemokine panel bead immunoassay.

Results: We report novel evidence that shows increased expression of fibronectin and fibrinogen in the extravascular and parenchyma and increased expression of fractalkine, CX3CR1, IL-1 and IL-10 in the injury epicenter in cases of acute and subacute human SCI but not in control cases. We also found significantly reduced expression of fibronectin and Evans blue at 3 days, reduced lesion core area and inflammatory response (Iba1 and galectin-3 expression) and increased levels of GFAP and Fibronectin in gld mice when compared to Wt mice. Furthermore, there was a significant increased in the level of MAP2, CNPase, anti-inflammatory cytokine IL-15 expression and improved neurological functional recovery in gld mice relative to Wt mice after SCI.

Conclusions: In conclusion, we report multiple lines of evidence that indicate that FasL activation plays a pivotal role in mediating BSCB disruption, glial scarring formation, the inflammatory response and neurological functional recovery after SCI. These data provided a compelling rationale for therapeutically targeting Fas/FasL in human SCI.

669. Creation and Utilization of a Neurotrauma Dashboard for Quality Improvement

Shelly D. Timmons, MD, PhD, FACS, FAANS; Megan Brosious, BA; Jennifer Hunt, RN; Loren Gorgol, MS; Nathaniel Stark, MS; C. Hanson, MS (Danville, PA)

Introduction: The complexity of medical decision-making is increasing, due to exponential growth in the medical literature and increasingly sub-specialized providers. Team-based medical care provides checks and balances, but also contributes to problems analyzing the effects of interventions by introducing unwarranted variability in care, especially where medical evidence is lacking. Creation of disease-specific quality improvement (QI) tools is therefore important.

Methods: A neurotrauma dashboard was constructed by a neurosurgeon-led team of information specialists and clinicians. Diagnosis buckets incorporating CPT codes for traumatic cranial, craniofacial, brain (TBI), spinal column, spinal cord, peripheral nerve, and neurovascular injuries were constructed and used to perform within-category and cross-category comparisons. Drill-down menus were constructed for a variety of neurocritical care procedures and other patient-specific data by diagnoses, which could then be used to complete specific PI projects. The dashboard was populated with electronic chart data.

Results: The dashboard was utilized to conduct QI projects such as appropriateness of anticonvulsant and deep venous thrombosis / venous thromboembolism prophylaxis in TBI. The results of these projects and suggested steps for ongoing implementation and exportability are demonstrated. Future projects are discussed, as well as issues of construct and data validity, and comparisons with other databases and other available PI tools.

Conclusions: Outcomes-based tools are of greater utility than process-measure tools. Disease-specific tools must be developed by specialists with content expertise in the area of interest. We successfully created a neurotrauma QI dashboard and utilized it to conduct disease-specific PI projects in a large hospital system.

670. The Brain at Altitude - Rewriting the pathogenesis of High Altitude Headache and its translation into trauma care - results of the Caudwell Xtreme Everest Expedition

Mark H. Wilson, FRCS (SN) MBChir (London, United Kingdom)

Introduction: We have undertaken a number of studies at altitude including taking over 200 people to Everest base camp, 20 higher and 8 summiting. The brain in hypoxia is a reproducible ethical brain injury model simulating physiological changes of critical care.

Methods: Studies summarised include field ($n = 198$ trekkers, $n=24$ climbers to 5300m and 7950m) and sea level hypoxic MRI studies. Four domains are addressed: i. Arterial: Hypobaric hypoxia: ($n=24$) Transcranial Doppler (TCD) measured middle cerebral artery diameter (MCAD) and blood velocity (MCAv). Sea-Level normobaric hypoxia: ($n=7$) A hypoxicator ($FiO_2 = 11\%$) for 3 hours with a 3T MRI scan measured MCAD and MCAv. ii. Brain Oxygenation: Near Infrared Spectroscopy (NIRS) monitored Regional Brain Oxygenation (rSO₂). iii. Venous: Retinal imaging and MRI studies. iv. Headache: Daily diary recording headache burden.

Results: Arterial: Hypobaric and normobaric hypoxia induced MCA dilatation. Mean ($\pm$ (SEM)) MCAD increased in hypoxia (from $5.23(\pm 0.23)$ mm (at 5300m) to $9.34(\pm 0.88)$ mm (at 7950m) ($p < 0.001$) (TCD). At sea-level, (after 3 hours $FiO_2 = 11\%$) MCAD increased from $3.04(\pm 0.13)$ mm to $3.27(\pm 0.13)$ mm (MRI).

Brain Oxygenation: rSO₂ decreased more than peripheral arterial saturation, especially during exercise. The percentage reduction in resting SaO₂ and rSO₂ from 75m to 5300m was $-22.23 \pm 0.56\%$ and $-30.61 \pm 1.28\%$ ($p < 0.001$). **Venous:** 23 of 24 subjects exhibited retinal venous distension (range 5-44%). Distension correlated with headache ($r = 0.553$, $p = 0.005$). Transverse sinus narrowing strongly correlated to retinal and cerebral venous distension and headache. **Headache:** Headache Severity Index correlated inversely to lateral and third ventricular volumes summed ($r = -0.5$, $p = 0.005$) and pericerebellar CSF volume ($r = -0.56$, $p = 0.03$).

Conclusions: Cerebral blood flow in hypoxia is greater than thought and venous hypertension from inadequate drainage is a cause of high altitude headache. This mechanism of intracranial hypertension occurs in critical care and clinical correlates are described.

671. Decreased Mortality in Traumatic Brain Injury following Regionalization of Trauma across Hospital Systems

Michael Liam Kelly, MD; Aman Banerjee, MD; Michael Nowak, PhD; Michael Steinmetz, MD; Jeffrey Claridge, MD (Cleveland, OH)

Introduction: The Northern Ohio Trauma System (NOTS) was established to improve outcomes of trauma patients across the region. We hypothesized that mortality in patients with traumatic brain injury (TBI) would improve after regionalization.

Methods: All patients <14 years with a TBI were identified from NOTS, a regional trauma system consisting of 2 large healthcare systems and regional EMS providers. Data from 2008 through 2012 were analyzed before and after NOTS formation in 2010. Multivariate regression analysis (RA) was performed to evaluate independent predictors of survival.

Results: 11,220 patients were identified with TBI in the NOTS database; 4,507 (40%) before NOTS and 6,713 (60%) after NOTS. Admissions to the regional level 1 center post-NOTS increased from 36% to 46% ($p < 0.0001$). Injury severity scores and Abbreviated Injury Scores (AIS) were similar between periods. The mortality rate decreased from 6.2% to 4.9% ($p = 0.005$) among all TBIs and from 19% to 14% ($p < 0.0001$) in TBIs with a Head AIS ≥ 3 ($N = 3,538$). Craniotomy procedures increased from 1.8% to 2.7% ($p = 0.003$) in TBIs and from 5.9% to 8.1% ($p = 0.02$) in TBIs with Head AIS ≥ 3 . RA demonstrated an independent effect on survival for post-NOTS period in TBI patients (OR: 1.3; 95% CI: 1.1-1.6; C-stat=0.96) and in TBIs with Head AIS ≥ 3 (OR: 1.4; 95% CI: 1.1-1.7; C-stat=0.86).

Conclusion: Regionalization of an urban trauma system is associated with a reduced mortality rate for patients with TBI, particularly for patients with a Head AIS ≥ 3 . These findings support regionalization of trauma in a spirit of collaboration across health care systems.

672. Incidence and risk factors for suicidal ideation after mild traumatic brain injury

Leo da Costa, MD; Allison Bethune; Scott McCullagh, MD; Elizabeth Waknine, BS; Wei Xiong, PhD; Anthony Feinstein, MD (Toronto, Canada)

Introduction: Mild traumatic brain injury (mTBI) is highly prevalent and has known association with depression and increased risk of suicidal ideation (SI). However, little attention is given during assessment of mTBI in ERs to the identification of possible risk factors for SI. We examined prospectively the prevalence and

risk factors for SI following mTBI in patients presenting to a large trauma hospital.

Methods: Prospective data was collected over 14 years. Radiological and clinical features were collected at admission; psychiatric and social assessment took place at 3 and 6 months. Over 50 demographic, outcome, and psychometric measures were evaluated. Chi-square analyses were used to determine correlates of SI. Logistic regression analysis was performed to model the predictors.

Results: 82% of 2296 patients (mean age = 34.7 years) seen were mild TBI (mTBI). The frequency of SI was high: 24% (3 months) and 53% (6 months), regardless of severity. Altered level of consciousness ($p = .008$) and female sex ($p = .01$) were correlated with higher probability of SI. Radiological and clinical variables (GCS, amnesia length, CT findings) commonly assessed in the ER by neurosurgeons were not. Interestingly, in follow-up there has been an increase in the incidence of SI. Again, at 6 months initial clinical and radiological findings were not predictive of SI. Mid-term predictors included unemployment ($p = .024$) and no past history TBI ($p = 0.0008$).

Conclusions: Suicidal intent following mTBI is frequent and risk does not decrease with time from injury. Current methods for ER assessment of patients with mTBI fail to identify patients at highest risk. Improvements can be made in the ER assessment of patients with mTBI with inclusion of demographic, psychiatric and socioeconomic factors in the initial evaluation. Our observation of a delayed increase in SI indicates a time window for therapeutic intervention.

International Travel Scholarship

673. Effect of IL-6-174 G/C polymorphism in predicting disability and functional outcome in patients with severe Traumatic Brain Injury (STBI)

Sumit Sinha, MD; Naseem Mansoori, PhD; A Mukhopadhyay, MD; Bhawani Sharma, MD (New Delhi, India)

Introduction: The role of IL-6-174 G/C polymorphism in predicting functional outcome as measured by Functional Independence Measure (FIM) and Glasgow Outcome Score (GOS) after severe traumatic brain injury (STBI), is analysed.

Methods: In this cross sectional study, all the patients of STBI, between 18-65 years of age, were included. The polymorphisms of IL-6-174 G/C genes were assessed using PCR-RFLP. Serum IL-6 level was measured by ELISA. The neurologic outcome, GOS and FIM score were evaluated at one month and six months after injury.

Results: 45 subjects (40 male and 5 female), were studied. The mean age was 32.7 ± 10.5 years. Serum IL-6 level did not show any statistically significant difference between patients with presence or absence of variant allele. Out of 45 subjects; 13 have GC genotype, 1 have CC and 31 have GG genotype. After first month of injury patient having variant C allele showed better outcome as compared to patients having wild G allele- (not statistically significant) (GOS: $p = 0.085$ and FIM: $p = 0.076$). This difference was statistically significant after 6 months of injury (GOS: $p = 0.024$ and FIM: $p = 0.030$). Patient having variant C allele showed 6.4-fold better outcome in term of GOS as compared to those having wild allele. It was also observed that in patients having wild allele, the FIM score is low as compared to variant allele.

Conclusions: Our study reveals for the first time that the C allele increased the odds of good clinical outcome 4.4 fold after

one month, and 6.4-fold after six months of injury. In addition, patients with wild G allele showed statistically more drop in FIM score. The preliminary data of ongoing study suggest that IL-6-174 G/C polymorphism play an important role in the clinical outcome of STBI.

674. The Head Injury Transportation Straight to Neurosurgery (HITS-NS) Trial

Damian Holliman, PhD MRCS (Newcastle-Upon-Tyne, United Kingdom); Wanda Russell, PhD (University of Manchester, United Kingdom); Fiona Lecky, MD, PhD (University of Sheffield, United Kingdom)

Introduction: Direct transport of traumatic brain injury (TBI) patients to a neuroscience centre (NC), bypassing non-specialist acute hospitals, could potentially improve outcomes following severe TBI. However, delays in stabilisation of airway, breathing and circulation may be deleterious, and the costs of implementing this strategy are unknown. This trial investigates the impact of bypass of acute hospitals to potentially facilitate earlier neurosurgery.

Methods: A feasibility cluster randomised controlled trial conducted in two paramedic ambulance services. Adult patients with signs of isolated TBI (GCS <13), injured nearest to a non-specialist acute hospital will be transported either to that hospital (control group), or to the nearest NC (intervention group). Primary outcomes included recruitment rate, protocol compliance, accuracy of paramedic TBI identification. Secondary outcomes included 30-day mortality, 6-month Extended Glasgow Outcome Scale.

Results: Recruitment ended in March 2013 with 277 patients recruited with paramedic compliance rates of 78.5% in the control group and 50% in the intervention group. For 117 control patients 30-day mortality was 8.8% compared with 9.9% ($p=.762$) of the 160 intervention group patients. The proportion of patients with TBI who underwent neurosurgical intervention was 27% in the control group and 9.4% ($p=.063$) in the intervention group.

Conclusions: The involvement of multiple healthcare providers highlights the challenges in conducting pre-hospital TBI trials. Initial results suggest no significant differences between the patients in each group. Collection of further secondary outcomes is being completed and will be presented. This feasibility study was essential in informing the direction of future pre-hospital TBI management research.

675. Expression of mitogen-activated protein kinases in the outer membranes of chronic subdural hematomas

Masahiro Aoyama; Koji Osuka, MD, PhD; Masakazu Takayasu, MD, PhD (Nagakute, Japan)

Introduction: Various growth factors are expressed in chronic subdural hematoma (CSDH) fluid and are associated with their growth. Growth factors activate the mitogen-activated protein kinase (MAPK) cascade. In this study, the presence of three major MAPK cascade transmitters in the outer membranes of CSDHs was assessed.

Methods: Samples of outer membrane and CSDH fluid obtained from eight patients during trepanation surgery were assessed in this study. The membranes were immediately homogenized in sample buffer. Expression of ERK, phosphorylated (p)-ERK, P38, p-P38, SAPK, p-SAPK and actin was assessed by western blot analysis. Expression of three p-MAPKs was also assessed by

immunostaining. Western blot analysis was performed on cultured fibroblast cells treated with CSDH fluid to detect p-MEK and p-ERK in fibroblasts in vitro.

Results: Western blot analysis detected ERK, P38 and SAPK in all cases. p-ERK was detected in all samples, whereas p-P38 and p-SAPK were detected in some of the samples. Immunostaining revealed all three p-MAPKs were expressed in vascular endothelium, whereas only p-ERK was expressed in fibroblasts. Compared with a control, CSDH fluid significantly induced expression of p-MEK and p-ERK in cultured fibroblast cells 15 min after treatment.

Conclusions: Growth factors in CSDH fluid might activate the MEK/ERK signaling pathway in fibroblasts in CSDH outer membranes, thus inducing growth of CSDHs. All three p-MAPKs may be associated with neovascularization in CSDH membranes. These MAPK pathways could become novel targets for treatment of CSDHs.

676. COMPLICATIONS IN CRANIOPLASTY: A RETROSPECTIVE ANALYSIS OF 212 PATIENTS

Ulrich Meier, MD PhD; Johannes Lemcke, MD; Christian von der Brölie, MD; Igor Stojanowski, MD; Leonie Götz (Berlin, Germany)

Introduction: The aim of the study is to investigate whether predictors of surgical complications are identifiable in a group of 212 consecutive patients after decompressive craniectomy due to different indications or bone resection for tumor surgery.

Methods: The hospital's electronic database was reviewed. Two hundred and thirty patients with cranial vault reconstruction could be identified. Parameters which could possibly predict the occurrence of complications after surgery were analysed. The endpoint of the study was the explantation of the bone flap resp. the implant due to epidural empyema or aseptic necrosis.

Results: 212 of the identified patients with a mean age of 42.8 (SD 17.89) years could be included in this retrospective study. We found a significant relation between epidural empyema after bone flap reimplantation and the presence of a VP shunt at the time of cranial vault reconstruction, the implantation of a VP shunt together ($p=0.001$) with the bone flap and the implantation of fragmented bone flaps ($p=0.016$). We also found a significant relation between aseptic necrosis and an open traumatic brain injury (open TBI) as primary diagnosis ($p=0.004$). Further alcoholism was identified as a risk factor for aseptic bone flap necrosis ($p=0.010$).

Conclusions: In order to avoid infectious complications after cranial vault reconstruction, indications for VP shunts should be carefully evaluated. The implantation of fragmented bone flaps should be avoided by the use of CAD implants. Patients after open TBI or with alcoholism should be carefully followed up since those patients are prone to develop aseptic necrosis.

677. Eye Movement Tracking Detects Subclinical Disconjugate Gaze in Structural and Concussive Brain Injury

Uzma Samadani, MD, PhD, FAANS (New York, NY); Robert Ritlop, BS; Marleen Reyes, BA; Elena Nehrbass, BS; Floyd Warren, MD; Elizabeth Lamm, BS; Julia Schneider; Radek Kolecki, MS; Sameer Farooq; Michael Jureller; Anastasia Alex; Rebecca Tran; David Shiunonov; Paige Burris; Chen Shi; Neil Mendhiratta; Meng Qian (New York); Jason Huang (Rochester); Christopher McStay; Paul Huang, MD; S. Rob Todd; Rob Fergus; R. Theodore Smith; Douglas Kondziolka, MD (New York)

Introduction: Quantitative tests to determine brain function after injury are limited. Eye movements may correlate with cerebral function. The purpose of this study is to determine whether structural and non-structural (concussive) brain injury result in disconjugate gaze, measured using a novel eye tracking algorithm performed while the subject watches television.

Methods: A prospective observational study of injured subjects age 18-60 was performed at Bellevue Hospital. Subjects were serially assessed as soon as possible after the injury, and at 1, 4 and 12 weeks post-injury with eye tracking and the validated concussion measure SCAT3. Injured subjects were divided into three groups: (1) structural brain injury evident on CT scan; (2) non-structural brain injury or negative findings on brain CT scan; (3) non-brain injured (negative control) trauma subjects not meeting criteria for obtaining a CT scan of the brain but with other traumatic injury(ies). Eye tracking findings were also compared to 125 non-injured control subjects who denied history of ocular motility disorder or neurologic disease.

Results: Non-brain injured trauma controls had a mean horizontal conjugacy of .0074+.0060. 8 of 9 subjects with structural brain injury had significantly disconjugate horizontal eye movement (greater than .0194) relative to trauma and non-injured controls. The subject who did not have disconjugate gaze had sustained minimal hemorrhage into a subdural hygroma without mass effect. 6 of 19 subjects with head CT scans negative for structural injury (concussion patients) had significantly disconjugate horizontal gaze relative to corporally injured and non-injured control subjects. Eye tracking improved to normal with time. Correlation with SCAT3 is in progress.

Conclusions: A novel algorithm for eye movement tracking while watching television reveals disconjugate gaze in structural and concussive brain injury.

678. Melatonin modulate the activities of antioxidant enzymes via the activation of Nrf2-ARE signaling pathway in a mice traumatic brain injury model.

Ding Ke (Nanjing, China); Chunxi Wang, PhD (Nanjing)

Introduction: This study was conducted to evaluate the possible involvement of melatonin in the activation of nuclear factor erythroid 2-related factor 2 and antioxidant responsive element (Nrf2-ARE) signaling pathway and the modulation of the activities of antioxidant enzymes in experimental TBI.

Methods: This work contained two experiments. Experiment 1, ICR mice were divided into four groups: sham group, TBI group, TBI+vehicle group and TBI+melatonin group. Melatonin was administered intraperitoneally at 10 mg/kg at 0, 1, 2, 3 and 4 hr post TBI. Experiment 2, Nrf2 wild-type and Nrf2 knock out mice were both received TBI insult and melatonin administration intraperitoneally at corresponding time-points and named Nrf2(+/+) group and Nrf2(-/-) group.

Results: Administration of melatonin following TBI significantly

ameliorated brain injury, such as oxidative stress (MDA, 3-NT), brain edema and cortical neuronal degeneration (FJC). And melatonin markedly promoted the translocation of Nrf2 protein from cytoplasm to the nucleus, increased the expressions of Nrf2-ARE pathway-related downstream factors, including hemoxygenase-1 (HO-1), NAD(P)H:quinone oxidoreductase 1 (NQO-1), and prevented the decline of the activities of antioxidant enzymes, superoxide dismutase (SOD) and glutathione peroxidase (GPx). Furthermore, melatonin administration could not prevent the decline of the activities of antioxidant enzymes in Nrf2 knock out mice.

Conclusions: Melatonin administration may attenuate brain injury in this TBI model, through modulating the activities of antioxidant enzymes by the media of Nrf2-ARE pathway.

Ronald L. Bittner Award

700. Awake craniotomy to maximize glioma resection: methods and technical nuances with 561 patients.

Shawn Level Hervey-Jumper, MD; Mitchel Berger, MD; Darryl Lau, MD (San Francisco, CA)

Introduction: Awake craniotomy is an established procedure for testing and identification of functional areas. Identification of these locations allows for more aggressive extent of brain tumor resection and therefore improved survival. The goal of this study was to examine the way in which these surgeries were performed including methods and optimal techniques.

Methods: We retrospectively studied 561 patients undergoing awake brain tumor surgery by a single author (M.B.) for tumors in functional regions between 1997-2013.

Results: The median patient age was 42. 75% percent of patients had KPS 90-100 and 25% KPS <80. Fifty-four percent of patients received surgery for high-grade gliomas, 43% low-grade gliomas, 1% metastatic lesions, and 2% other (cortical dysplasia, etc). The majority of patients were ASA class 1 or 2 (mild systemic disease) however patients with severe systemic disease were not excluded representing 29% of study participants. Preoperative airway analysis revealed complete visualization of soft palate and uvula in 79% of patients (Mallampati score 1-2). Laryngeal mask airway (LMA) was used in 7 patients (1.2%), most commonly used in large vascular tumors with mass effect. Mannitol was given in 68% of cases and used more commonly in high-grade tumors (p=0.03). Sixteen percent of patients were active smokers, which did not impact mapping or length of stay. Intraoperative seizures occurred in 3% of patients. Preoperative seizure history and number of preoperative antiepileptic drugs had no effect on the frequency or control of intraoperative stimulation induced seizures. Mapping was aborted in 3 cases (0.5%) due to intraoperative seizures (2 cases) and patient emotional intolerance (1 case).

Conclusions: These findings suggest that awake brain tumor surgery can be safely performed with an extremely low failure rate regardless of ASA classification, Mallampati score, BMI, smoking status, psychiatric, seizure history, vascularity, or tumor mass effect.

701. Increasing Rate of Publication Misrepresentation Among Neurosurgery Residency Applicants

Heather Kistka, MD; Arash Nayeri, BA; Jamie Dow; Lola Chambless, MD (Nashville, TN)

Introduction: Misrepresentation of scholarly achievements is a recognized phenomenon; well-documented in numerous fields. We identified a trend towards increasing numbers of publications among applicants for neurosurgery residency at Vanderbilt University and sought to determine whether this was a result of increased academic productivity or inflated reporting.

Methods: The Electronic Residency Application Service applications from 2012 (n=194) and SF Match applications from 2006 (n=148) were reviewed. Demographic data were collected including: age, gender, medical school, advanced degrees, Alpha Omega Alpha membership, and USMLE® Step 1 score. Publications reported as accepted or in press were verified via PubMed, journal websites, Google search, and direct journal contact. Works were misrepresented if they did not exist, incorrectly reported the author order, or were incorrectly listed as peer-reviewed.

Results: Between 2006 and 2012 there was a significant increase ($p < 0.0001$) in number of total works per applicant (4.05 vs. 13.25) and percentage of applicants with misrepresentations (16.2% vs. 43.2%, $p < 0.0001$). In 2012 applicants with <10 works and those from the top ten medical schools (US News & World Report) had a significantly higher rate of misrepresentation ($p < 0.0001$ and $p = 0.0004$). No other demographic variables were statistically significant.

Conclusion: The incidence of legitimate and misrepresented scholarly works reported by applicants to our program has dramatically increased since 2006. This trend is concerning in a profession where trustworthiness is of paramount importance. In order to preserve the integrity of the field of neurosurgery, programs should consider verifying citations prior to submitting their rank lists particularly in applicants with more reported works.

702. Abnormal white matter integrity related to head impact exposure in a season of high school varsity football

Alexander K. Powers, MD; Elizabeth Davenport, MS; Jillian Urban, MS; Christopher Whitlow, MD, PhD; Mark Espeland, PhD; Joseph Maldjian, MD; Youngkyoo Jung, PhD; Joel Stitzel, PhD (Winston Salem, NC)

Introduction: This study's purpose is to determine if the cumulative effects of head impacts from a season of football produce measurable changes in the brain in the absence of clinically diagnosed concussion.

Methods: 45 players from a local high school football team were enrolled for the 2012 season. None of the players in the analysis experienced clinical concussion. All players were instrumented with the Head Impact Telemetry System (HITS). All players received pre- and post-season MRI scans. Total impacts and Risk Weighted cumulative Exposure (RWE) were computed from the helmet sensor data for each player. DTI scalars were computed. Voxel-wise delta maps were computed for each scalar (post-season–pre-season) and converted to Z-maps using the group mean and standard deviation. Abnormal voxels were defined as 2 SD above or below the mean with a minimum cluster threshold of 1 ml to reduce false positives. Total number of abnormal voxels was computed for each subject and DTI scalar. Linear regression was performed between the biomechanical metrics and number of abnormal voxels for each DTI scalar.

Results: Regression analyses revealed a statistically significant

linear relationship between RWECP and all the DTI measures. RWELinear also demonstrated a statistically significant association with the DTI measures. RWERotational and the total number of head impacts did not demonstrate a statistically significant association with any of the DTI scalars.

Conclusions: We demonstrate that a single season of football play can produce MRI measurable brain changes that have been previously associated with mTBI. This adds to the growing body of literature providing evidence that a season of play in a contact sport can show brain changes in the absence of concussion or clinical findings.

American Brain Tumor Association Young Investigator Award

703. The Clinical Importance of Extent of Resection in Medulloblastoma is Dependent on Molecular Subgroup

Eric M. Thompson, MD (Toronto, Canada); Michael Taylor, MD, PhD (Toronto)

Introduction: Medulloblastoma is now acknowledged to comprise 4 distinct molecular subgroups (WNT, SHH, Group 3, and Group 4) that are clinically and genetically distinct. Traditionally, increased extent of resection (EOR) has been associated with improved prognosis for medulloblastoma. This study sought to determine the clinical importance of EOR and metastatic stage by medulloblastoma subgroup.

Methods: Medulloblastoma subgroup affiliation was determined using nanosString profiling. Extent of resection was classified as gross total (GTR), near total (NTR, <1.5cm²), or subtotal (STR, ≥1.5cm²) based on post-operative contrast-enhanced CT or MRI. Presence (M+) or absence (M0) of metastases was determined at initial staging. Mantel-Cox log-rank was used to compare overall survival (OS) and ANOVA to compare EOR.

Results: We analyzed 518 medulloblastoma samples: 55 WNT, 150 SHH, 108 Group 3, and 205 Group 4. There was no difference in distribution of GTR, NTR, STR between the 4 subgroups ($P = 0.3126$). Increased EOR was associated with increased OS only in Group 4 patients ($P = 0.0118$). For the M0 subset of patients, EOR was associated with OS only in Group 4 patients ($P = 0.0055$). Extent of resection had no impact on OS in patients with metastasis (M+) regardless of subgroup. M+ patients had a worse OS than M0 patients in the SHH group ($P = 0.0191$) and Group 4 ($P = 0.0455$).

Conclusions: Obtaining a GTR has prognostic significance only in Group 4 patients. Intraoperative medulloblastoma subgrouping will guide surgical resection in the near future. EOR has no impact on M+ patients regardless of subgroup and aggressive surgical resection should not be attempted at the cost of potential morbidity.

704. Deep Brain Stimulation for Moderate and Severe Disability Due to Traumatic Brain Injury (TBI)

Ali R. Rezai, MD, FAANS; W Mysiw, MD; Michael Knopp, MD; Per Sederberg, PhD; Jennifer Bogner, PhD; Dylan Nielsen, MD, PhD; John Corrigan, PhD (Columbus, OH)

Introduction: Annually, more than 100,000 Americans sustain a TBI that requires hospitalization and results in prolonged disability. Deep brain stimulation (DBS) for TBI has been studied

for those in vegetative or minimally conscious state (MCS) with mixed results. This study is the first to investigate DBS in TBI patients who recovered beyond MCS but have persistent severe cognitive and behavioral disability marked by poor regulation of executive functions.

Methods: FDA and IRB approval was granted to study four subjects with disability defined by a Glasgow Outcome Scale-Extended 3-6 (moderate or severe). Average age was 40 years, and patients were 6-21 years post TBI. Patients underwent bilateral DBS electrode placement in the internal capsule and striatum. Assessments were conducted at five phases (baseline to one year post-surgery) measuring cognitive performance and functional independence; serial EEG and 18F-FDG PET images were also acquired.

Results: Cognition and function improved significantly over the 5 phases of the study with two of the four patients meeting responder criteria. Clinical improvements correlated with changes on PET scans involving the prefrontal and orbitofrontal cortex. Patients tolerated the procedure well with no significant adverse events. Details of the safety, clinical and physiological outcome data will be provided.

Conclusions: DBS for severe disability from TBI can improve cognitive, behavioral and functional independence outcomes. Clinical improvements were sustained one year post DBS implantation and were associated with PET changes in physiological activation of frontal lobe networks implicated in behavioral control.

Cone Pevehouse Young Neurosurgeons Award

705. The role of large administrative ICD-9 databases in evaluating surgical practice

Yakov Gologorsky, MD (Brookline, MA); John Knightly, MD (Morristown, NJ); John Chi, MD, MPH; Michael Groff, MD (Boston, MA)

Introduction: Healthcare-policy research is increasingly reliant on large administrative databases such as the Nationwide Inpatient Sample (NIS). Recent studies have suggested that the most rapidly rising indications for lumbar fusion are degenerative disc disease and disc herniation, neither of which is a well-accepted indication. Administrative databases typically classify cases using primary ICD-9-CM discharge codes which are not generated by surgeons, but are rather assigned by hospital coders. It is unclear how accurately the coders capture the surgeon's indication for fusion. We sought to compare the ICD-9-CM code(s) assigned by hospital coders to the surgeon's indication based on review of the medical chart.

Methods: All lumbar fusions performed by our department between 8/1/2011 and 8/31/2013 were retrospectively reviewed. Indication for fusion was categorized as: spondylolisthesis, deformity, tumor, infection, trauma, pseudarthrosis, adjacent-level degeneration, stenosis, or degenerative disc pathology. These surgeons' diagnoses were compared against the primary ICD-9-CM codes that were submitted to the NIS.

Results: 170 hospital admissions resulting in 178 lumbar fusions were identified. The indication for fusion in 43 hospitalizations were tumor, infection, or trauma; the remaining 127 were for degenerative diagnoses. The primary ICD-9-CM code matched the surgeon's diagnosis in 101/170 (59%) cases. Of the 127 cases

that were degenerative in nature, the primary ICD-9-CM diagnosis matched the surgeon's diagnosis in only 59 cases (45%).

Conclusions: Evaluating indications for fusion based on ICD-9-CM codes extracted from administrative databases does not accurately reflect the surgeon's indication. If the primary diagnosis codes obtained from the NIS are inherently incorrect 50% of the time, it certainly calls into question the validity of conclusions derived from mining this database. The underlying causes of data corruption are numerous and cannot be traced to a single source. Researchers, policy-makers, government/third-party payers, and physicians should note these limitations when reviewing studies using hospital claims data.

Robert Florin Resident Award

706. Neurosurgical Decision Making: Personal and Professional Preferences

Omar Tanweer, MD (New York, NY); Taylor Wilson, BS; Stephen Kalhorn, MD; John Golfinos, MD; Paul Huang, MD; Douglas Kondziolka, MD (New York)

Introduction: It is known that physicians sometimes recommend treatment that, in a similar clinical scenario, they might not choose for themselves. We sought to understand this dynamic across neurosurgical practice and examine how neurosurgeons value the procedures they offer.

Methods: We conducted an online survey sent to a large cohort of neurosurgeons in May 2013. Respondents were randomized to answer either as the surgeon or as the patient. Questions encompassed an array of distinct neurosurgical scenarios. Data on practice parameters and experience levels was also collected.

Results: We obtained 534 survey responses, 279 responding as the neurosurgeon, and 255 as the patient. For both vestibular schwannoma and arteriovenous malformation management, more respondents chose resection for their patient but radiosurgery for self ($p=.002$ and $.001$). Aneurysm coiling was chosen more often over clipping for self than patient, but surgeons with a $<30\%$ open cerebrovascular practice had less of a tendency to do so. In a case of large spontaneous intracranial and intraventricular hemorrhage neurosurgeons were more likely to place a ventricular drain in a patient than himself or herself. Overall, surgeons with a predominant tumor surgery focus were more aggressive in terms of glioma, vestibular schwannoma, AVM, and trauma management. Neurosurgeons in practice <10 years since residency were more likely to recommend against interventions for spinal pain, aneurysms, AVMs or intracranial hemorrhage.

Conclusions: In certain clinical scenarios neurosurgeons would choose treatment options for themselves that are different from options they would recommend to patients. Amongst the management of our provided scenarios of vestibular schwannoma, arteriovenous malformation, intracranial aneurysm and intracranial hemorrhage responses favored less invasive interventions when the surgeon themselves was the patient. These findings are likely a result of cognitive biases, previous training, areas of expertise and personal values.

707. The national chronic subdural hematoma audit of the United Kingdom and Ireland

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Introduction: Chronic subdural hematoma (CSDH) represents one of the commonest neurosurgical conditions. Despite this, optimal patient management remains controversial. We have undertaken a prospective multicentre audit in order to establish current practice, national benchmarks and identify areas for future research.

Methods: Neurosurgical units (NSU) in the United Kingdom (UK) and Ireland were invited to enrol patients prospectively from June to December 2013. All adult patients with a primary or recurrent CSDH were eligible for inclusion. Data on pre-operative baseline, surgical parameters and overall outcome were entered onto a secure online database.

Results: Audit standards were established from published systematic reviews and a randomized controlled trial. These include: clinical recurrence rate less than 20%; unfavourable modified Rankin score (mRS) (4-6) at discharge from NSU less than 30%; morbidity rate in NSU less than 10% and mortality rate in NSU less than 5%. The outcome measures were: (1) clinical recurrence requiring re-operation within 60 days; (2) mRS score at discharge from NSU; (3) morbidity and mortality in the NSU; (4) destination at discharge from NSU; (5) length of stay in NSU. To date 770 patients from 26 NSUs have been enrolled. National outcomes comply with the audit standards. Complete results of the audit will be presented at the AANS Annual Meeting.

Conclusions: This represents the largest prospective study of patients with CSDH. The audit determines, for the first time the contemporary management and outcomes of patients with CSDH across the UK and Ireland. This will help inform national and international guidelines, clinical practice and future research.

708. Attrition Rates in Neurosurgery Residency: Analysis of 1361

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Introduction: The objective of this study is to determine neurosurgery residency attrition rates by gender of matched applicant and by type and rank of medical school attended.

Methods: The study follows a cohort of 1361 individuals who matched into a neurosurgery from 1990 – 1999. The main outcome measure was certification by the American Board of Neurological Surgeons. A secondary outcome measure was documentation of practicing medicine as per the American Medical Association Physician Finder and National Provider Index websites. 10.7% (n=146) of the cohort were women. 20% (n=266) graduated from a top ten medical school. 45% (n=618) were graduates of public school, 50% (n=680) of private school and 5% (n=63) of international schools. At the end of the study, 0.2% of subjects (n=3) were deceased and 0.3% (n=4) were lost to follow-up.

Results: The residency completion rate was 86.0% (n=1171) overall, with 76.0% (n=111/146) of women and 87.2% (n=1059/1215) of men completing residency. Board certification was obtained by 78.3% (n=1,065). 61.0% (n=89/146) of women and 80.3% (n=976/1215) of men were board certified. Women were found to be significantly more at risk (p <.005) of not completing residency or becoming board certified than men. Public medical school alumni had significantly higher board certification rates than private and international alumni. (502/618 for public = 81.2%; 515/680 for private = 75.7%; 48/63 for international = 76.2%; (p <.05). There was no significant difference in attrition for graduates of top ten ranked institutions versus other institutions. There was no difference in number of years to achieve neurosurgical board certification for men versus women.

Conclusions: Women have greater attrition than men during and after neurosurgery residency training. International and private medical school alumni had higher attrition than public medical school alumni.

709. Spine Care and the CERTAIN Learning Healthcare System: The Spine Surgical Care and Outcomes Assessment Program

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Introduction: Variability in the use, care and outcomes of spine surgery has been an important quality improvement (QI) target for healthcare patients, providers, payers, and policy makers.

Methods: Starting in August 2011, Washington State's clinical community organized into a voluntary collaborative for prospective data collection of consecutive spine surgical cases aimed at benchmarking the indications for, process and outcomes of spine surgery across 20 WA State hospitals.

Results: 6407 patients (57.7 ±15.8 years, 48.7% men) underwent index spine surgical procedures of interest at 20 SCOAP hospital (through December 2012) including 4087 lumbar and 2273 cervical procedures. 9.5% were part of the Labor and Industries program, with the majority (56%) having a form of tax-payer supported payment coverage (Medicare, Medicaid, Tricare, WA State Department of Corrections and the state's employee coverage program). 38% were working at the time of the procedure, 8.2% were disabled and 17% unemployed. The most common indications for procedures were stenosis (72.5%) and what surgeons described as spinal instability (41.9%). Neurologic symptoms were described in 92.5% of patients with baseline limb pain scores of 5.9. The mean NRS for back pain was 5.9 with an ODI/NDI of 44. Death was an uncommon event (<1%) and transfer to a skilled nursing facility ranged from 3.8-10.7%, based on procedure. Adjusting for demographic, clinical and procedural characteristics the odds of a combined adverse event (CAE) were significantly greater among older patients, those with taxpayer supported healthcare coverage, higher ASA status and those undergoing fusions, multi-level treatments. There was considerable variation in the odds of a CAE across hospitals.

Conclusion: Considerable variation in the indications, process and outcome of spine surgery poses an opportunity for QI across WA State and highlight the value of this community-based, performance surveillance initiative. An immediate target for QI includes cigarette cessation to improve functional outcomes.

710. Readmission Rates for Cranial Neurosurgical Patients by Surgical Indication

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Introduction: Reducing readmissions is one means of controlling health care costs. Understanding 30-day readmission rates and predictive factors is valuable for quality improvement efforts. Rates of readmission for cranial neurosurgery are currently unknown.

Methods: Using 2010-2011 HCUP State Inpatient and State Emergency Department Databases from CA, FL, and NY, we identified patients undergoing cranial neurosurgery and their 30-day all-cause readmissions. Multivariate analyses were developed to identify characteristics associated with readmissions.

Results: 53,328 patients underwent cranial neurosurgery for neoplasm (50.65%), seizure (5.32%), vascular condition (25.03%) and trauma (18.99%). Inpatient mortality was highest in vascular (7.98%) and lowest in seizure (0.78%) $p < 0.0001$. 30-day all-cause readmissions were 21.57% in neoplasm, 23.43% in seizure, 22.23% in vascular and 21.93% in trauma $p < 0.0001$. Strong significant predictors of early readmission for neoplasm were Medicaid payer (OR 1.42, 95% CI 1.57–1.30) and diabetes (OR 1.20, 95% CI 1.30–1.10); for seizure were Medicaid payer (OR 1.72, 95% CI 2.20–1.34) and initial ED admission (OR 1.62, 95% CI 1.98–1.33); for vascular were MediCare payer (OR 1.28, 95% CI 1.45–1.11) and liver disease (OR 1.46, 95% CI 1.856–1.15); and for trauma were Medicaid payer (OR 1.45, 95% CI 1.75–1.20) and renal failure (OR 1.54, 95% CI 1.88–1.25).

Conclusions: This study represents a comprehensive look at 30-day all-cause readmissions for cranial neurosurgery. The data indicate that 30-day readmission rates were greater than 20% and patient characteristics, especially race and payer, were associated with an increased readmission risk. These baseline readmission rates will inform future quality improvement and readmission reduction efforts.

711. Disparities in patient population with different type of insurance: Does it affect outcomes

Saniya Siraj Godil; Scott Zuckerman, MD (Nashville, TN); Matthew McGirt (Charlotte, NC)

Introduction: Socioeconomic disparities are known to exist amongst government and private health plans. However, the effect these population variances have on the quality and cost of care remains unknown. We set out to determine whether disparities between private and government health plans were associated with differences in outcomes.

Methods: All patients undergoing elective lumbar surgery were enrolled into a prospective longitudinal registry. Data was collected on patient demographics, treatment variables, morbidity, patient reported outcomes and patient satisfaction.

Results: A total of 519 patients were included. Mean age was higher in public insurance group ($p < 0.001$). Significant racial disparity was seen between two groups ($p = 0.03$). Public insurance group comprised of significantly comorbid ($p < 0.001$) and unemployed patients ($p < 0.001$). There was no difference in baseline PROs between groups. Number of motion segments involved was higher in public insurance group ($p < 0.001$). There was significant difference in the types of surgeries between the two groups ($p < 0.001$). Length of surgery ($p = 0.004$) and hospital stay ($p = 0.006$) was significantly higher in public insurance group. 90-day morbidity was higher in public insurance group, but

not statistically significant. Mean improvement in PROs was significantly higher in private insurance group ($p < 0.05$).

Conclusions: Significant disparities exist in patient population with public vs private insurance. Patients with public plan comprise of a significantly older, comorbid and unemployed group, undergoing extensive spine surgery with less improvement in outcomes as compared to private insurance group. In surgical treatment of low back pathology, bundled payment amounts and benchmarks of quality should be different for public and private plans due to the different patient populations with unique risks and differing outcomes.

712. A socioeconomic analysis of intraoperative neurophysiologic monitoring in spine surgery: National utilization, regional variation, costs and outcomes

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Introduction: Anecdotal observations suggest a recent surge in use of intraoperative neurophysiological monitoring (IONM) in spine surgery. To our knowledge, there is no clear evidence to indicate why this is occurring and to what extent the occurrence is regional.

Methods: The Nationwide Inpatient Sample (NIS) was queried for all spine procedures performed in the United States from 2007-2011. Utilization of IONM (ICD-9 00.94) was compared between years and geographic regions. Mean hospital charges, patient independence at discharge, and iatrogenic nerve injury were compared with and without use of IONM.

Results: A total of 408,255 spine procedures were identified. IONM was reported in 28,925 cases. Utilization of IONM increased each calendar year, from 1% of all cases in 2007 to 13% of all cases in 2011. Use of IONM ranged from a regional low of 8% of spine cases in the northeast region to 21% of spine cases in the west in 2011. Even discectomy for 'disc displacement' saw a steady rise in utilization from nearly 0% in 2007 to 8% in 2011. Mean hospital costs were greater with IONM for both elective ($\$94,043 \pm \490 versus $\$62,601 \pm \102 , $p < 0.001$) and nonelective ($\$128,049 \pm \$2,426$ versus $\$99,090 \pm \522 , $p < 0.001$) admissions. Despite an increase in hospital costs, patients were independent at discharge more frequently when no IONM was performed for both elective (82% versus 76%, $p < 0.001$) and non-elective (63% versus 56%, $p < 0.001$) hospitalizations. Iatrogenic nerve injury was extraordinarily rare, occurring in 27 cases, with no significant decrease in cases where IONM was employed.

Conclusions: There has been a dramatic increase in use of IONM over recent years, with marked regional variation. Interestingly, utilization increased steadily even in the context of discectomy. Reasons for these trends and their financial implications warrant further exploration.

713. Assessing comorbidities that contribute to patient satisfaction and hospital cost following lumbar spine surgery

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Introduction: A subset of a national data base of lumbar spine outcome data including a combination of financial and patient

satisfaction data were analyzed to discern whether preoperative factors can be identified that would predict cost as well as the likelihood of satisfaction following surgery.

Methods: A total of 120 patients as a subset of the National Neurosurgery Quality and Outcomes Lumbar Database (N2QOD) were assessed pre-operatively, at 3 months (120 patients) and 12 months (48 patients). Patient's satisfaction, Oswestry Disability Index and EuroQol-5D were included and co-morbidities including diabetes, smoking, and depression were examined to see whether any predicted patient satisfaction following surgery. In addition to the N2QOD data, detailed financial records were compared between comorbidity groups.

Results: The frequency of post-operative patient satisfaction was compared to pre-operative comorbidities including depression, smoking, diabetes, obesity (BMI <30), and morbid obesity (BMI <40). Pre-op depression correlated significantly with significantly worse ODI and EQ5D scores at Baseline, 3 months, and 12 months ($p < 0.05$). Depressed patients also had significantly longer lengths of stay following lumbar surgery. Smoking was a significant factor in patient dissatisfaction at 12 months ($p < 0.05$). Smokers also had significantly greater BMI values and worse ODI and EQ5D scores than non-smokers. Despite previous reports of comorbidities such as morbid obesity causing higher hospital costs, we found no significant differences comparing multiple measures of surgical costs between comorbidity groups.

Conclusions: Smoking and pre-op depression are factors in worse ODI and EQ5D scores at baseline and up to a year after lumbar surgery. Smoking is a significant factor in patient dissatisfaction at 12 months following surgery. No comorbidity that we evaluated caused a significant change in the cost of surgery.

714. The association of unfavorable outcomes with the intensity of neurosurgical care in the United States

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Introduction: There is wide regional variability in the volume of procedures performed for similar surgical patients throughout the United States. We investigated the association of the intensity of neurosurgical care (defined as the average annual number of neurosurgical procedures per capita) with mortality, length of stay (LOS), and rate of unfavorable discharge for inpatients after neurosurgical procedures.

Methods: We performed a retrospective cohort study involving the 222,851 patients who underwent cranial neurosurgical procedures from 2005-2010 and were registered in the National Inpatient Sample (NIS) database. Regression techniques were used to investigate the association of the average intensity of neurosurgical care with the average mortality, LOS, and rate of unfavorable discharge.

Results: The inpatient neurosurgical mortality, rate of unfavorable discharge, and average LOS varied significantly among several states. In a multivariate analysis higher age, male gender, coverage by Medicaid, minority racial status, and urban non-teaching hospitals were associated with increased mortality, rate of unfavorable discharge, and LOS. The opposite was true for coverage by private insurance, higher income, fewer comorbidities and small hospital size. There was no correlation of the intensity of neurosurgical care with the mortality (Pearson's $\rho = -0.18$, $P = 0.26$), rate of unfavorable discharge (Pearson's $\rho = 0.12$, $P = 0.48$), and LOS of cranial neurosurgical procedures (Pearson's $\rho = -0.17$, $P = 0.32$).

Conclusions: We observed significant disparities in mortality, LOS, and rate of unfavorable discharge for cranial neurosurgical

procedures in the United States. Increased intensity of neurosurgical care was not associated with improved outcomes.

715. Neurosurgery Jury Verdicts and Settlements: 2012 Prevalence by Case Type

Christopher L. Taylor, MD, MBA, FAANS (Albuquerque, NM)

Introduction: Spine surgery is the most common type of procedure resulting in litigation, but it is also the most common type of procedure in neurosurgical practice. To identify all publically reported legal cases resulting from neurosurgery practice for a single year, two data sources were reviewed. This study determines the relative risk of court trial or settlement by type of procedure.

Methods: The WestLawNext™ database and Medical Malpractice Verdicts, Settlements, & Experts reports were comprehensively searched to identify any case involving a neurosurgeon completed in 2012. Statistical analysis was performed.

Results: Forty-four cases involving an allegation of malpractice against a neurosurgeon were completed in 2012. Death or paraplegia/quadruplegia was present in 43% of cases. Cases related to spine surgery were most common, however, there was a lower risk of litigation following cranial surgery as compared to spine surgery (p -value = 0.058). The primary allegation in 55% of cases was directly related to surgery, however, all other aspects of care including pre-operative (14%), post-operative (14%), and non-operative (18%) management were substantial contributors to lawsuits. Twenty-eight (64%) cases resulted in a verdict for the defense, seven (16%) resulted in a verdict for the plaintiff, and nine (20%) resulted in a settlement. Median award after verdict for the plaintiff was \$691,565. Median reported settlement was \$777,500. The average time to closure was 68 months; the maximum was 142 months.

Conclusions: Death or spinal cord injury is probably the most powerful predictor of litigation in neurosurgery. Cranial surgery may be significantly less likely than spine surgery to result in litigation. Avoiding cranial surgery in an attempt to decrease the risk of litigation in a neurosurgical practice is not a rational decision. Civil litigation is an inefficient way to compensate victims of malpractice and an expensive way to promote quality.

716. Intraoperative Application of Topical Vancomycin Powder Is Safe and Reduces Infection Rate in Craniotomies

Mark A. Attiah, BA; Andrew Olsen, BA; Andrew Richardson, PhD; Timothy Lucas, MD, PhD (Philadelphia, PA)

Introduction: Cranial infections following craniotomy are an important cause of morbidity, increased hospital length of stay and health care cost. Furthermore, metrics on hospital infection rates are increasingly being made public, incentivizing hospitals to aggressively reduce infection. In an effort to improve patient care by reducing infections, we examined the safety and efficacy of topical vancomycin during craniotomy as an adjunct to routine systemic antibiotics prophylaxis.

Methods: A retrospective review of 150 patients who underwent elective cranial surgeries over a 2-year period at a single academic center was performed. The control group received standard systemic prophylaxis, whereas the treatment group received standard prophylaxis plus 1g of topical vancomycin powder applied into the surgical wound before closure. The primary outcome measure was incidence of cranial infections. Sub-analyses examined type

of surgery, history of prior surgeries and medical comorbidities. Patients with cranial implants (e.g. shunts, cranioplasties) or an allergy to vancomycin were excluded.

Results: A total of five cranial infections (6.7%; 5/75) were observed in the control group. One patient in the treatment group experienced a cranial infection (1.3%; 1/75). The reduction in cranial infections was statistically significant (p less than 0.05). There were no adverse clinical events or wound complications related to the use of the vancomycin powder. Patient demographics were balanced between the two groups.

Conclusions: The use of topical vancomycin powder in craniotomy wounds is a safe and effective method to significantly reduce the incidence of infection in patients undergoing cranial surgery.

717. National Socioeconomic Indicators are associated with Neurological Outcomes Following Aneurysmal Subarachnoid Hemorrhage: A Mixed-Effects Analysis

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Introduction: Although heterogeneity exists in patient outcomes following subarachnoid hemorrhage (SAH) across different centers and countries, it is unclear which factors contribute to such disparities. We performed a post-hoc analysis of a large international database to evaluate the association between national socioeconomic indicators and patient outcome following aneurysmal SAH.

Methods: Analysis was performed on a database of 3552 patients in studies of tirilazad for aneurysmal SAH from 1991-1997, including 162 neurosurgical centres in North and Central America, Australia, Europe and Africa. Two primary outcomes were assessed at 3 months post-SAH, mortality, and Glasgow Outcome Score. The association between these outcomes and nation-level socioeconomic indicators (per-capita gross domestic product (GDP), population-to-neurosurgeon ratio, and health care funding model), as well as patient-level covariates were assessed using a hierarchical mixed-effects logistic regression.

Results: Multiple previously-identified patient-level covariates were significantly associated with increased mortality and worse neurologic outcome, including age, intraventricular hemorrhage and initial neurologic grade. Among nation-level covariates, a higher per-capita GDP was associated with reduced mortality and improved neurologic outcome ($p < 0.05$). A higher population-to-neurosurgeon ratio was also associated with better neurologic outcome ($p < 0.01$). Health care funding model was not a significant predictor of either primary outcome.

Conclusions: Higher per-capita GDP and population-to-neurosurgeon ratio were associated with improved outcome after aneurysmal SAH. The former may speak to resource availability, while the latter may reflect better outcomes with centralized care. Although patient clinical and radiographic phenotypes remain the primary predictors of outcome, national socioeconomic disparities may also explain heterogeneity in outcomes following SAH.

718. Laminectomy with Fusion is cost-effective versus laminectomy alone for Grade I Degenerative Lumbar Spondylolisthesis with Spinal Stenosis: Cost-Utility Analysis over a 5 year time horizon

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Introduction: Grade I degenerative lumbar spondylolisthesis with spinal stenosis is a common cause of spinal morbidity. It remains unclear whether to treat this condition with laminectomy alone or lumbar fusion with laminectomy. This study reports a cost-utility analysis of these two procedures at five-year follow-up.

Methods: Patients were obtained from a single site participating in a randomized trial comparing patients aged 50-81 years, receiving laminectomy alone or laminectomy with instrumented fusion between 2002-2009. Short Form-36 (SF-36) and Oswestry Lower Back Disability Index (ODI) were collected prior to surgery and post-operatively at 3 months, 6 months, 1 year, and annually to 5 years. Direct costs were calculated from a hospital perspective using total charges and year-specific cost-to-charge ratios, adjusted to 2012 dollars. 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 area under the utility curve relative to the baseline.

Results: 39 patients received laminectomy and 37 patients received laminectomy with fusion. All patients showed significant improvements in the SF-36 and ODI relative to baseline ($p < 0.01$). Patients receiving fusion showed greater gain in QALYs at 5 years compared to laminectomy alone ($0.83 + 0.20$ vs. $0.46 + 0.24$; $p = 0.001$). Patients who received laminectomy alone had higher reoperation rate (38.5% vs. 18.9%; $p = 0.06$). Total costs, including reoperations, were lower for laminectomy alone compared to fusion ($\$23,428 + \$18,651$ vs. $\$41,019 + \$17,164$, $p < 0.00006$). Cost/QALY ratios were comparable for each procedure (laminectomy: $\$50,297$; fusion: $\$49,498$). Incremental cost-effectiveness ratio (ICER) of fusion compared to laminectomy alone was $\$48,473$, and below societal willingness-to-pay threshold.

Conclusions: Laminectomy with fusion is associated with greater gain in QALYs at 5 years compared to laminectomy alone and is a cost-effective procedure for Grade I degenerative lumbar spondylolisthesis.

719. Familial Occurrence of Brain Arteriovenous Malformation: A Novel ACVRL1 Mutation Detected by Whole Exome Sequencing

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Introduction: Brain arteriovenous malformations (BAVM) can occur in patients with familial hereditary hemorrhagic telangiectasia (HHT), but familial occurrence of this condition has also been described in the absence of HHT stigmata. This study examined a family with three affected cases without HHT using whole exome sequencing, in an attempt to provide a comprehensive genomic characterization.

Methods: A Turkish family with six members was included in the study. One sibling had both spinal and brain AVM while two siblings had BAVM only. The parents and the fourth sibling were not affected as confirmed by cranial MRI. We performed whole exome capture and Illumina sequencing on blood samples from the two family members with BAVMs, one from the proband and one from his affected sister.

Results: Whole exome sequencing performed on 2 of the affected patients revealed an ACVRL1p.Lys332Glu mutation. Variant segregation in family members was confirmed by direct Sanger sequencing.

Conclusions: A novel mutation in ACVRL1 was found to be associated with BAVM in a familial occurrence and in the absence of HHT stigmata. Furthermore, this study demonstrates whole exome sequencing technology can be particularly useful for gene discovery in conditions where mapping can be confounded by locus heterogeneity and uncertain diagnostic classification schemes.

720. Epidemiology of a Large Telestroke Cohort in the Delaware Valley

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Introduction: The American Heart Association/American Stroke Association has recently endorsed Telestroke. It has enhanced stroke diagnosis, increased tPA administration and improved long-term outcomes. However, many of the publications on telestroke so far have been review articles. We investigated the epidemiological features of telestroke patients and evaluated the difference between the transferred and non-transferred cohorts.

Methods: We collected data on telestroke consultation, between January 2012 and June 2013, regarding patient's age, gender, diagnosis, NIHSS, onset-to-spoke time (OTS), tPA administration and transfer status. Further data was obtained on transferred patients regarding discharge and endovascular interventions.

Results: The means of age, NIHSS and OTS time were the following: 67.59 years, 7.65 and 11.28 hours respectively. The proportion of transferred patients was 12.03%, lower than what was previously reported. The overall rate of IV tPA administration was 11.98%. Transferred patients had a significantly higher NIHSS mean (10.93 vs 6.73; $P < 0.001$), and were more likely to have received IV-tPA on onset (25.57 vs 9.67; $P < 0.001$). The age, gender proportion, stroke mimic proportion, and the mean of OTS did not differ between the two-groups (0.49 vs. 0.31 $P = 0.3779$). A logistic regression showed that NIHSS and tPA administration at onset predict the transfer. The odds ratios were 1.06 and 2.78 respectively ($P < 0.001$). Of the transferred patients, 4.5% received endovascular intervention. The mortality rate of transferred patients was 12.9%. Other outcomes were the following: 52% discharge to rehabilitation facilities, 29% discharge to home, and 8% discharge to long-term nursing facilities.

Conclusions: Telestroke network is increasing the frequency of tPA usage in acute ischemic stroke and decreasing the need for transfer. Our aim was to optimize the stroke therapy to shorten the hospital stay and to increase the discharge home. This allows, a better functional outcome and an additional benefit of cost-saving for the hospital.

721. Pipeline Embolization Device for Internal Carotid Artery Aneurysms: Does Size and Location Affect Occlusion Rates?

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Introduction: Pipeline Embolization Device represents a breakthrough in the treatment of aneurysms. Despite widespread enthusiasm, data is limited to determine whether aneurysm size and location in the internal carotid artery (ICA) affect the rate of aneurysm occlusion.

Methods: We reviewed 137 unruptured ICA aneurysms. Aneurysms were stratified according to size and location into on-label and off-label (FDA). The later was subdivided into three groups. A) less than 10 mm located from the petrous to the superior hypophyseal ICA. B) more than 10 mm located from the posterior communicating to the ICA bifurcation. C) less than 10 mm located similarly to group B. Rate of aneurysm occlusion was determined/divided into complete (100%) and near-complete ($< 90\%$).

Results: Groups were on-label ($n=28$), group A ($n=80$), group B ($n=8$), group C ($n=21$). The most common locations were ophthalmic (35%), cavernous (20%), and posterior communicating (20%). Aneurysm size was 7.7 mm (17.5 mm on-label; 4.7 mm group A; 13.4 mm group B; 4.2 mm group C). Follow-up was available for 127 aneurysms with mean duration of 9.6 months. Complete occlusion occurred in 65% (on-label); 72% (group A); 87% (group B); 52% (group C). Near-complete occlusion occurred in 23% (on-label) and 7% (group A).

Conclusions: Occlusion rates were similar for small and large proximal ICA aneurysms. Use of single PED resulted in lower occlusion rates compared to PUFs trial. Small aneurysms located from the posterior communicating to the ICA bifurcation showed lower occlusion rates. The position of the posterior communicating artery with retrograde filling may account for these findings.

722. AQUAPORIN-4 GENE VARIANT INDEPENDENTLY PREDICTS COMBINED EDEMA VOLUME AFTER INTRACEREBRAL HEMORRHAGE

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Introduction: Aquaporin-4 (AQP4) is the prominent water-channel protein in the brain playing a critical role in controlling cell water content. After intracerebral hemorrhage (ICH), perihematomal edema (PHE) formation leads to a rapid increase in intracranial pressure after the initial bleed. We sought to investigate the effect of a common genomic variant in the AQP4 gene on PHE formation after ICH.

Methods: We reviewed the literature and identified a candidate polymorphism in AQP4 genes previously reported in GWAS studies. Between February 2009 and March 2011, 128 patients consented to genetic testing and were genotyped for single nucleotide polymorphism (SNP) rs1058427 on the AQP4 gene. Genomic DNA was extracted from buccal swabs using MasterAmp extraction kits (Epicentre, Madison, WI). DNA extracted from buffy coats of whole blood samples was amplified via PCR. Linear regression with log-transformed ICH+PHE volume as the response variable was used to determine the association of SNP rs1058427 controlled for admission variables age, GCS,

infratentorial location, hypertension, systolic blood pressure, blood urea nitrogen, glucose, and alkaline phosphatase.

Results: Nine of 128 patients had the minor allele for SNP rs1058427. Presence of the minor allele was significant in the model ($p=0.010$), and associated with an increase of 239% in ICH+PHE volume ($\beta=1.22$, $\exp(\beta)=3.39$) after controlling for admission variables. Other significant variables included in the model were age ($p=0.034$) and GCS ($p=0.001$).

Conclusion: The establishment of an independent association between rs1058427 and ICH+PHE volume provides evidence implicating the AQP4 gene in hematoma and edema formation after ICH.

723. BMP signaling modulation inhibits cerebral arteriovenous malformations in a vertebrate model

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Introduction: Cerebral arteriovenous malformations (AVMs) are vascular anomalies that carry a high risk of stroke and death. Current treatment options for these lesions are limited to surgery, external beam radiation, and/or endovascular embolization; they carry substantial risks. In order to test potential AVM therapies, we utilized a reverse genetics approach to model AVMs in zebrafish.

Methods: In a zebrafish line with endothelial expression of EGFP (Tg(flk1:EGFP)) we used antisense morpholino oligonucleotides to knockdown activin receptor-like kinase I (alk1), which encodes a TGF-beta family type I receptor implicated in human AVMs. Organisms were subjected to drug treatment and then experimental groups were assessed by whole embryo morphometrics, fluorescent vessel histology, and phosphorylated SMAD1 enzyme-linked immunosorbent assay.

Results: Knockdown of alk1 caused a spectrum of morphological, functional, and molecular defects that resemble those seen in humans with AVMs. We found that losartan, an angiotensin II receptor antagonist, normalizes blood vessel morphology and systemic manifestations of high-output arteriovenous shunting in vivo. SMAD1 phosphorylation was significantly decreased in alk1 morphants compared to uninjected organisms (0.189 ± 0.0201 , 0.429 ± 0.0164 , $p=0.0002$). After treatment with losartan, morphant SMAD1 levels approached uninjected levels (0.326 ± 0.0360 , $p=0.0355$) and were significantly higher than those seen in the morphant-control group ($p=0.0294$).

Conclusions: These data suggest that modulating the BMP signaling pathway with losartan, a drug in widespread clinical use in humans as an anti-hypertensive, may be an effective therapeutic strategy for patients with AVMs.

724. The fate of cranial neuropathy after flow diverter treatment of carotid aneurysms

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Introduction: Although endovascular treatment of brain aneurysms has gained popularity over the last decade,

microsurgery has been the gold standard for decompression of cranial nerves (CN) affected by aneurysmal mass effect. Recovery of visual symptoms has been quoted as high as 79% with open treatment of compressive cerebral aneurysms. The question as to whether endovascular flow diversion can equal microsurgical decompression in restoring function in cranial neuropathy remains unanswered.

Methods: The medical records of patients presenting with cranial neuropathy (2, 3, 4 and 6th CN) due to cerebral aneurysm and treated with the pipeline embolization device (PED) between November 2009 and October 2013 were retrospectively reviewed. Nine institutions from North America, led by the Endovascular Neurosurgery Research Group contributed patient data. Demographics, cranial neuropathy outcome (improved, unchanged, or worse), clinical complications, and radiographic outcome were recorded.

Results: Forty-three patients met inclusion criteria for the study representing 43 treated aneurysms of the internal carotid artery (ICA). There were 40 females (93%) and 3 males (7%). The mean age was 64.5 (33-89). Of the 43 aneurysms, 24 (56%) were of the cavernous segment while 19 (44%) were distal to the cavernous segment. At last follow-up 86.1% of aneurysms had complete or near complete occlusion. The 30 day morbidity was 14%. The rate of cranial nerve improvement after PED was 39.5%, 69.2%, and 81.25% at 3, 6, and 12 months, respectively. Thirty-eight patients had known duration of symptoms prior to treatment. At last follow-up, 100% ($n=12$) of patients improved if treated within one month of symptom onset, while 38.5% ($n=26$) improved if treated after one month of symptom onset.

Conclusions: Cranial neuropathy due to cerebral aneurysm responds similarly when treated with pipeline embolization when compared to open surgery.

725. A Critical Assessment of Complications Associated with Use of the Pipeline Embolization Device

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Introduction: The Pipeline Embolization Device (PED) has become an important tool in the treatment of complex cerebrovascular pathology since its FDA approval in April 2011. We sought to determine the overall complication rate (permanent and transient) associated with the use of this new device from a single institution.

Methods: We retrospectively examined a prospectively maintained database of our patients treated with the PED since its availability to the current time. One hundred and twenty six patients (22 male, 104 female; Age range 14-83 yrs, Ave 59.6 yrs) were treated for a total of 137 intracranial aneurysms, one cervical internal carotid artery dissection, one cervical vertebral artery dissection, and one carotid-cavernous fistula with a total of 221 PED (1.75 PED/pt).

Results: There were a total of 40 complications experienced by 33 patients in our cohort. Four complications (4/126, 3.2%) in four patients were permanent, resulting in three deaths and one permanent disability. There were an additional 36 complications (36/126, 28.6%) in 29 patients, all of whom went on to recover completely. The total complication rate associated with the use of the PED was 31.7% (40/126).

Conclusions: Despite a low rate of permanent complications associated with the PED in this series, the total complication rate was high. This finding supports the conclusion that this device should be reserved for the most challenging aneurysms. Patients

should be advised of this higher rate of transient, peri-procedural complications.

726. Treatment of Intracranial Atherosclerosis with Stenting: A Review of Outcomes in the Post-SAMMPRIS Era

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Introduction: Intracranial atherosclerotic disease (ICAD) represents a significant global health burden. The proportion of ischemic strokes attributable to ICAD ranges from 10-50% depending on geographic location, ethnicity and medical comorbidities. The initial promise of endovascular stenting for the treatment of ICAD has been tempered by the results of the SAMMPRIS trial which demonstrated better outcomes with medical management compared to stenting for symptomatic ICAD. We review the ICAD stenting outcomes following the publication of SAMMPRIS.

Methods: A comprehensive literature search was performed using Pubmed to identify all case series of stenting for ICAD after the publication of SAMMPRIS in September 2011. The type and design of the stent, number of patients and lesions, inclusion criteria, and clinical and angiographic outcomes were noted.

Results: From October 2011 to August 2013, 19 ICAD stenting series were identified describing the interventional outcomes for 2,196 patients with 2,314 lesions. Of the 38 different stents used, 87% were balloon-expandable stents (BES) and 13% were self-expanding stents (SES). The median minimum stenosis was 50%. The median rates of technical success rate, postprocedural ischemic events, and symptomatic in-stent restenosis (ISR) were 98% (range 87-100%), 9.4% (range 0-25%), and 2.7% (range 0-11.1%), respectively. The median follow-up durations were one to 67 months. Despite the advantages and disadvantages associated with the versatility and durability of BESs compared to SESs, there has yet to be definitive evidence that the clinical outcomes of either stent design is superior to its counterpart.

Conclusions: The management of severe ICAD remains controversial. Future ICAD trials are needed to better define the optimal stent design, lesion location and morphology, and patient population which will portend the best outcomes with intervention. Advances in endovascular technology and medical therapy remain necessary to combat this cerebrovascular pathology.

727. Patient phenotypes associated with outcomes following aneurysmal subarachnoid hemorrhage: A principal component analysis

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Introduction: Predictors of outcome following aneurysmal subarachnoid hemorrhage have been previously determined through hypothesis-driven methods that often exclude putative covariates and require a priori knowledge of potential confounders. Here, we apply a data-driven approach, principal component analysis (PCA), to identify baseline patient phenotypes that may predict neurological outcomes.

Methods: PCA was performed on 120 subjects enrolled in CONSCIOUS-1, a prospective randomized trial of clazosentan for the prevention of angiographic vasospasm. Correlation matrices were created using a combination of Pearson, polyserial and polychoric regressions among 46 variables. Scores of significant

components (with eigenvalues greater than 1) were included in multivariate logistic regression models with incidence of severe vasospasm, delayed ischemic neurological deficit (DIND) and long term outcome as outcomes of interest.

Results: Sixteen significant principal components accounting for 74.6% of the variance were identified. A single component, dominated by the patients' initial hemodynamic status, World Federation of Neurosurgical Societies score, neurological injury and initial neutrophil/leukocyte counts was significantly associated with poor outcome. Two additional components were associated with angiographic vasospasm, of which one was also associated with DIND. The first was dominated by the aneurysm-securing procedure, subarachnoid clot clearance and intracerebral hemorrhage, while the second had high contributions from markers of anemia and albumin levels.

Conclusions: PCA, a data-driven approach, identified patient phenotypes that are associated with worse neurological outcomes. Such data reduction methods may provide a better approximation of unique patient phenotypes and may inform clinical care as well as patient recruitment into clinical trials.

728. Extracellular RNAs as biomarkers for the cerebral vasospasm after aneurysmal subarachnoid hemorrhage

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Introduction: Recent evidence suggests that RNAs may function as extracellular signaling molecules, allowing intracellular communication both during development and disease. We sought to identify and study alterations in exRNAs in blood and cerebrospinal fluid (CSF) after aneurysmal subarachnoid hemorrhage, with the goal of identifying biomarkers for cerebral vasospasm and neurological decline.

Methods: We enrolled 20 patients who presented with aneurysmal subarachnoid hemorrhage and had an external ventricular drain (EVD) placed. We prospectively collected clinical information, including imaging and laboratory studies. We collected daily blood and CSF samples from each patient from the time of admission until the removal of the EVD. Blood and CSF samples were analyzed and processed to isolate exRNAs. Cluster analysis was used to group patients into those with poor and good clinical grades based on exRNA signatures.

Results: We identified a robust increase in a cohort of microRNAs in the blood and CSF of patients after hemorrhage. Notably, we identified a 12 fold increase in the levels of microRNA92 in samples from patients on post-bleed day 2 after hemorrhage relative to controls. The levels of this microRNA returned to baseline on post-bleed day 7. MicroRNA92 is a regulator of endothelial nitrous oxide synthase (eNOS). Increased levels of this microRNA results in decrease of the eNOS transcript and the ability to generate nitrous oxide. Using cluster analysis of patient samples on post-bleed day 2 we were able to predict with 80% accuracy the likelihood of cerebral vasospasm and neurological decline.

Conclusions: exRNAs are secreted into the blood and CSF of patients after aneurysmal subarachnoid hemorrhage. These molecules may serve as biomarkers to help predict likelihood of decline after aneurysm rupture. Identification of biological targets of some of these molecules, specifically microRNAs, may provide new insight into the biological pathways activated after aneurysm rupture.

729. Clinical and Radiographic Analysis of an Artificial Cervical Disc: Seven Year Clinical and Radiographic Outcomes from a Prospective Randomized Controlled Clinical Trial

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Introduction: To determine its safety and efficacy, we examined the clinical and radiographic outcomes of patients enrolled in a prospective, randomized, multicenter trial of an artificial cervical disc device at 7 years of follow up.

Methods: At 32 investigational sites, 541 patients with single-level cervical disc disease with radiculopathy were randomized to 1 of 2 treatment groups: 276 investigational group patients underwent anterior cervical discectomy and arthroplasty with an artificial cervical disc, and 265 control group patients underwent anterior cervical discectomy and fusion. Clinical and radiographic follow-ups were completed preoperatively, intraoperatively, and at 1.5, 3, 6, 12, 24, 36, 60 and 84 months.

Results: Of the 541 patients enrolled, 395 patients (212 investigational and 183 control patients) have completed 7 years of clinical follow-up. Significant improvements achieved by 1.5 months in both groups were sustained at 7 years. In the investigational group, mean Neck Disability Index improvements from preoperative scores were 38.2 and 37.5 at 60 and 84 months, respectively. In the control group, the corresponding means were 33.8 and 31.9. The differences between the investigational and control groups at 60-month and 84-month periods were significant ($P = 0.014$ and 0.002 , respectively). The overall rates of maintenance or improvement in neurological status in the investigational group were significantly higher: 92.2% and 8.2% at 60 months and 84 months as compared with 85.7% and 79.7% in the control group ($P = 0.017$ and 0.0011 , respectively). At 84 months, the percentage of working patients in the investigational group was 73.9%, and in the control group, 73.1%. Postoperatively, the implant effectively maintained average angular motion of 6.67° at 60 months and 6.75° at 84 months. At 84 months, one implant migration was observed. Rates for surgery at the index level trended lower in the investigational group (11/276; 4%) when compared to the control group (29/265; 10.9%), and there were statistical differences between the investigational and control groups with specific regard to the rate of subsequent revision and supplemental fixation surgical procedures. Additional surgical procedures for adjacent segment disease were observed in both treatment groups. Rates for surgery at adjacent levels trended lower in the investigational group.

Discussion: Cervical disc arthroplasty has the potential for preserving motion at the operated level while providing biomechanical stability and global neck mobility and may result in a reduction in adjacent segment degeneration.

Conclusion: The PRESTIGE Disc maintains improved clinical outcomes and segmental motion after implantation at 7-year follow-up.

730. No Difference in Postoperative Complications, Pain and Functional Outcomes Up to 2 Years After Incidental Durotomy in Lumbar Spinal Fusion: A Prospective, Multi-Institutional, Propensity Matched Analysis of 1741 Patients

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Introduction: Incidental durotomies occur in up to 17% of

spinal operations. Controversy exists regarding the short and long-term consequences of durotomies. The primary aim of this study was to assess the effect of incidental durotomies on the immediate postoperative complications and patient reported outcomes measures

Methods: 1741 patients were selected from a multi-institutional prospective data registry, who underwent primary lumbar fusion for low back pain and /or radiculopathy between January 2003 and December 2010. We collected and analyzed data on patient demographics, postoperative complications, back pain, leg pain, and functional disability over two years, with risk adjusted propensity score modeling.

Results: Incidental durotomies occurred in 70 patients (4%). Compared to the control group ($n = 1671$), there was no significant difference in postoperative infection ($p = 0.32$), need for reoperation ($p = 0.85$), or symptomatic neurologic damage ($p = 0.66$). At one and two year follow up, there was no difference in patient reported outcomes of back pain (BP-Visual Analog Scale), leg pain (LP-Visual Analog Scale), or functional disability (Owestry Disability Index) ($p < 0.3$), with results remaining consistent in the propensity-matched cohort analysis ($p < 0.4$).

Conclusions: Within the context of an on-going debate on the consequences of incidental durotomy, we found no difference in neurologic symptoms, infection, re-operation, back pain, leg pain, or functional disability over a two year follow up period.

731. Improvement in Pain After Lumbar Surgery in Cancer Patients with Mechanical Radiculopathy

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Introduction: Lumbar metastases can result in spinal instability and mechanical radiculopathy, characterized by radicular pain produced by axial loading. This pain pattern represents a definitive symptom of neoplastic instability and may serve as a reliable indication for surgical stabilization. We examined the results of surgical decompression and fixation in the treatment of mechanical radiculopathy.

Methods: The Memorial Sloan-Kettering Cancer Center Department of Neurosurgery internally maintained spine neurosurgery operative database was queried over an 8-year period to identify all patients with spinal metastases who underwent lumbar surgery. Patients were identified and deemed eligible for inclusion in this study based on the presence of all of the following: (1) metastatic tumor, (2) lumbar surgery and (3) lumbar radiculopathy. Only patients whose operative indication included mechanical radiculopathy were included. Pre- and post-operative pain was assessed with the Visual Analog Scale (VAS) of pain, while pre- and post-operative performance status was evaluated using the Eastern Cooperative Oncology Group (ECOG).

Results: 55 patients were included in the cohort. L2 and L3 were the most common levels involved and most patients underwent multi-level posterior decompression and instrumented fusion. Following surgery, 98% of patients reported pain relief. A significant difference between average pre- and post-operative pain scores was found ($p < 0.01$). Overall, 41.5% of patients experienced improvement in their ECOG score post-operatively.

Conclusions: Mechanical radiculopathy in patients with spinal metastases represents a highly reliable surgical indication. Spinal decompression and fixation is an effective treatment for pain palliation in this patient population.

732. Prevalence and Type of Cervical Deformity Among 470 Adults with Thoracolumbar Deformity

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Introduction: Deformity may present in multiple spinal regions in a single patient. Our objective was to assess the prevalence of cervical deformity among adults presenting for evaluation of thoracolumbar (TL) deformity.

Methods: Multicenter, prospective, consecutive series. Inclusion criteria: TL deformity and age <18. Parameters included pelvic tilt (PT), pelvic incidence (PI), lumbar lordosis (LL), C2-C7 sagittal vertical axis (C2-C7 SVA), C7-S1 SVA and C2-C7 lordosis (CL). Cervical deformity was defined as CL <0° (cervical kyphosis [CK]) or C2-C7 SVA <4cm (cervical positive sagittal malalignment [CPSM]). Patients were stratified by SRS-Schwab deformity classification, including curve type (N=sagittal deformity, T=thoracic scoliosis, L=lumbar scoliosis, D=T+L scoliosis) and modifier grades: PT (0: <20°, +:20-30°, ++: >30°), C7-S1 SVA (0: <4cm, +:4-9.5cm, ++: >9.5cm), PI-LL mismatch (0: <10°, +:10-20°, ++: >20°).

Results: 470 patients met criteria (mean age=52), with mean CL=-8° and mean C2-C7 SVA=3.2cm. Prevalence of CK and CPSM was 31% and 29%, respectively, and 53% had CK and/or CPSM. Prevalence of CK differed by curve type: N=15%, L=27%, D=37%, T=49% (p <0.001); prevalence of CPSM did not differ by curve type (p=0.19). Higher PT grades had lower prevalence of CK (0=40%, +=27%, ++=15%; p <0.001) but greater prevalence of CPSM (0=23%, +=28%, ++=45%, p=0.001). Similarly, higher SVA grades had lower prevalence of CK (0=40%, +=23%, ++=11%; p <0.001) but greater prevalence of CPSM (0=24%, +=24%, ++=48%, p <0.001). Higher PI-LL grades had lower prevalence of CK (0=35%, +=31%, ++=22%; p=0.034) but no association with CPSM (p=0.46).

Conclusions: Cervical deformity is highly prevalent (53%) among adults with TL deformity. Its prevalence and type differs significantly based on SRS-Schwab curve type and sagittal spinopelvic modifier grades. Evaluation of TL deformity should include assessment of cervical parameters for evidence of concurrent cervical deformity.

733. Defining Substantial Clinical Benefit (SCB) in Patients Undergoing Decompression Surgery for Cervical Myelopathy

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Introduction: Validated patient derived outcome measures are now being applied routinely to assess outcomes following spine surgery. To date few criteria are well accepted as defining clinical success. The minimal clinically important difference is an important hypothetical threshold which has been difficult to estimate. More recently measures of SCB have been sought as a better measure of success. Few reports have established SCB thresholds in the specific context of cervical myelopathy.

Methods: Prospectively collected patient derived outcome measures were obtained from 46 patients who underwent decompression for cervical myelopathy. SCB thresholds for neck

disability index (NDI), neck and arm visual analog scores (VAS), Nurick score (N), modified JOA score (mJOA), Short Form-12 physical (PCS) and mental component (MCS) scores were calculated using receiver operating characteristic (ROC) curve analysis to discriminate between reports of not sure and definitely yes on the question, Would you have the same treatment again for the same condition? Threshold levels for the raw score and the area under the curve (AUC) for the ROC curve are presented.

Results: SCB thresholds from most to least discriminate were as follows: PCS of 30.1 (AUC of 0.8978); NDI of 34.0 (AUC of 0.8263); MCS of 46.2 (AUC of 0.7530); mJOA of 13.0 (AUC of 0.7344); Neck VAS of 2.8 (AUC of 0.6773); Right arm VAS of 1.8 (AUC of 0.6593); Left arm VAS of 2.4 (AUC of 0.6148); and N of 2.0 (AUC of 0.3606).

Conclusions: To our knowledge this study is the first time SCB thresholds were defined for a series of patients specifically undergoing surgery for cervical myelopathy including the disease specific measures of N and mJOA. Good discrimination was observed for PCS and NDI while only fair discrimination was observed for MCS and mJOA. N and VAS provided poor discrimination.

735. Outcomes of surgical management of cervical spondylotic myelopathy: Results of the Prospective, Multicentre, AOSpine International Study in 479 Patients

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Introduction: The efficacy of surgical decompression for cervical spondylotic myelopathy (CSM) has been recently reported for the North American population in prospective multicenter study. However, data are lacking regarding international variations in patient presentation, management and outcomes for CSM. Here, we present results of a prospective, international multicentre study of the management of CSM.

Methods: Between 2007 and 2011, 479 patients with CSM were prospectively enrolled in 16 sites based in Asia Pacific (AP) n=150, Europe (E) n=126, Latin America (LA) n= 80 and North America (NA) n=123. Demographic information, surgical technique and functional outcome parameters including the mJOA, Nurick Score, NDI, SF36v2 were collected.

Results: The mean age at presentation was 56.4 years (± 11.91) and 65% were males. There were no significant regional differences in baseline mJOA, Nurick and NDI scores (p <0.1) but LA patients had a significantly lower SF36 PCS and a much higher SF36 MCS (p <0.008). Across the regions there were significant differences in presenting age (p <0.0003) and etiology (p <0.001). There were regional differences in surgical approach: in E (71.43%), AP (61.07%) and NA (56%) underwent anterior surgery whereas in LA most (66.25%) had posterior surgery. Overall, most patients had anterior surgery (57.7%). All outcome measures (mJOA, Nurick, NDI and SF36v2) showed significant improvement (P < 0.001) at 1 year. mJOA improved from 12.48 to 14.9, NDI improved from 37.33 to 25.24 and Nurick score improved from 3.28 to 2.00. Both the SF36v2 PCS and SF36v2 MCS also improved from 34.23 to 41.18 and from 39.52 to 46.22 respectively. There were regional differences in outcome with patients from AP and NA showing greater functional improvement in mJOA and Nurick than patients from Europe.

Conclusions: In a large international study we have shown that surgical decompression for patients with CSM was beneficial despite the differences in presentation and surgical techniques.

736. Postoperative Cervical Sagittal Imbalance Affects Outcome and Outpatient Costs Following Surgery for Cervical Spondylotic Myelopathy

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Introduction: The purpose was to determine if postoperative cervical sagittal balance following surgery for cervical spondylotic myelopathy (CSM) affects outcome and outpatient health costs.

Methods: A prospective non-randomized 4-center study enrolled patients over 2 years. Outcome assessments (mJOA, Oswestry Neck Disability Index, EQ-5D, and SF-36 PCS) were obtained preoperatively, 3 months, 6 months, and 1 year postoperatively. Sagittal balance, measured preoperatively and 1 year postoperatively, was defined as the distance between a C2 and C7 plum lines (standing lateral cervical spine radiograph). Health cost diaries were completed to assess outpatient health costs.

Results: 21 ventral and 28 dorsal patients were enrolled. Average age (62 years; 39% female). Baseline cervical sagittal balance was +28.5 mm. Significant improvement in mJOA and SF-36 PCS scores were observed following surgery regardless of approach. A lower cervical sagittal balance value postoperatively was an independent predictor of clinical improvement (≥ 5 points) in SF-36 PCS score ($P = 0.02$). A greater sagittal imbalance value was inversely associated with clinical improvement in SF-36 outcome ($P = 0.02$) and was observed more frequently in patients treated with dorsal surgery. Sagittal balance value of greater than +45 mm postoperatively was associated with no improvement in HR-QOL following surgery even though myelopathy improved. An increase in post-operative sagittal balance was associated with an increase in outpatient costs following surgery.

Conclusions: Cervical sagittal balance is an important independent factor that significantly affects patient outcome and outpatient costs following surgery for CSM.

737. Preoperative Predictors of 3-Month/1-Year Change in Quality-of-Life (EQ-5D) Following Multilevel Lumbar Laminectomy and Fusion

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Introduction: There is a paucity of data examining patient characteristics that affect improvement in quality-of-life following lumbar laminectomy and fusion(LLF).

Methods: 332 patients undergoing LLF in 3 or fewer levels were included. Patient demographics, perioperative data, and 90-day postoperative complications were gathered from the medical record. Patient reported outcomes (PROs) including EQ-5D, ODI, NRS-back/NRS-leg pain, ZUNG depression rating, and MSPQ anxiety rating were collected prospectively at baseline, 3-months, and 1-year. Multivariate analysis was used to assess the association between EQ-5D change scores at 3-months/1-year with age, gender, BMI, ASA grade, blood loss, primary vs. revision surgery, use of an interbody fusion, history of smoking, history of diabetes, 90-day complications, and preoperative PROs measures as covariates.

Results: Univariate analysis revealed significant improvement from baseline at 3-/12-month follow-up for EQ-5D, ODI,

NRS-back pain, and NRS-leg pain(p less than 0.001). Multivariate analysis at 3-months demonstrated that increased age(p less than 0.001), increased preoperative NRS-back pain($p=0.001$), and worse preoperative ODI($p=0.001$) resulted in greater improvement in EQ-5D, whereas increased anxiety(MSPQ, $p=0.015$) resulted in less improvement in EQ-5D. Multivariate analysis at 1-year demonstrated that increased age($p=0.012$) and worse preoperative ODI($p <0.001$) resulted in greater improvement in EQ-5D, whereas increased anxiety(MSPQ, $p <0.001$) and 90-day complications($p=0.006$) resulted in less improvement in EQ-5D.

Conclusions: Our work demonstrates significant improvement in all PROs at 3-months/1-year following LLF. Older patients and those with higher levels of back specific disability(ODI) have greater gains in quality-of-life at both 3-months/1-year after surgery. Patients with higher anxiety preoperatively have decreased improvement in quality-of-life at both 3-months/1-year postoperatively.

738. Survival and recurrence following resection of chordoma in the mobile spine: Results of 171 patients from the AOSpine Primary Tumor Knowledge Forum

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Introduction: Chordomas are primary spinal tumors that grow via an indolent course but have devastating effects on patients' lives. The location of the tumor along the neuroaxis plays an important role in the feasibility of surgical resection. Boriani and colleagues published a series of 52 patients with mobile spine chordoma in 2006 reaffirming the importance of en bloc resection for this population. The present study reviews recurrence and survival data from 171 patients with mobile spine chordoma across multiple international centers.

Methods: Descriptive statistics were summarized using mean/standard deviation or frequency and percentage. Enneking appropriate (EA) resection was designated if the preoperative classification was S1 or S2 and the resection by pathology report was intralesional, or if the classification was S3-IIB and the resection was classified as marginal or metastatic and the pathology report was marginal or wide.

Results: Fifty-seven patients (33%) were female, 114 patients were male (67%). The mean age at diagnosis was 58 ± 14 years (range 17-86 years). Median survival after surgery was 6.9 years for all patients. Surgeon's postoperative assessment of an en bloc resection ($p=0.041$) and Enneking appropriate resection ($p=0.034$) were associated with significantly increased survival. Patients with intralesional transgression on the surgical pathology specimen were 7.4 times more likely to experience a recurrence within 10 years (HR 7.442, $p=0.002$). Age at diagnosis, tumor volume and level (cervical, thoracic, lumbar) did not significantly impact survival or tumor recurrence.

Conclusions: Achievement of en bloc resection with no evidence of contamination on the surgical pathology specimen affords increased survival and decreased risk of recurrence for patients with mobile spine chordoma. Patient age, tumor volume

and the level of the lesion do not appear to influence patient survival or tumor recurrence.

739. The Nationwide Inpatient Sample Database does not Accurately Reflect Surgical Indications for Fusion

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Introduction: Several studies based on administrative databases such as the Nationwide Inpatient Sample (NIS) have suggested that the greatest recent rise in lumbar spinal fusion operations has been in the general categories of degenerative disc disease and disc herniation, neither of which is a well-accepted indication for lumbar fusion. Administrative databases typically classify cases using ICD-9-CM discharge codes. These codes are not generated by surgeons, but are rather assigned by hospital medical coders. It is unclear how accurately they capture the surgeon's indication for fusion. We sought to compare the ICD-9-CM code(s) assigned by the medical coder to the surgeon's indication based on a review of the medical chart.

Methods: A retrospective review was undertaken of all lumbar fusions performed by our department between 8/1/2011 and 8/31/2013. Indication for fusion was categorized as: spondylolisthesis, deformity, tumor, infection, trauma, pseudarthrosis, adjacent-level degeneration, stenosis, or degenerative disc pathology. These surgeon diagnoses were compared with the primary ICD-9-CM code that was submitted to the NIS.

Results: 178 lumbar fusion operations were performed over 170 hospital admissions. There were 43 hospitalizations for fusion, whose indications were tumor, infection, or trauma; the remaining 127 were for degenerative diagnoses. The primary ICD-9-CM diagnosis matched the surgeon's diagnosis in 101/170 (59%) cases. Excluding the 43 whose indication for fusion we believe are well accepted, the primary ICD-9-CM diagnosis matched the surgeon's diagnosis only 59 of 127 (45%) cases.

Conclusions: Characterizing indications for fusion based on ICD-9-CM codes extracted from large administrative databases does not accurately reflect the surgeon's indication. While these databases may accurately describe national rates of lumbar fusion surgery, the lack of fidelity in the source codes limits their role in accurately identifying indications for surgery. Studying relationships between indications, complications and outcomes stratified solely by ICD-9-CM codes is not well founded.

DePuySynthes Resident Craniofacial Award

740. The Spectrum of Neuro-behavioral Sequelae Following Repetitive Mild Traumatic Brain Injury: A Novel Mouse Model of Chronic Traumatic Encephalopathy (CTE)

Anthony Liberato Petraglia, MD; Benjamin Plog, BA; Samantha Dayawansa, MD, PhD; Michael Chen, BS; Matthew Dashnaw, MD; Katarzyna Czerniecka, MD; Corey Walker, BS; Jeffrey Iliff, PhD; Rashid Deane, PhD; Maiken Nedergaard, MD, PhD; Jason Huang, MD (Rochester, NY)

Introduction: There has been an increased focus on the neurological sequelae of repetitive mild traumatic brain injury (TBI), particularly chronic traumatic encephalopathy (CTE);

however, no animal model exists that captures the characteristic presentation of this phenomenon. We sought to develop an animal model of CTE.

Methods: Our model is a modification and fusion of two of the most popular models of TBI and allows for controlled closed-head impacts to un-anesthetized mice. Two-hundred eighty, 12-week old mice were divided into control, single mild-TBI, and repetitive mild-TBI groups. Repetitive mild-TBI mice received six concussive impacts daily, for 7-days. Behavior was assessed. Neurological severity score (NSS) was computed and vestibulo-motor function tested with the wire grip test (WGT). Cognitive function was assessed with Morris water maze (MWM); anxiety/risk-taking behavior with the elevated-plus-maze (EPM); and depression with the forced swim/tail suspension tests. Sleep EEG/EMG studies were performed at 1-month.

Results: NSS was elevated compared to controls in both TBI groups and improved over time. Repetitive mild-TBI mice demonstrated transient vestibulo-motor deficits on WGT. Repetitive mild-TBI mice demonstrated deficits in MWM acutely and persisting out to 6-months. Both mild-TBI groups demonstrated increased anxiety at 2-weeks but repetitive mild-TBI mice develop increased risk-taking behaviors at 1-month that persists at 6-months. Repetitive mild-TBI mice exhibit depression at 1-month. Both mild-TBI groups demonstrate sleep disturbances.

Conclusions: We describe the neurological sequelae of repetitive mild-TBI in a novel mouse model. The behavior exhibited by repetitive mild-TBI mice, in this model, resembles the characteristic neuro-psychiatric behavioral picture seen in CTE.

741. Thromboembolic Complications Associated with a Transfusion Threshold of 10 g/dl in TBI Patients

Shankar P. Gopinath, MD, FAANS (Houston, TX); Julia Hannay, PhD; Jose-Miguel Yamal; J Clay Goodman, MD; Barbara Tilley, PhD; Claudia Robertson, MD (Houston)

Introduction: Optimal hemoglobin concentration for TBI patients is controversial. Many advocate maintaining a hemoglobin concentration of at least 10 g/dl to optimize cerebral oxygen delivery. However, the transfusions that are required may have some adverse effects. The goal of this analysis was to compare the complication rates in patients enrolled in a clinical trial where two treatments (administration of erythropoietin and transfusion threshold) were randomized using a factorial design.

Methods: Patients were randomly assigned to either the 7 or 10 g/dl transfusion threshold during the acute post-injury recovery period. This report describes the prespecified secondary safety endpoints for the trial including mortality, incidence of ARDS and of nosocomial infections. The incidence of thromboembolic events was also examined because of an imbalance observed in the reporting of adverse events.

Results: Two hundred patients with closed head injury who were not able to follow commands after resuscitation were enrolled in the study. Kaplan-Meier survival curves showed no difference in the two treatment groups (log rank test, $p=.72$). The incidence of ARDS was 16% and 25% in the 7 g/dl and 10 g/dl groups, respectively ($p=.16$). There was no difference in the incidence of infections. The patients in the 10 g/dl group had a significantly higher incidence of thromboembolic events (20% vs. 8%, $p=.009$).

Conclusions: There was no long-term benefit with maintaining a higher hemoglobin concentration, and an increased risk of thromboembolic events. Guidelines for transfusion in hemodynamically stable TBI patients should follow the restrictive strategy recommended for other critically ill patients.

742. Gender and the Effects of TBI/Polytrauma: Comparative Analysis of Female TBI/Polytrauma Cohort Characteristics and Outcomes

Odette Althea Harris, MD, MPH, FAANS (Stanford, CA); David Horton, BA; Joyce Chung, PhD; Jennifer Zahm, BS; Carmelinda Mann, PhD (Palo Alto, CA); Odette Harris, MD, MPH (Stanford, CA)

Introduction: Traumatic Brain Injury (TBI) often secondary to blast explosions in conjunction with multiple systemic injuries is defined as Polytrauma. The characterization and management of TBI/Polytrauma injuries is often directed by data derived from the larger cohort, comprised almost entirely of males (< 95%). This raises concern as to whether these data can be generalized. We hypothesize, that as females represent such small numbers of TBI/Polytrauma patients, their experience is not wholly represented in published outcomes that inform data driven treatment, management, and funding decisions.

Methods: Retrospective cohort study of all female veterans who sustained TBI, and were treated at VA Palo Alto Health Care System, Polytrauma System of Care (VAPAHCS PSC) in context of comparative analysis with published data. Demographics, injury, post-concussive/neurobehavioral symptoms, neuropsychological domains and quality of life data were examined. These data were compared to established prevalence rates in the Polytrauma literature.

Results: Females represent 6% of TBI/Polytrauma patients at VAPAHCS. Female TBI/Polytrauma patients were diagnosed significantly ($p < 0.05$) more often than the general Polytrauma cohort with depression (69% vs. 33%), cognitive disorders (34% vs. 15%), substance abuse (24% vs. 8%). Females were more often homeless (10% vs. 2%) and unemployed (42% vs. 20%), despite higher levels of education.

Conclusions: Females represent small numbers in the general TBI/Polytrauma cohort. Current available data do not wholly represent this subpopulation. Diagnostic/demographic factors and outcomes emerge as significantly different than the general Polytrauma cohort. Since these data drive management algorithms and funding allocations for TBI, improved Methodology and a Gendered approach to research is imperative.

743. Impaired functional networks characterize coma after hemorrhagic stroke

Chuck Mikell, MD; Garrett Banks, BSE; Brett Youngerman, MD; Patrick Karas, BS; Andrew Chan, BS; Henning Voss, PhD; E. Connolly, MD; Jan Claassen, MD, PhD (New York, NY)

Introduction: Hemorrhagic stroke characteristically presents with depressed level of consciousness; yet mechanisms underlying mental status impairment are incompletely understood. Though prior studies have demonstrated resting state network (RSN) alterations in other disorders of consciousness, it is not known what networks are disrupted in coma acutely after brain hemorrhage.

Methods: Resting fMRI was performed on twenty-five acute intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH) patients, nine of whom were comatose. RSN connectivity differences between comatose and non-comatose patients were analyzed by applying dual regression against a template of standard RSNs. Seed-based analyses were also performed.

Results: Seven resting state networks (RSNs) were disrupted in comatose patients: 1.) visual occipital (VO), 2.) visual medial

(VM), 3.) visual lateral (VL), 4.) cognitive control (CC), 5.) right executive control network (RECN), 6.) sensorimotor network (SMN), and 7.) salience network (SN). Loss of within-network connectivity characterized coma, with specific loss of functional connections to several areas, including Broca's area, supplementary motor area, anterior cingulate gyrus, and visual areas. Additionally, aberrant connectivity was seen in comatose patients, including to the frontal pole, visual areas, and the angular gyrus. These correlations were not found within normal resting network architecture.

Conclusions: Cognitive, visual, and sensorimotor networks were disrupted in comatose patients after hemorrhagic stroke; coma was associated with loss of established connections and formation of aberrant connections not seen in awake patients. These insights aid in understanding the underlying biological processes of coma and may help design interventions to recover consciousness after acute brain injury.

744. Venous Sinus Thrombosis with occipital skull fractures - 2 years experience at a London Major Trauma Centre

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Introduction: Damage to cerebral venous sinuses restricting venous outflow is often not considered following Traumatic Brain Injury (TBI), however, it is an important cause of refractory intracranial hypertension and persisting headache.

Methods: We retrospectively analysed CT venograms performed for patients at a London Major Trauma Centre with skull fractures crossing venous sinuses, persisting unexplained refractory intracranial pressure elevation or persisting headache out of keeping with plain CT findings.

Results: Between September 2011 and October 2013, 41 patients underwent CT venograms (32 male; mean age 45.2 range 21-81). Mechanisms of Injury comprised: falls (16), road traffic collisions (10), assault (9), collapse with trauma (4) and unknown (2). Twelve patients had thrombus within transverse or sigmoid sinuses. A further 4 had significant extraluminal compression of a sinus. Only one patient had thrombus and no associated fractures. The 11 with thrombus and additional 4 with sinus compression all had a fracture crossing a venous sinus or lambdoid diastasis. Ten of this group also had base of skull fractures. Of the remaining 25 studies with normal venous drainage 11 had fractures crossing a venous sinus, 8 had base of skull fractures only and the remainder either had no fractures or fractures elsewhere (e.g. facial). Three of the 41 patients died in hospital.

Conclusions: In this series 16 out of 41 patients studied had compromised venous sinus drainage (9 falls, 5 assaults and 2 RTCs). In the sub-group of 27 patients with a fracture/diastasis crossing a sinus 16 (59%) had venous pathology. Knowledge of this can explain refractory intracranial hypertension or headache and assist further management planning. Criteria for CT Venography in trauma are suggested.

745. Functional and structural correlates of persistent postconcussive syndrome

James Harvey Hedges, BS; Yushi Wang, BS; Brett Yarusi, BA (New York, NY); Daniel Graham, BS; Julia Owen, PhD (San Francisco, CA); Jun Maruta, PhD; Lisa Spielman, PhD (New York, NY); Pratik Mukherjee, MD, PhD (San Francisco, CA); Jamshid Ghajar, MD, PhD (New York, NY)

Introduction: People who sustain a concussion may continue to experience symptoms, including headache, dizziness, and fatigue, long after their injury. These symptoms define persistent postconcussive syndrome (PPCS), the etiology and manifestations of which remain unclear. Varied and undefined impairments in neurocognitive function, including in memory and attention, may coincide with PPCS.

Methods: We applied neurocognitive testing and diffusion tensor imaging in 30 PPCS patients and 140 healthy controls to address the following questions: How does PPCS impact neurocognitive function and how is it related to depression and PTSD symptomatology? What are the neuroanatomical correlates of functional decrements in PPCS?

Results: PPCS patients had specific impairments in visual tracking, some impairments in visual attention, and more general impairments in response timing. They had greater variability in gaze position error in a circular tracking task, which may reflect greater fatigability, but did not have impairments in predictive timing. Patients had slower responses and reduced accuracy in the Attention Network Test and generally took longer to complete tasks at normal performance levels. PTSD and depression symptomatology was related to this slowing effect. Microstructural integrity of tracts in anterior and posterior brain regions was associated with some response timing measures, but only the right posterior thalamic radiation showed a group difference.

Conclusions: Neurocognitive deficits seen in PPCS may be part of a subset of deficits that fail to recover shortly after a concussion. Associations with comorbid conditions may reflect overlapping mechanisms. Minor neuroanatomical differences may contribute to PPCS, but do not account for its functional effects.

746. Predicted Poor Neurological Outcome is Overestimated by the IMPACT Prognosis Calculator in Severe TBI Patients After Early Decompressive Craniectomy in Latin America.

Andres Mariano Rubiano, MD (Neiva Huila, Colombia); Jose Charry, MS (Neiva, Colombia); Nancy Carney, PhD (Portland, OR); Juan Puyana, MD (Pittsburgh, PA); P. David Adelson, MD (Phoenix, AZ)

Introduction: In 2007, a prognosis calculator was developed, based on analysis of 8,509 patients with TBI from the International Mission for Prognosis Analysis of Clinical Trials in TBI (IMPACT) study, including data of trials between 1984 and 1997. The calculator model predicts outcomes based on clinical, laboratory and imaging findings. The aim of this study was to compare the estimation of outcome at 6 months in severe TBI patients that underwent early decompressive craniotomy (EDC) in a hospital in Latin America (LA).

Methods: 106 severe TBI patients managed by a damage control approach with EDC between 2009 and 2013 were analyzed. Outcome was evaluated using the Glasgow Outcome Scale (GOS) dichotomizing results as good outcome (GOS 4-5) and poor outcome (GOS 1-3). The IMPACT calculator was used in order to analyze outcome in the same group of patients. Results were

compared and measures of frequency were obtained to identify differences.

Results: Poor global neurological outcome at 6 months was seen in 36/106 patients (33.9%), with mortality (GOS 1) in 26/106 (25.4%). Variables associated with poor outcome included: unreactive pupils at ER presentation, midline shift, compressed basal cisterns and non-evacuated hematoma on initial CT. In contrast, poor neurological outcome predicted by the IMPACT calculator was 65.6%, with a mortality of 48.2%.

Conclusions: The IMPACT prognosis calculator overestimates poor neurological outcome and mortality at 6 months, compared with observed outcome from patients with severe TBI after EDC in a university hospital in LA. Differences in management including intensity of surgical treatment in 1997 as compared with present day may be a variable that should be taken into consideration to understand differences. Prediction of outcome with the IMPACT calculator needs to be analyzed with caution in different contexts, including areas where EDC as a damage control approach is used.

747. Luteolin provides neuroprotection in the models of traumatic brain injury through Nrf2-ARE pathway

Jianguo Xu, Handong Wang, MD, PhD; Ke Ding; Xinyu Lu (Nanjing, Jiangsu Province, China)

Introduction: This study was aimed to investigate whether luteolin could exert neuroprotection in the models of TBI and the possible role of Nrf2-ARE pathway in the putative neuroprotection.

Methods: A modified Marmarou's weight-drop model in mice and scratch model in mice primary cultured neuron were used to induce TBI. Luteolin was given in one subgroup. In vivo, motor performance, permeability of blood-brain barrier and brain water content were evaluated 24h after injury. Moreover, neuronal apoptosis and oxidative stress markers were also examined. We further studied the expression of Nrf2 and its downstream factors via western blot, EMSA and immunofluorescence. In vitro, neuron survival, intracellular ROS and nuclear translocation of Nrf2 were detected. Finally, the effects of luteolin in Nrf2-/- mice were investigated.

Results: In vivo, luteolin administration following TBI significantly ameliorated secondary brain injury, including brain water content, BBB impairment, neuronal apoptosis and neurological deficits. Furthermore, the levels of MDA, SOD and GPX were restored in the group with luteolin treatment. And luteolin could enhance the translocation of Nrf2 to the nucleus both in vivo and in vitro, which subsequently up-regulated the expression of the downstream factors such as HO-1 and NQO1. In vitro, luteolin administration also lowered the intracellular ROS level and increased the neuron survival. However, luteolin treatment failed to provide neuroprotection after TBI in Nrf2-/- mice.

Conclusions: These in vivo and in vitro data demonstrate luteolin can provide neuroprotective effects in the models of TBI, possibly through the activation of Nrf2-ARE pathway.

748. The Rapid Deployment Neuro Team: A Specialized Neurotrauma Team for Combat Casualty Care

Anthony Peter Trenga, BA (Charlottesville, VA); Geoffrey Ling, MD, PhD (Bethesda, MD); Beverly Walters, MD (Fairfax, VA); Leon Moores, MD, MS (Bethesda, MD); James Ecklund, MD (Fairfax, VA)

Introduction: Initially conceived in 1999, the Rapid Deployment Neurological Team (RDNT) was designed to provide a highly

skilled specialty trained neurotrauma team capable of deploying within 24 hours from the US to a military theater in response to changing battlefield needs. The goal was to provide advanced neurosurgical and neuro critical care in anticipation of increased brain-injured casualties. The team was initially comprised of a neurosurgeon, a neurologist with critical care specialization, and a neurosurgical OR technician. This concept was inaugurated in 2003 for deployment to Operation Enduring Freedom (OEF) in Afghanistan, and deployed in 2005 to Iraq for Operation Iraqi Freedom (OIF).

Methods: A comprehensive literature review of modern wartime neurotrauma methodology and first-hand accounts from neurological specialists deployed to OEF and OIF were used to establish the historical context of the RDNT. A retrospective chart review was performed to highlight the incidence of neurotrauma and polytrauma in OEF and OIF and the efficiency of the RDNT model.

Results: During the initial 3½-week deployment in OEF, the RDNT emergently operated on 7 casualties, including civilians and US and allied military personnel. An additional 38 surgeries were performed over 3 months in OIF. Patients were treated for open depressed skull fracture, subdural and subarachnoid hematoma, and pneumocephalus, among others.

Conclusions: Treating over 300 war-injured patients, the RDNT demonstrated its effectiveness in providing surge mission support and underscored the importance of neurotrauma specialty care in war theater. It also provided evidence of the importance of neuro critical care in optimizing patient care and outcome.

Medical Student Summer Research Foundation Award

749. A Dose-Dependent Response of Neuroinflammation after Repetitive Mild Traumatic Brain Injury

Stephen Miranda, Benjamin Plog, BA; Matthew Dashnaw, MD (Rochester, NY)

Introduction: Repetitive mild traumatic brain injury (mTBI) has become an epidemic among athletes and military personnel, but the pathophysiologic processes leading from trauma to chronic neurodegeneration remain unclear. The purpose of this study was to examine, in a dose-response manner, the relationship between the number of mTBI events and the induction of a pathologic process leading to neurologic changes.

Methods: In adapting our previously characterized 'Hit-and-Run' model of repetitive mTBI, mice were suspended in a plastic cone without anesthesia and subjected to an impact over the left temporoparietal lobe by a pneumatic piston with a rubberized tip. Mice received 3 hits every 2 hours for 1, 2, 3, or 4 consecutive days, totaling either 3, 6, 9, or 12 hits. Neurological severity scores were assigned one hour after injury, confirming that all mice underwent mild injury (NSS less than 5/10). Immunohistochemical staining of cerebral tissue was performed to assess levels of GFAP, an established biomarker for astrogliosis following TBI.

Results: Immunostaining revealed a dose-dependent response in GFAP+ area across tissue sections from the ipsilateral and contralateral hemisphere, cortex, white matter, and subcortex. When compared to sham-injured controls, GFAP+ area was not significantly elevated in the 3-hit or 6-hit groups, but was greatly increased in the 9-hit and 12-hit groups, as high as threefold.

Conclusions: These data suggest that the degree of astrogliosis correlates closely with the number of repetitive mTBI events, and

that there may be a threshold number of traumatic events, which when reached initiates a pathologic pathway leading to long-term neurologic injury.

750. Human subthalamic nucleus recordings during high conflict decisions reveal increased spike-LFP interactions in the beta and theta bands

Kareem Zaghloul, MD PhD; Baltazar Zavala, BS; Srikanth Damera, BS; Jian Dong, BS; Codrin Lungu, MD (Bethesda, MD); Peter Brown, PhD (Oxford, United Kingdom)

Introduction: Recent clinical and physiologic evidence suggests that the most common target for deep brain stimulation (DBS), the subthalamic nucleus (STN), may play a crucial role in decision-making. Human STN recordings have demonstrated increases in firing rate and theta (4-8 Hz) band oscillatory power and decreases in beta power (12-30 Hz) during decisions, with greater changes occurring during conflict. It is unclear, however, how conflict related changes in STN oscillations relate to and modulate single-unit spiking.

Methods: We simultaneously captured STN single-unit spiking and local field potential (LFP) activity during DBS surgery as patients performed a sensory-motor task involving low and high conflict decisions.

Results: We found decreases in STN beta power and increases in theta power and firing rate during the decision period, consistent with previous studies. In addition, we found significant interactions between STN spiking activity and beta oscillatory phase during the baseline period that disappeared during low conflict trials. Conversely, this relationship persisted during high conflict trials and was associated with increased spiking. Similarly, we found significant spike-phase locking in the theta band during high conflict trials, which was associated with elevated theta power.

Conclusions: Our results are the first to tie together STN LFP oscillations and firing rates during decision-making. They suggest that the phase of the LFP oscillations may determine the firing of STN neurons, and that this relationship plays a critical role during conflict. Our data yield insight into the neural mechanisms of decision-making in the STN, and have implications for understanding how DBS may disrupt these circuits.

751. Brain computer interface (BCI) controlled prosthetic arm movement is possible in the absence of visual input with proprioceptive feedback

Elizabeth C. Tyler-Kabara, MD, PhD, FAANS; Jenifer Collinger, PhD (Pittsburgh, PA); Brian Wodlinger, PhD (Toronto, Canada); Douglas Weber, PhD; Andrew Schwartz, PhD; Michael Boninger, MD, PhD; Robert Gaunt, PhD (Pittsburgh, PA)

Introduction: Proprioception is a crucial component of the motor control system. Loss of proprioceptive input leads to gross deficits in motor performance. Proprioceptive feedback is beneficial during motor learning in rehabilitation following brain injury. Deficiencies in arm movements in patients lacking proprioception showed significant limitations in their ability to make reaching movements without visual guidance. Intracortical microelectrode brain-computer interface (BCI) achieved high quality control of a robotic prosthetic arm. However, BCI controlled prosthetic limbs are currently operated without somatosensory feedback.

Methods: Experiments were conducted with a single subject implanted with two 96-channel microelectrode arrays in motor cortex. The subject has complete paralysis with essentially intact

sensation. Reaching movements were conducted under visual guidance with and without proprioception, or blindfolded with and without proprioception. Proprioception was provided by moving the subject's limb in coordination with the movement of the prosthetic limb. Task conditions were randomized and each task type was performed five times within a session. After a standard 2-dimensional calibration trial, the subject was asked to move the prosthetic limb back and forth across two lines in the horizontal plane as many times as possible within one minute.

Results: With vision alone, the median number of line crossings was 25 (22-32). Without vision only 6 (2-9) line crossings were achieved. With vision and proprioception 19 (11-26) line crossing were achieved and with proprioception alone 18 (16-20) line crossing were achieved.

Conclusions: In this study proprioception significantly improved prosthetic control in the absence of vision. Importantly, the decoders were trained without proprioception, which we believe accounts for some of the decreased performance when vision and proprioception were used simultaneously. These data demonstrate that proprioception can have a powerful impact on BCI controlled prosthetic arm movements and should be an important target for sensory restoration.

752. Beta Oscillations Modulate High-Frequency Oscillations and Neuronal Firing in the Parkinsonian Subthalamic Nucleus

Andrew Il Yang (New York, NY); Shervin Rahimpour, BA; Codrin Lungu, MD; Kareem Zaghloul, MD, PhD (Bethesda, MD)

Introduction: Pathologic oscillations and neuronal synchrony are hallmarks of the Parkinsonian basal ganglia. Despite being the most common target for deep brain stimulation (DBS), the precise interactions between oscillatory bands of different frequencies and between oscillatory and spiking activity, within and around the human subthalamic nucleus (STN), remain unclear.

Methods: Local field potential and single-unit spiking were recorded from fourteen patients receiving bilateral DBS of the STN for Parkinson's disease (PD). We quantified phase-amplitude coupling (PAC) between low and high frequency oscillations, and synchronization of spiking activity to the phase of those oscillations. Simultaneous activity was recorded from microelectrodes at multiple depths above, within, and below the STN to characterize the spatial topography of these interactions.

Results: There was stronger coupling between beta (12-30Hz) phase and high-frequency oscillation (150-500Hz; HFO) amplitude within the STN versus outside ($p < 0.01$). Notably, the strength of this coupling was correlated with the power of the beta band ($p < 0.01$). Similarly, we found stronger spike-phase locking (SPL) with beta oscillations in the STN ($p < 0.01$). Although the degree of PAC and SPL was correlated ($R=0.17$; $p=0.01$), the preferred phases of beta-coupled HFOs and beta-synchronous spikes were different ($p < 0.00001$). DBS electrodes that were most clinically effective were in the region of maximal PAC in 80% of hemispheres.

Conclusion: We characterized the spatial extent of PAC and the relationship between PAC and SPL. Our results suggest that beta modulation of neuronal spikes and HFOs represent distinct processes, and that PAC may be a clinically-relevant marker of the dorsolateral STN.

753. Robust transient dynamics for lexical selection in Broca's Area

Christopher Richard Conner; Nitin Tandon, MD (Houston, TX)

Introduction: Studies of the left inferior frontal gyrus (LIFG) during language have found distinct sub-regions: pars opercularis (POp), pars triangularis (PT), pars orbitalis (POr), and sub-central gyrus (sCG). However, an understanding of how these regions select and produce appropriate articulation is unknown. We performed electrocorticography (ECoG) in 27 left-hemisphere dominant patients to evaluate LIFG dynamics.

Methods: Subjects overtly named pictures of nouns, verbs or scrambled images during ECoG recording. Subdural electrodes were localized in LIFG using individual anatomy. Data were filtered into the gamma band (70-110Hz) and Hilbert transformed to obtain the power envelope. Amplitude envelope correlations were calculated between each region to assess functional connectivity. Directionality was estimated by using time-lagged correlations. Attractor state dynamics were modeled using k-means clustering of information flow between LIFG sub-regions.

Results: At 250ms after onset, we found a dramatic decrease in gamma power in POr that preceded concurrent activation of PT, POp and sCG. Between 300-600ms, negative correlation from POr-to-PT and from POr-to-POp was noted during noun and verb generation. Around 400ms, connectivity increased bi-directionally between POp and sCG until articulation, after which, sCG became negatively correlated with PT, suggestive of a stop signal. Verb naming alone significantly increased positive correlation between POr and sCG. Clustering revealed that parallel network interactions occurred in serial and that system state was determined by functional connectivity.

Conclusions: Negative correlations were observed both rostral-to-caudal and caudal-to-rostral, rejecting hierarchical models of LIFG. We found rapidly fluctuating network dynamics occur bi-directionally and in parallel, and that grammatical distinctions are reflected in information flow.

754. Ventrolateral prefrontal cortical neuronal activity during intertemporal choice

David Barrett Weintraub, MD; Barry Richmond, MD (Bethesda, MD)

Introduction: To investigate the influence of reward valuation on neuronal responses, we are recording single unit neuronal activity during an intertemporal choice task, in which the size of a reward and the time delay required to obtain it are varied in a crossed-design. Here we report the effects of reward size and delay on ventrolateral prefrontal cortical neuronal activity during intertemporal choice.

Methods: A rhesus monkey was trained to associate visual cues with various combinations of liquid reward amount and delay during a bar touch and release task. In each trial, a visual cue indicates the reward size:delay combination. Following the cue, the monkey may accept or skip the trial by releasing the bar on an indicated instruction. The monkey accepted the trials in a predictable and reliable manner.

Results: We recorded extracellular activity from 96 neurons from the ventrolateral prefrontal cortex using a chronically implanted array. We analyzed the neuronal firing rates following cue presentation and reward delivery. Following cue presentation, 43% and 30% of neurons encoded reward size and reward delay, respectively, and 58% encoded at least one component. Following reward delivery, 47% and 72% of neurons encoded reward size

and delay, respectively, and 80% encoded at least one component.

Conclusions: Both reward size and delay are encoded by neurons in the ventrolateral prefrontal cortex during intertemporal choice. Delay encoding following reward delivery is most common. This activity may contribute to strategies of rule based decision making.

755. Safety and Efficacy of using stereotactic laser ablation (SLA) for MR negative epileptic foci

Samuel F. Ciricillo, MD, FAANS, FACS; Michael Chez, MD; Azad Ghassemi, MD (Sacramento, CA)

Introduction: 20–30% of temporal lobe epilepsy patients (TLE) and 20–40% of those with extratemporal lobe epilepsy (ETLE) show no evidence of underlying lesion on MRI (MRI-negative) (Carne2004). The current study evaluates the safety and efficacy of using stereotactic laser ablation (SLA) for MR negative epileptic foci.

Methods: 22 children and 6-adults with medically refractory focal epilepsy were evaluated with video EEG, 3-Tesla MRI, fMRI, MEG (22-patients) and PET (3-patient) with 6 temporal and 21 extra-temporal foci. The patients had SLA (Visualase, Inc. Houston, TX) with frameless navigation (Brainlab, Inc.). All had intraoperative EEG monitoring in MRI, thereby showing pre-ablation and post-ablation spike data. 10 patients had depth electrodes through laser placement burr holes. The cooled laser applicator is MR-compatible (1.6mm in diameter), which enabled real time MR temperature imaging. Seizure outcome was noted for 4–24 months post-ablation.

Results: 17 patients showed seizure freedom (65%), 5 had < 75 % reduction, 2 had no improvement, and 4 had very short follow up (< 4 months). All the mesial temporal and focal frontal cases (100%) remain seizure free and 11/21 (53%) extra-temporal cases are seizure free. 1-mesial temporal patient had a superior quadrantanopsia. Other minor complications were placement hemorrhage of no clinical significance in 2 patients. The average LOS was < 24 hours.

Conclusions: SLA, in combination with MEG, is a valuable safe new tool to achieve seizure freedom in MR negative cases (both temporal and extra-temporal). Additionally, SLA may offer options to those patients resistant to traditional craniotomy option.

756. Anatomical predictors of response to dorsal anterior cingulotomy for obsessive-compulsive disorder

Garrett P. Banks; Charles Mikell, MD; Brett Youngerman, MD; Andrew Chan (New York, NY); Christopher Filippi, MD (New York, USA); Emad Eskandar, MD (Boston, MA); Darin Dougherty, MD (Boston, NY); Sameer Sheth, MD, PhD (New York, NY)

Introduction: Whereas dorsal anterior cingulotomy has been performed for decades to treat severe, refractory obsessive-compulsive disorder (OCD), the reasons for patient response heterogeneity remain poorly understood. We hypothesized that pre-surgical gray or white matter structural differences may predict patient response.

Methods: We performed voxel-based morphometry and probabilistic tractography on preoperative imaging from fifteen patients who underwent standard bilateral cingulotomy. Outcomes were measured using the Yale-Brown Obsessive Compulsive Scale (Y-BOCS). Volumetric T1 scans were pre-processed, tissue segmented, and transformed to standard space. Whole brain cluster-based gray matter analysis was used to compare responders to non-responders. Using probabilistic tractography, we calculated connectivity between the average cingulotomy area and brain

structures involved in the pathophysiology of OCD. For each structure, left-sided connectivity and right-sided connectivity were compared. This laterality difference was compared between responders and non-responders using Wilcoxon rank-sum and linear regression.

Results: Decreased right anterior cingulate cortex (ACC) grey matter, centered at Talairach coordinates $x=1, y=40, z=20$ (anterior to the eventual lesion), correlated with superior response ($p < 0.01$ Bonferroni corrected). Tractography analysis showed that in responders, connectivity from lesion area to thalamus, caudate, globus pallidus, and hippocampus was greater on the right ($p < 0.05$ Bonferroni corrected). Average laterality of these four structures regressed against Y-BOCS change yielded a linear relationship ($R^2=0.72, p=2.9 \times 10^{-4}$).

Conclusion: Decreased right ACC grey matter and greater right-sided connectivity from lesion area to specific sub-cortical structures predicted superior clinical response. These results suggest that preoperative structural metrics may help identify patients more likely to respond to surgical intervention for severe, refractory OCD.

Integra Foundation Award

757. Gamma Knife Radiosurgery for Sellar and Parasellar Meningiomas: A Multicenter Study of 763 Patients

Jason P. Sheehan, MD, PhD, FAANS (Charlottesville, VA); Robert Starke (Charlottesville); Hideyuki Kano (Pittsburgh); Anthony Kaufmann (Winnipeg); David Mathieu (Sherbrooke); Fred Zeiler; Michael West (Winnipeg); Samuel Chao; Gandhi Varma (Cleveland); Veronica Chang; James Yu (New Haven); Heyoung McBride; Peter Nakaji; Emad Yousef; Norissa Honea (Phoenix); Stephen Rush; Douglas Kondziolka (New York); John Lee; Robert Bailey (Philadelphia); Sandeep Kunwar; Paula Petti (Fremont); Lawrence Lunsford (Pittsburgh)

Introduction: Parasellar and sellar meningiomas are challenging tumors owing in part to their close proximity to important neurovascular and endocrine structures. Complete resection can be associated with significant morbidity, and incomplete resections are common. We evaluate the outcomes of parasellar and sellar meningiomas managed with Gamma Knife radiosurgery (GKRS).

Methods: A 10 center study of benign sellar and parasellar meningioma patients was conducted through the North American Gamma Knife Consortium. From a period of 1988 to 2011, 763 GKRS patients with sellar and/or parasellar meningiomas were identified. The median follow up was 66.7 months (range 6 to 216 months). Three-hundred and fifty-five (50.7%) underwent at least one prior resection, and 3.9% had prior radiation therapy (RT). Factors predictive of new neurological deficits following GKRS were assessed via univariate and multivariate analysis. Kaplan-Meier and Cox regression analyses were used to assess factors predictive of tumor progression.

Results: Overall, tumor volumes remained stable or decreased in 90.2% of patients. Actuarial progression free survival rates at 3, 5, 8 and 10 years were 98%, 95%, 88%, and 82%, respectively. More than one prior surgery, prior RT, or a margin dose less than 13 Gy significantly increased the likelihood of tumor progression after GKRS. At last clinical follow-up, 86.2% of patients demonstrated no change or improvement in their neurological condition whereas 13.8% of patients experienced progression of symptoms. New or worsening cranial nerve deficits were seen in 9.6% of patients with CN V being the most adversely affected nerve. Cranial nerve functional improvement (especially

in CN V and VI) was observed in 34% of patients with pre-existing deficits. New or worsened endocrinopathies were demonstrated in 1.6% of patients. Unfavorable outcome with tumor growth and accompanying neurological decline was statistically more likely in those patients with larger tumor volumes ($p=0.022$) and more than 1 prior surgery ($p=0.021$).

Conclusions: GKRS provides a high rate of tumor control for patients with parasellar or sellar meningiomas; it is accompanied by neurological preservation or improvement in most patients.

Preuss Research Award

758. Signal Transducer and Activator of Transcription 5b Promotes Malignant Progression In Glioma

Loyola Veronique Gressot, MD; Tiffany Doucette, PhD; Yuhui Yang, MS; Gregory Fuller, MD, PhD; Khatri Latha, PhD; Ganesh Rao, MD (Houston, TX)

Introduction: STAT5b expression induces anti-apoptotic signaling pathways that mediate tumor cell proliferation and invasion in cancer. We hypothesized that overexpression of STAT5b contributes to the transition of gliomas from low- to high-grade; a progression that is poorly understood.

Methods: We analyzed the TCGA data set to determine expression patterns of STAT5b in glioma subtypes. We modeled STAT5b expression in vivo and assessed tumor latency, grade, and apoptotic and mitotic indices.

Results: We found that STAT5b expression correlates with the Proneural(PN) relative to Mesenchymal and Neural subtypes of GBM($p < 0.05$). Therefore, we modeled STAT5b expression in a PDGFB-dependent PN model of glioma. In mice co-expressing PDGFB + STAT5b, 33/34(97%) formed tumors whereas 28/29(96%) tumor expressing PDGFB alone formed tumors. However, the cohort coexpressing STAT5b and PDGFB developed 8(24.2%) low-grade and 25(75.8%) high-grade tumors while the PDGFB alone cohort developed 21(75%) low grade and 7(25%) high-grade tumors($p = < 0.0001$; 95% CI: 2.91-30.17; OR: 9.38). Mice co-expressing STAT5b and PDGFB had a shorter survival time($p = 0.0011$; 95% CI: 1.66-4.57; HR: 1.97). Tumors from the STAT5b+PDGFB injection set had a significantly lower rate of apoptosis (as quantified by CC3 staining) than tumors induced by PDGFB alone($p = 0.0001$). The mitotic index (based on pHH3) was similar between injection sets($p = 0.2$). Ectopic expression of STAT5b alone was insufficient to induce tumors.

Conclusions: We show that STAT5b expression is more prominent in the PN subtype. We also show that STAT5b promotes the malignant progression of gliomas from low- to high-grade tumors in vivo. For the PN subtype of GBM, STAT5b may be a relevant therapeutic target.

Leksell Radiosurgery Award

759. Clinical Outcome and Risk of spine deformity and vertebral compression fracture after Spine radiosurgery

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Introduction: Single fraction radiosurgery (SRS) is successfully

used to manage traditionally radioresistant cancer while sparing the cord. High rates of local control and effectiveness on pain compared to conventional radiotherapy make this treatment increasingly more frequently used. The risk of vertebral compression fracture (VCF) is reported. The aim of this study is to determine the risk of VCF and identify predictive factors.

Methods: We evaluated 84 consecutive spine metastases treated with single fraction SRS on the Novalis as outpatients. MRI were evaluated for the 6 Spine Instability Neoplastic (SINS) criteria and changes in vertebral body height (VBH) at baseline, 3, and 6-9 months after SRS. Pain was evaluated with Visual Analog Scale (VAS); improvement/worsening considered a 2point change on VAS for score < 3 . VCF was considered a loss of VBH $< 10\%$; radiographic progression was considered loss of VBH $< 25\%$.

Results: Pain was present in 82% of patients prior to SRS. After SRS, pain was improved in 85% of patients at 7days and persisted at 30 days. Radiographic control occurred in 98% of cases at 3 months and 88% at 6-9 months. VCF was present in 33% of cases prior to SRS. Overall rate of VCF after SRS was 20%. Rate of de novo VCF and progression was identical, more frequently occurring at 3 than 6-9months 3 after SRS. Worsening pain was present in only 20% of patients with VCF after SRS, yet 66% underwent a procedure: vertebroplasty (62%) and surgery (38%). SINS score, histology, and age did not correlate with VCF risk and/or intervention rate.

Conclusions: Spine SRS provide excellent radiographic and pain control. We report 80% probability of VCF-free outcome up to 9 months after SRS. Additional studies are needed to determine if in the presence of an asymptomatic VCF interventions to prevent radiographic progression are necessary.

760. An analysis for the role of telomerase (hTERT) promoter mutations in gliomagenesis

Koray Ozduman, MD, Assoc.Prof of Neurosurgery; Cemaliye Akyerli, PhD; Sirin Yuksel, BS; Ozge Can, PhD; Yavuz Oktay, PhD (Istanbul, Turkey); Paolo Nanni, PhD; Nathalie Selevsek, PhD; Jonas Grossmann, PhD (Zurich, Switzerland); Aysel Ozpinar, PhD; Aydin Sav, MD; Cengiz Yakicier, MD, PhD; M Necmettin Pamir, MD (Istanbul, Turkey)

Introduction: Telomerase reverse transcriptase (hTERT) hTERT promoter mutations (C228T and C250T) are common in gliomas and result in enzyme overexpression. This study aimed at identification of oncogenic processes associated with the expression of hTERT in gliomas and its effects on patient outcome.

Methods: A total of 171 glioma tumor samples [62 oligodendrogliomas, 27 oligoastrocytomas, 25 astrocytomas, 54 glioblastomas, and 3 gliomatosis cases] were screened for hTERT promoter mutations by Sanger sequencing or DNA mini-sequencing. Findings were correlated with IDH, Olig-2, Ki67, EGFR, VEGF, pBRAF, c-myc PTEN, p16, TP53 protein expressions and MGMT methylation; and 1p19q co-deletions. To screen the effects of hTERT expression on the proteome, 8 hTERT promoter mutant and 2 wild-type WHO grade II oligodendrogliomas (all IDH-mutant) were compared using LC-MS/MS.

Results: hTERT promoter mutations were detected in 52.6% of gliomas. These mutations were common in oligodendroglial tumors and primary glioblastomas but far less frequent in astrocytic and oligoastrocytic gliomas or secondary glioblastomas. In oligodendrogliomas, hTERT promoter mutations were correlated with higher incidence of R132 IDH mutations, higher incidence of 1p19q co-deletions and lower incidence of TP53 mutations. There

were no differences in tumor localization, laterality, overall- or progression free- survival. When hTERT mutant and wild-type WHO grade II oligodendrogliomas were compared using LC-MS/MS analysis, a total of 1606 proteins were identified (false discovery rate of 0.2%). 75 of these proteins were significantly differentially expressed in the 2 subgroups ($p < 0.05$). 11 of the proteins had been associated with glioma development previously. Pathway analysis revealed involvement of transcriptional silencing, cell cycle and cell-adhesion.

Conclusions: The presence of hTERT mutations may point to a different oncogenic program in oligodendrogliomas.

761. Intraoperative mass spectrometry imaging of an onco-metabolite to guide brain tumor surgery

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Introduction: For many intraoperative decisions, surgeons depend on frozen section pathology, a technique developed over 150 years ago. Technical innovations that permit rapid molecular characterization of tissue samples at the time of surgery are needed and in most cases, during the surgical procedure.

Methods: Using desorption electrospray ionization mass spectrometry (DESI MS), we rapidly detect the tumor metabolite 2-hydroxyglutarate (2-HG) from tissue sections of surgically-resected gliomas, under ambient conditions and without complex or time-consuming preparation. The method was validated by correlating 2D mass spectrometry imaging of glioma specimens with histopathology, and genetic profiling of discordant cases.

Results: With DESI MS, we identify IDH1-mutant tumors with both high sensitivity and specificity within seconds to minutes, immediately providing critical diagnostic, prognostic and predictive information. Imaging tissue sections with DESI MS shows that the 2-HG signal overlaps with areas of tumor and that 2-HG levels correlate with tumor content, thereby indicating tumor margins. Mapping the 2-HG signal onto three-dimensional MRI reconstructions of tumors allows the integration of molecular and radiologic information for enhanced clinical decision-making. We also validate the methodology and its deployment in the operating room – we have installed a mass spectrometer in our Advanced Multimodality Image Guided Operating (AMIGO) suite and demonstrate the molecular analysis of surgical tissue during brain surgery.

Conclusions: Mass spectrometry provides a new tool for the direct surgical imaging of tissue during neurosurgery. This work indicates that metabolite-imaging mass spectrometry could transform many aspects of surgical decision-making.

762. The utility and predictability of immediate postoperative prolactin levels in patients undergoing surgery for prolactinomas

Michael Edward Ivan, MD (San Francisco, CA); Michael Ivan, MD, MS; Jason Cheng; Manish Aghi; Sandeep Kumar; Lewis Blevins (San Francisco)

Introduction: Surgery is only one step in the treatment plan of prolactinomas and is commonly not curative. To date, the

predictability of postoperative prolactin levels in identifying patients who will have tumor residual, tumor progression, or need adjuvant therapy is unknown. We aimed to understand if there was a correlation to either tumor residual, progression and/or the need of adjuvant therapy.

Methods: A retrospective analysis of pathologically confirmed prolactinomas from the University of California, San Francisco was performed. From 2001 to 2011, this resulted in 181 cases of prolactinomas. All patients where preoperative medical therapy was not halted for more than 30 days were excluded. 144 patients were included in this study who had a postoperative prolactin level taken 24 hours after surgery and a postoperative MRI at 6 weeks to inspect for residual tumor. Adjuvant therapy was defined as either radiotherapy or medical therapy.

Results: 144 patients were evaluated with an average followup of 768 days and the sensitivity and specificity of an elevated immediate postoperative prolactin level predicting radiographic residual was 88% and 86%. The sensitivity and specificity of an immediate elevated postoperative prolactin level predicting postoperative adjuvant therapy was 91% and 59%. The rate of tumor progression was 3.1% and the rate of patients requiring adjuvant therapy was 22.6%.

Conclusion: Immediate postoperative prolactin aids in the prediction of tumor residual. This level also assists in predicting patients who will have tumor progression although we did not have enough patients to confirm this statistically. In addition to immediate prolactin levels, continued radiographic and prolactin levels are also needed to screen for tumor progression and/or the need for adjuvant therapy.

763. Surgery, stereotactic radiosurgery and observation provide comparable long-term quality of life for patients with small to medium sized vestibular schwannomas: An international, multi-center, cross-sectional, observational study

Michael J. Link, MD, FAANS (Rochester, MN); Morten Lund-Johansen, MD, PhD (Bergen, Norway); Matthew Carlson, MD (Rochester, MN); Oystein Tveiten, MD (Bergen, Norway); Colin Driscoll, MD (Rochester, MN); Frederik Goplen, MD (Bergen, Norway); Bruce Pollock, MD; Jay Mandrekar, PhD (Rochester, MN)

Introduction: To determine which treatment strategy provides best long-term quality of life (QoL) for patients with small-to-medium sized vestibular schwannoma (VS).

Methods: Patients who underwent primary microsurgery, stereotactic radiosurgery (SRS) or observation for sporadic small-to-medium sized (less than 3.0 cm) VS between 1998 and 2008 at one of two tertiary academic referral centers were surveyed using the SF36, PROMIS, and Penn Acoustic Neuroma Quality-of-Life (PANQOL) scale. Additionally, general population adults were surveyed, providing a non-tumor control group for comparison. Pairwise comparisons between groups were performed using Wilcoxon rank sum test. Multivariable regression analysis was used to assess associations between outcome and treatment groups adjusting for age and tumor size.

Results: A total of 643 (144 surgery, 248 SRS, 148 observation, 103 controls) consecutive respondents were analyzed. The mean overall response rate was 79% and the mean time interval between treatment and survey was 7.7 years. Patients in the microsurgery cohort were younger and had larger tumors compared to those who received SRS or observation ($p < 0.0001$). When adjusting for differences in age and tumor size, there were no statistically significant difference between treatments groups with respect to PROMIS physical or mental summary subscales,

SF36 physical or mental health dimensions, or PANQOL anxiety, general, hearing or energy subdomains. Patients who received microsurgery reported worse PANQOL facial, balance, and pain subdomain scores and total PANQOL score compared to SRS and observation cohorts (P less than 0.01). The differences between the non-tumor control group and patients with VS were substantially greater than differences observed between individual treatment groups for the majority of measures.

Conclusions: The diagnosis of VS more significantly impacts patient QOL than treatment strategy. Patients with small-to-medium sized VS enjoy comparable long-term QOL whether managed with observation, microsurgery, or SRS.

764. mTOR And Its Interacting Signaling Pathways As A Therapeutic Target For Medulloblastoma

Michael LaBagnara, MD (Hawthorne, NY); Paul Lee, BA; Avinash Mohan, MD; Raj Murali, MD (Valhalla, NY); Meena Jhanwar-Uniyal (New York, NY)

Introduction: Medulloblastoma (MB) is genetically defined in 4 subgroups with distinct prognostic outcomes. Despite advancements in treatment which includes surgical resection, radiation, and chemotherapy for all subtypes, current adjuvant therapies carry significant morbidity and adverse side-effects. Recently identified HIPPO pathway components that regulate mTOR via PI3K signaling and Sonic Hedgehog (SHH) may play an important role in MB. Their suppression may offer a better combined inhibition of these pathways and provide a targeted treatment which may improve prognosis.

Methods: Protein expression involved in AKT/mTOR and HIPPO pathways was measured using Immunohistochemistry in MB cells. Scratch and chemotactic migration was used to assess the motility of MB cells following treatment with inhibitors of aforementioned pathways. Cell cycle analysis and proliferation was measured using EdU and MTT techniques, respectively. siRNA treatment was used to inhibit HIPPO pathway.

Results: IHC suggested that a significant number of tumors had over-expression of AKT, mTOR, and interestingly YAP. Treatment with inhibitors of PI3K/AKT (LY294002) and mTOR (rapamycin) given with EGF, significantly reduced cellular motility. Importantly, SHH inhibitor cyclopamine given with LY or rapamycin significantly reduced cellular motility. Cell proliferation was suppressed by inhibition of HIPPO pathway using 3 unique 27mer duplexes of YAP1 siRNA treatments. Additionally, the combined treatment of SHH with either LY or Rapa caused maximum suppression of cellular growth.

Conclusions: Results demonstrated combined targeting of mTOR/HIPPO and SHH pathways may provide superior strategies for treatment of MB.

765. Dose-Volume Analysis of Radiation-Induced Optic Neuropathy after Single-Fraction Pituitary Adenoma Radiosurgery

Bruce E. Pollock, MD, FAANS; Michael Link, MD; Jacqueline Leavitt, MD; Scott Stafford, MD (Rochester, MN)

Introduction: The normal tissue complication probability (NTCP) of the anterior visual pathways (AVP) remains poorly defined after single-fraction stereotactic radiosurgery (SRS).

Methods: One hundred sixteen patients with pituitary adenomas having single-fraction SRS between October 2007 and December 2011. Excluded were patients with prior radiation therapy ($n=12$),

CT-based dose planning ($n=2$), refused research authorization ($n=3$) and less than 12 months of follow-up ($n=10$). The maximum point dose, 8-Gy volume, 10-Gy volume, and 12-Gy volumes for the right and left optic nerves/chiasm were determined for the study group (232 sides). Visual function of the study group was compared before and after SRS. The median follow-up after SRS was 37 months (range, 12-70).

Results: The median maximum point dose to the AVP was 9.2 Gy (range, 2.4-14.5). One hundred forty-nine sides (64%) received < 8 Gy; the median 8-Gy volume in this group was 17.6 mm³ (range, 0.1-150.7). Eighty-one sides received < 10 Gy (35%); the median 10-Gy volume in this group was 1.8 mm³ (range, 0.1-51.6). Twenty-seven sides (12%) received < 12 Gy; the median 12-Gy volume in this group was 0.1 mm³ (range, 0.1-5.4). No patient had a decline in their visual function after SRS. The 95% confidence interval of developing a radiation-induced optic neuropathy (RION) at the 8-Gy, 10-Gy, and 12-Gy volumes were 0-3.0%, 0-5.4%, and 0-14.8%, respectively.

Conclusions: The AVP in patients without prior radiation treatments can safely receive radiation doses up to 12 Gy with a low risk of RION. Additional studies are needed to better delineate the NTCP of the AVP.

800. The National Neurosurgery Quality and Outcomes Database (N2QOD): Predictors of Persistent 12 month Disability Following Lumbar Surgery

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Introduction: Up to \$850 billion annually is expended on ineffective treatments in the U.S. (IOM) Quality registries are central to emerging evidence-driven reforms. The National Neurosurgery Quality and Outcomes Database (N2QOD) Lumbar Pilot aims to measure safety and effectiveness of everyday neurosurgical spine care. In this study, we aimed to determine predictors of 12 month surgical outcomes for lumbar disc herniation and spondylolisthesis.

Methods: A nationwide, prospective, longitudinal outcomes registry was introduced in March 2012. Using standardized sampling, baseline, peri-operative, 3- and 12-month medical record and patient-reported outcomes (PROs) data was entered prospectively. Linear regression identified variables associated with worse or unchanged 12 month disability (ODI) scores after surgery.

Results: 376 disc herniation and 247 spondylolisthesis patients have reached 12 month followup at 43 sites. Aggregate improvement in all PROs (back pain, leg pain, ODI, EQ5D) was observed at 3 and 12 months ($p < 0.05$). However, 13.8% of patients in both groups did not show ODI improvement. Educational level, liability claim, and baseline ODI were significant predictors of worse/unchanged ODI at 12mos in both groups. Unique predictors were seen for both disc herniation (age, duration of symptoms, and depression) and spondylolisthesis (gender, smoking, and diabetes).

Conclusions: Lumbar surgery for disc herniation and spondylolisthesis is highly effective in the real-world setting. However, a significant subset of patients does not report improved disability scores at 12 months. N2QOD, a comprehensive national outcomes registry, is feasible, shows excellent data integrity, and promises to facilitate shared decision-making and improved utilization of increasingly scarce healthcare resources.

801. The Barrow Ruptured Aneurysm Trial: 6-year results

Robert F. Spetzler, MD, FAANS; Cameron McDougall, MD; Joe Zabramski, MD; Felipe Albuquerque, MD; Peter Nakaji, MD (Phoenix, AZ); Nancy Hills, PhD (San Francisco, CA); Robert Wallace, MD (Phoenix, AZ) Discussant: Robert H. Rosenwasser, MD, FAANS, FACS

Introduction: The Barrow Ruptured Aneurysm Trial (BRAT) compares the safety and efficacy of clipping and coiling for patients presenting with a SAH.

Methods: 238 patients and 233 patients with aneurysms were assigned to clipping and coiling respectively. Dedicated nurse practitioners collected the data. Cross overs were at the discretion of the treating physician. Primary poor outcome was defined by the modified Rankin Scale (mRS) < 2 and was independently adjudicated. Six years after randomization 336 patients who had received treatment were available for evaluation. Thirty eight percent of patients assigned to coiling were crossed over to clipping.

Results: Based on mRS < 2 , similar to the results at three years there was no significant difference in outcomes ($p=0.33$) between the two cohorts. Complete aneurysm obliteration at six years was present in 96% of clipped vs 48% of coiled patients. Retreatments had occurred in 13% of coiled vs 4% of clipped patients ($p=0.001$).

Conclusions: Based on mRS scores at six years there is no significant difference between the two treatment modalities. However the significant difference in aneurysm obliteration, aneurysm recurrence and required retreatment favor clipping.

802. Black Holes, White Dwarfs, and Supernovas: The Complications of Radiosurgery

Douglas S. Kondziolka, MD, FAANS (New York, NY); L. Lunsford, MD (Pittsburgh, PA) Discussant: Bruce E. Pollock, MD, FAANS

Introduction: Complications after stereotactic radiosurgery pose challenges in clinical identification, imaging interpretation, and management, and affect outcomes. Incidence varies with the target volume, anatomic location, dose delivered, patient age, and

poorly understood genetic factors. From our 26 year experience with over 13,000 patients, we studied complication identification and management approaches.

Methods: A continuously maintained prospective registry was used to record outcomes after stereotactic radiosurgery for patients with brain tumors, vascular malformations, pain, movement or behavioral disorders. We evaluated methods to detect and to define such adverse events, including MRI, FDG-PET, other nuclear medicine techniques, and in selected cases biopsy. We also used medications including corticosteroids, non-steroidal anti-inflammatory drugs, vitamin E, pentoxifylline, and bevacizumab.

Results: Adverse radiation effects (ARE) were found in 1-8% of tumors and were most common in larger lesions, and supratentorial meningiomas with peritumoral edema. Late ARE in brain metastases were rare for tumors less than 10mm. ARE was documented in brain AVMs (30% with asymptomatic imaging and 6-15% with symptomatic changes depending on location). Cranial nerve effects for I,II, III-VI,V,VII,IX-XII were uncommon with careful dose selection. Visual deficits without prior irradiation and a point radiosurgery dose less than 10 Gy, occurred in less than 1%. Cochlear dose, tumor volume and age affected hearing. No imaging test to date provides diagnostic specificity of an ARE above 90%. T1/T2 matching, perfusion imaging, and quantitative diffusion measurements correlate with the parenchymal responses of inflammation or recurrent tumor.

Conclusions: Using current selection criteria and techniques, the ARE risks of radiosurgery are now better established. The most severe complications occur even when standard techniques were used, and may represent a poorly understood genetic susceptibility to radiation. In such patients, use of bevacizumab provides unique advantages over extended use corticosteroids. Other agents have modest benefit that can be utilized in patients with lesser symptoms.

803. Endoscopic Third Ventriculostomy with Choroid Plexus Cauterization in Hydrocephalic Infants: A Prospective North American Series

Scellig S. D. Stone, MD, PhD (Brookline, MA); Benjamin Warf, MD (Boston, MA) Discussant: Mark M. Souweidane, MD, FAANS

Introduction: Choroid plexus cauterization (CPC) is a potential adjunct to endoscopic third ventriculostomy (ETV) in the treatment of obstructive hydrocephalus. This combined treatment may promote shunt independence in infants who generally suffer lower success rates from ETV alone versus their older counterparts. Most published series suggesting a benefit from this combined approach stem from experience in developing countries. Here, we review the senior author's North American series of hydrocephalic infants treated by ETV+CPC.

Methods: Patients were prospectively collected and reviewed for accuracy. Treatment success was the absence of any subsequent surgical procedure for definitive CSF diversion or death related to hydrocephalus management. Data were analyzed using Kaplan-Meier survival plots and log-rank tests. Predicted success with ETV alone was determined using the ETV Success Score.

Results: Since 2009, 83 patients (46 M, 37 F) of mean age 162 days (range 2-908 days) underwent ETV+CPC for hydrocephalus related to aqueductal stenosis (19), Dandy-Walker spectrum (7), myelomeningocele (21), hemorrhage (22), infection (5), or other (9). Median overall CSF diversion-free survival was 612 days, with significantly worse results post infection (21 days), with age < 6 months (215 days) and in females (189 days, though all infection cases were female). The 6 month ETV+CPC success

rate (60%) was significantly greater than predicted for ETV alone (46%). Complications included 1 CSF leak and 1 transient SIADH.

Conclusions: ETV+CPC safely increased shunt independent survival over that predicted for ETV alone in a North American prospective series of hydrocephalic infants, adding impetus to conduct a prospective randomized trial.

804. Intravenous Acetaminophen for Postoperative Supratentorial Craniotomy Pain – A Randomized, Double-Blinded, Placebo-Controlled Trial

William H. Sweet Award

Walavan Sivakumar, MD; Paul House, MD (Salt Lake City, UT); Robert Hoesch, MD, PhD (Murray, UT); Julie Martinez, RN; Nancy Duncan, NP; Safdar Ansari, MD; Craig Kilburg, MD (Salt Lake City, UT) Discussant: Kim J. Burchiel, MD, FAANS, FACS

Introduction: Pain control after craniotomy is often difficult. Narcotic medication use can impair the evaluation of brain function. Studies have shown that post-craniotomy patients experience inadequate pain control. Additionally, postoperative nausea and vomiting delays the use of oral medication. Few nonnarcotic intravenous (IV) medications exist. The recently approved IV formulation of acetaminophen might serve as a safe, potent non-opioid adjunct to narcotic medications in this patient population. No studies on IV acetaminophen in post-craniotomy patients have been performed.

Methods: This is a randomized, double-blinded, placebo-controlled trial enrolling 150 patients. Adults undergoing elective, supratentorial craniotomies are randomized into one of two groups: 1) 1000mg/100mL IV acetaminophen every 8 hours with the standard-pain protocol or 2) 100mL 0.9% normal-saline with the standard-pain protocol. Primary outcome measures are narcotic consumption in morphine equivalents at 24 and 48-hours after surgery.

Results: An independent statistician performed an early interim analysis. To date, 19 patients have been enrolled in the study. Large differences were noted in narcotic consumption between the IV acetaminophen and placebo groups at all time-points (morphine equivalents 24/48 hours were 49.5/70.5 and 120.1/172.6, respectively.) Additionally, IV acetaminophen group patients reported pain scores 1.38 points lower than the placebo group. Both groups reported decreased pain scores over time, by 1.41 points per day. Statistical significance values will be calculated at the next interim analysis.

Conclusions: Patients who receive postoperative IV acetaminophen after craniotomy had lower narcotic consumption and reported lower pain scores in an interim analysis. It is anticipated the results from 75 patients will be available by March 2014.

Vesalius Award

805. Julius Caesar Arantius (Giulio Cesare Aranzi, 1530-1589) and the hippocampus of the human brain; history behind discovery

Shyamal C. Bir, MD, PhD, FAHA (Shreveport, LA); Sudheer Ambekar, MD (Shreveport, USA); Sunil Kukreja; Papireddy Bollam, MD; Anil Nanda, MD, MPH (Shreveport)

Introduction: Julius Caesar Arantius is one of the pioneer anatomists and surgeons of the 16th century who discovered the different anatomical structures of the human body. In the current

historical article, we present the details of Arantius' life and his pioneering work on hippocampal discovery.

Hippocampus: One of his prominent discoveries is the hippocampus. At that time, Arantius gave the term hippocampus, from the Greek word for seahorse (hippokampus: hippos, horse; and kampos, sea monster). Arantius published his description of the hippocampus in 1587, in the first chapter of his work entitled *De Humano Foetu Liber*. Numerous nomenclatures of this structure, including white silk worm, Amon's horn, Ram's horn, were proposed by different scholars at that time. However, the term hippocampus has become popular in the literature.

Other anatomical structure: Other contribution in anatomical discovery includes fourth ventricle, choroid plexus, superior levator pulpebral muscle, coracobrachialis, cartilaginous nodules in the semilunar valve, foramen ovale, ductus arteriosus and ductus venosus, characteristics of the gravid uterus, deformed pelvis, and details about fetus, fetal circulation.

Publications: As a famous anatomist, Arantius had numerous publications including *De Humano Foetu Liber*, *Obsevationes Anatomicae*, and *De Tumoribus Secundum Locos Affectos*. Arantius also wrote a commentary called *Hippocraitis Librum de Vulneribus Capitis Commentarius Brevis*.

Conclusion: Acanthus should be highly honored in the field of neuroanatomy for his contribution in anatomical discovery of the hippocampus and other structures of the human brain.

806. The Story of John F. Kennedy's Spine Surgeries

Justin T. Dowdy, MD; T. Glenn Pait, MD (Little Rock, AR)

The 35th president of the United States, John F. Kennedy (JFK), experienced chronic back pain from an early age amongst other significant health issues. Lieutenant Kennedy underwent a lumbar discectomy at L5-S1 on June 23, 1944 which failed to provide significant relief. Due to continuing pain in his back, Senator Kennedy underwent a lumbosacral fusion in October of 1953 with implantation of a Wilson metallic plate with wire and bolt fixation. His post-operative course was complicated by a life-threatening urinary tract infection and he subsequently underwent removal of his plate four months later in addition to drainage of a surgical site abscess several years thereafter. Recent biographical literature has identified osteoporotic compression fractures as a major source of JFK's lower back pain resulting from chronic corticosteroid usage in the treatment of Addison's disease. However, upon direct review of his medical records and radiographs, we conclude that there is no compelling evidence to support this theory. Furthermore, the use of an external orthotic on November 22, 1963 may have contributed to his death. In this presentation, we will explain the story of his back problems, the surgical and non-surgical management undertaken in attempt to provide relief and seek to clarify the details surrounding the etiology and treatment of his chronic back pain as well as the ultimate role his pain played on the day of his assassination.

807. Cushing at His Prime - Brigham Surgical Records from 1922

Edward R. Laws, Jr., MD, FAANS(L); E. Chiocca, MD, PhD (Boston, MA)

Introduction: The Peter Bent Brigham Hospital opened in 1913, with Harvey Cushing, The Moseley Professor, as Surgeon in Chief. There Cushing built upon his previous successes in developing the field of Neurosurgery. By 1922 he had become

world renowned, trainees flocked to Boston to learn from him, and to adopt his methods techniques and insights.

Methods: Original case records for the year 1922 were carefully reviewed for identification of Neurosurgical and other surgical cases done in that year. The diagnoses, operations and outcomes were analyzed. The participation of residents and voluntary assistants and visiting surgeons was noted. Representative examples of case records, Cushing's own illustrations, photographs and pathology are presented

Results: Clearly, Cushing's scope of practice, and his successes in surgical outcomes were steadily growing. His dependence on his surgical colleagues, especially Gil Horrax, his orderly, his anesthetist, his pathologists, secretarial help and the voluntary assistants was integral to his success.

Still in the future were the introduction of electrocautery, the characterization of Cushing's Disease, and the book on Meningiomas.

Conclusions: This glimpse of Cushing's experience in the middle of his career at the Brigham enlightens the surgical milieu that he created, and some of the elements of his success. A table of the cases, general and neurosurgical is presented, with accompanying illustrations and photos.

808. From Galen to 'Gasserian' Ganglion: The revelation of mislabeled 'Third & Fourth Nerve' to the unlocking of 'Gasserian'-'Meckel' Complex

Jai Deep Thakur, MD; Matthew Hefner; Richard Menger, MD; Rimal Hanif, MD; Anil Nanda, MD, MPH (Shreveport, LA)

The second century saw the first description of the fifth-cranial nerve by the Greek physician Claudius Galen. Motor and sensory roots of the fifth nerve were described as two separate pairs of cranial nerve and henceforth contributed towards erroneous nomenclature in the literature as third and fourth cranial nerves. This notion was carried forward in time across 1500 years until the human cadaveric dissections caught up in the medieval era. Galen's description was found to be based on transference of anatomical observations in animal on to humans. In the 17th century, novel work of Thomas Willis published in his neuroanatomical treatise 'Cerebri Anatome' described the Trigeminal nerve as the fifth cranial nerve. Notably, there was no mention of trigeminal ganglion. Strongly influenced by Willis's work, French physician Raymond Vieussens, in 1685 fostered his dissection to elucidate the 'plexus ganglio-formis' (ganglion). The first accurate description of the three branches arising from the trigeminal ganglion was given in 1695 by a British physician Humphrey Ridley. However, it was Jacques B Winslow who coined the term 'nerf trijmeaux', after which the term 'Trigeminal Nerve' entered the anatomical books. Johann Friedrich Meckel in 1748 gave the most accurate description of the ganglion with the surrounding dura; henceforth an eponym in skull base anatomy; meckel's cave. In 1765, Austrian physician Antonius Hirsch dedicated his magnificent dissection treatise to his mentor Johann Lorenz Gasser, and with his explicit illustrations, the anatomical evolution of the trigeminal nerve, its ganglion and three branches was completed in the history of medicine.

809. The Rise and Fall of Hyperosmolar Urea to Decrease Brain Edema

Balint Otvos; Varun Kshetry, MD; Edward Benzel, MD (Cleveland, OH)

In 1919, it was observed that intravascular osmolar shifts could collapse the thecal sac and prevent fluid from being withdrawn from the lumbar cistern. This led to the idea that hyperosmolar compounds could ameliorate, if not reverse, brain swelling. Since then, various compounds have been used for the reduction of cerebral edema.

Urea was first utilized as an osmotic agent for the reduction of cerebral edema in 1950. It was shown to be a superior alternative to hyperosmolar glucose and was the first compound to be shown to be consistently effective at decreasing brain swelling. Its use became the standard of clinical practice in 1957, in both the intensive care unit and operating room, to rapidly reverse vasogenic edema. However, the prime of urea was rather short lived. Reports of side effects and complications of urea emerged. These included hematuria and coagulopathies in large doses, the potential for improper administration, the inability for use in patients with impaired renal function, and a significant potential for a rebound intracranial pressure escalation phenomenon.

Mannitol was first described in 1962 as a comparable and potentially superior alternative to urea. However, mannitol was purported to be a less effective hyperosmolar agent at rapidly reducing intracranial pressure. Therefore, urea was not immediately replaced by mannitol. The debate over the two compounds continued for a decade until mannitol eventually replaced urea by the mid 1970's as the hyperosmolar agent of choice due to ease of preparation and chemical stability.

Although urea is not currently the standard of care today, its rise and eventual replacement by mannitol have played a seminal role in both our understanding of cerebral edema and the establishment of the strategies for its management.

810. Maitland Baldwin: a secret life

Ronald P. Pokrupa, MD, FAANS, FRCSC (Kingston, Canada)

Maitland Baldwin was born in New York City in September 29 1918. He attended Choate School and then attended Harvard University for an Undergraduate degree. Extra-curricular activities included fencing, shooting and military training. He applied to the University of Edinburgh to study medicine but in 1939, with war looming it was not possible so he came to Queen's University Canada. A visit by Wilder Penfield to Queen's crystallized his desire to be a Neurosurgeon. He graduated from Queen's in 1943 and interned at the Massachusetts General Hospital and went to military service in the Pacific. He returned to Canada to enter Neurosurgical Residency at the Montreal Neurological Institute in 1947 completing this in 1952 and obtaining an MSc. After a short stay in Denver he was recruited to the position of Chief of Neurological Surgery at the newly founded National Institute of Neurological Diseases and Blindness in Bethesda Maryland. He remained at NINDS until his premature death at age 52 from a cerebral hemorrhage Feb. 9 1970. He was a captain in the US Naval Reserve and is buried in Gettysburg National Cemetery. It has been suggested that in addition to medical activities that he was an agent of the Central Intelligence Agency. This presentation explores the circumstances that led to these allegations.

811. Scythian Neurosurgery in Hippocratic Times

Alexey L. Krivoshapkin, MD (Mumbai, Russian Federation); Vladislav Kurbatov, MD, PhD; Tatyana Chikisheva, PhD (Novosibirsk, Russian Federation); Alice Zubova, PhD (Novosibirsk, Russia)

Introduction: The Scythian tribes of Siberia in 5th – 3rd centuries BC were quite familiar with animal and human anatomy embalming the deceased and had a system of ideas concerning the human body.

Methods: Three skulls with evidences of trepanation were discovered from 36 necropolises of Scythian tribes in Altai region of Russia. Skulls inspection and examination under magnification, 320 slices MSCT, spectroscopy of skull bone samples at trepanation site and the distance were exploited.

Results: In two cases trepanation was made for severe head injury. In the first case linear fracture of temporal and parietal bones going up to sagittal suture was found. The trepanation window 40x41mm was made with fine cutting technique directly at the fracture line 12 mm deviation from sagittal suture. MSCT showed complete bone healing. In the second case skull base and right temporal bone fracture were discovered. 23X16mm trepanation window was performed with rough technique directly at the sagittal suture. There was no bone regeneration in MSCT. In the third case with no signs of trauma 22x34 mm skull opening was put over the motor area of the left hemisphere with good technique. The bone regeneration was demonstrated by MSCT. Higher concentration of copper and tin at the site of trepanation window was found.

Conclusions: The population of Scythian Siberia performed skull trepanations more likely for the curative purposes with high efficacy. Scythian surgeons used scraping technique with bronze tools.

812. Radiosurgery Before Dr. Leksell

Raj Murali, MD, FAANS (Valhalla, NY); Herbert Oestreich, MD (Mamaroneck, NY)

Introduction: Dr. John G. Trump, professor of electrical engineering at the MIT in US, made significant contributions in the field of deep x-ray therapy which ultimately led to the development of radiosurgery by Dr. Leksell.

Methods: The archives at the physics department at MIT and New York Times was used to search the contributions of Dr. John G. Trump.

Results: Dr. Leksell demonstrated that functional lesions of the brain could be created by multiportal radiation in 1951. Dr. Oestreich, the senior author of this paper, spent time with Dr. John G. Trump at MIT in 1953. Dr. Trump had been publishing several articles regarding radiation treatment since 1930. He had appreciated that the penetrating characteristics of mega voltage x-rays is better in sparing intervening tissues while treating a lesion. Using this principle, Dr. Trump along with Dr. Van de Graaf designed and built an electrostatic generator in 1937. They also formed a company after World War II for a technique of radiating deep tumors where the patient was rotated 360 degrees about the tumor site. We will show pictures of this radiation equipment and also show the isodose curves for treating a pituitary tumor at that time. Incidentally, Dr. John G. Trump was the uncle of New York State Real Estate developer Donald Trump.

Conclusions: Dr. John G. Trump, electrical engineer and physicist from MIT in the US, described rotational radiation therapy for the treatment of deep lesions at least 10 to 20 years before Dr. Leksell described stereotactic radiosurgery in 1951.

813. Silas Weir Mitchell's Life Revisited

David G. Kline, MD, FAANS(L) (Lenoir, NC); David Kline, MD (New Orleans, LA)

Renowned for his contributions concerning nerve disorders such as causalgia and phantom limb syndrome resulting from the Civil War and observed at the Turner Lane Hospital in Philadelphia, Silas Weir Mitchell (1829-1914) made other unusual contributions. Raised by a Neurologist in an eclectic fashion, SWM published poetry by the age of 15 and later as a physician a fictional account of a wounded Civil War officer in the Atlantic Monthly under a nom de plume. In a similar fashion and again without acknowledgement until his later years, he published 13 novels about society of the 1800's. Due to a keen interest in mental disorders, Mitchell's literary characters often displayed such behavior and yet he was able to relate them and their stories to civilian life of this era. Some of the interesting details of novels such as Hugh Wynne (1896) and The Red City (1907) will be summarized.

Mitchell's interest in a neurotic disorder known as the vapors generated an unusual and yet controversial method of management. As a Neurologist, he campaigned to modernize insane asylums and initiated one of the first departments of Mental Disorders in a medical school where he became a trustee for 35 years despite graduating from another institution in his city. Indeed, his curiosity about human nature was stronger than his desire for social pleasure or prominence. He even founded an exclusive literary club which still exists on Camac Street in Philadelphia.

SWM's maturation as a physician as well as a fictional author and poet will be presented.

814. Peripheral Hypersensitivity to Subthreshold Stimuli Persists after Resolution of Acute Experimental Disc-Herniation Neuropathy and is Mediated by Heightened TRPV1 Receptor Expression and Activity

Mohammed Farid Shamji, MD PhD FAANS (Toronto, Canada); Yu Shan Tu; Michael Salter (Toronto)

Introduction: While acute disc-herniation induced radiculopathy most frequently resolves without clinical sequelae, a fraction of patients experience long-term sensory dysfunction. This study examined chronic sensitivity of the rodent hindpaw following resolution of acute inflammatory neuropathy.

Methods: C57BL/6 mice underwent mid-high sciatic nerve dissection, with either exposure only (control) or placement of nucleus pulposus (NP). Animals were evaluated throughout one, three, and five weeks for mechanical allodynia, thermal hyperalgesia, cold allodynia, and gait stability. At each time point, animals received intraplantar injection of capsaicin (0.1mg) or vehicle alone, thereafter the same behavioral testing. Immunohistochemistry was performed of sciatic nerve, dorsal root ganglion (DRG), and spinal cord for inflammatory activation as well as TRPV1-receptor expression. Ex vivo DRG explants were assessed for capsaicin sensitivity to TRPV1 activation (cobalt staining).

Results: Upon resolution of acute inflammatory pain, mice at three and five weeks (but not one week) demonstrated profound mechanical allodynia to subthreshold capsaicin than sham controls or NP animals delivered vehicle only ($p=0.02$). Conversely, perineural lymphocyte and intraneural macrophage infiltration was only observed at one week. Heightened spinal cord dorsal horn and DRG TRPV1 expression were seen, and DRG explants derived from NP-treated animals exhibited greater cobalt staining upon capsaicin stimulation than controls ($p=0.01$).

Conclusions: Non-compressive disc herniation sensitizes the sciatic nerve distribution in this animal model, despite resolution of intraneural macrophage migration. Heightened TRPV1 activity may explain transformation of acute inflammatory pain into chronic neuropathic pain, and may thus be a target for treating the long-term painful phenotype.

815. Percutaneous C1-C2 cordotomy for refractory cancer pain: a multicenter experience

Ashwin Viswanathan, MD (Houston, TX); Ahmed Raslan, MD (Portland); Parag Patil, MD, PhD (Ann Arbor); Erich Richter, MD (Morgantown); William Rosenberg, MD (Kansas City)

Introduction: CT-guided percutaneous C1-C2 cordotomy has been shown in two series from Turkey and Egypt to be useful for refractory cancer pain. However, no large series have been reported from America. Through an initiative of the Cancer Pain Research Consortium, multiple institutions are collaborating to form a registry of patients undergoing ablative neurosurgical procedures for cancer pain.

Methods: A retrospective chart review was performed of patients who had undergone CT-guided cordotomy at four participating institutions between July 2011 and October 2013. CT-guided cordotomy was performed with a radiofrequency electrode (Cosman Medical, Inc.) applied to the C1-C2 level.

Results: Thirty-nine patients were included in this study, and detailed followup data was available for 26 patients. The median age at the time of cordotomy was 56 years (range, 9-79), and the median postoperative survival was 90 days (range, 10 days - 17 months). The most common pathologies included lung cancer (n=7), melanoma (n=5), and sarcoma (n=5). Twenty-one patients experienced significant improvement after cordotomy with a mean preoperative pain intensity of 8.7 and a mean postoperative pain intensity of 3.3. At a median followup of 140 days, the mean pain intensity was 3.8. Five patients did not experience sustained improvement after cordotomy. Complications included mirror pain syndrome in 2 patients, and transient dysesthetic sensations in 3 patients. No patients had worse pain or developed neurological deficits.

Conclusions: CT-guided percutaneous cordotomy is safe, and for properly selected patients can lead to dramatic pain relief with low morbidity.

816. A National Survey of Spinal Cord Stimulation Trial to Permanent Conversion Rates

Gustavo Chagoya; Kevin T. Huang; Jeffrey Hatef; Andrew Marky, MD; Steven Thomas; Yulia Lokhnygina, PhD; Shivanand Lad, MD, PhD (Durham, NC)

Introduction: Conversion rates from trial to permanent spinal cord stimulation (SCS) systems have recently been scrutinized. Most reports to date have been small cohort, single-institution series and national level data across a variety of settings is currently lacking.

Methods: We designed a large, retrospective analysis using the Thomson Reuter's MarketScan database. Patients having a percutaneous implantation of neurostimulation electrode array (CPT code: 63650) without simultaneous implantation of a permanent pulse generator (CPT: 63685) were selected. Patients were analyzed for predictors of successful conversion according to age, gender, insurance status, employment status, geographic location, number of previous percutaneous trial attempts, and primary diagnosis.

Results: A total of 21,672 percutaneous trials were identified. The most common indications were radiculitis/neuritis (43.8%) and postlaminectomy syndrome (38.6%). Overall, 41.4% of those undergoing trials received a permanent SCS system within three months. Factors associated with increased likelihood of successful conversion included having commercial insurance (43% vs. 37%, $p < 0.0001$), younger age (43% for ages 35-44 vs. 39% for ages 65 and older, $p < 0.0001$), and no previous percutaneous trial attempts (44% after first-time vs. 27% after second vs. 14% after third or subsequent trial, $p < 0.0001$). Multivariate analysis revealed significant variation in conversion rates by geographic area (North Central vs. Northeast region: OR 1.48, 95%CI 1.31, 1.66, $p < 0.0001$).

Conclusions: Recent changes in healthcare policy and coverage decisions for SCS trials include procedure setting, trial-permanent conversion ratios, and proposed limitation to a single trial per patient per lifetime. As a field, this will necessitate improved patient selection by physicians who perform neuromodulation.

817. Dual occipital and supraorbital nerve stimulation for chronic migraine

Shannon Wang Hann, MD; Sharan Sharan, MD (Philadelphia, PA)

Introduction: Occipital nerve stimulation (ONS) has been studied in a few clinical trials for treatment of chronic migraine (CM) with failure to prove sufficient efficacy. To date, use of peripheral nerve stimulation (PNS) for treatment of primary headache is limited to off-label use only. We report our institutional experience in CM therapy with combined ONS and supraorbital nerve stimulation (SONS).

Methods: Fourteen patients treated with dual ONS and SONS for CM were studied with follow-up ranging from 3 - 60 months.

Results: 71% achieved successful stimulation as defined by $\geq 50\%$ decrease in pain severity. Average reduction in headache related visual analog scale (VAS) score was $-3.92 (\pm 2.4)$. Half of the patients also had resolution of migraine associated neurologic symptoms and returned to normal functional capacity. Main adverse events included lead migration (42.8%), supraorbital lead allodynia (21.4%), and infection (14.2%) with resultant high reoperation rate (35.7%).

Conclusions: Our stimulation efficacy was superior to the combined 33% positive response rates (greater than 50% pain reduction) from the published studies of ONS for CM. This is likely due to topographical paresthesia induced by combined ONS and SONS covers migraine pain area better than with ONS alone. We also discuss effective surgical techniques to prevent patient morbidities.

818. Efficacy of Spinal Cord Stimulation for Neuropathic Pain due to Spinal Cord Lesions

Toru Sasamori, MD; Shunsuke Yano, MD, PhD; Kazutoshi Hida, MD, PhD (Sapporo, Japan); Yasuhiro Chiba, MD, PhD; Daijiro Morimoto, MD, PhD (Kushiro, Japan); Toshitaka Seki, MD, PhD (Sapporo, Japan); Toyohiko Isu, MD, PhD (Kushiro, Japan); Hisatoshi Saito, MD, PhD; Kiyohiro Houkin, MD, PhD (Sapporo, Japan)

Introduction: Spinal cord stimulation (SCS) has been considered less effective for central neuropathic pain. However, recent advancements in SCS equipment may provide more favorable outcomes in patients with intractable pain.

Methods: We retrospectively analyzed 11 consecutive patients (mean age 62.2; 6 men, 5 women) with neuropathic pain due to spinal cord lesions, who underwent SCS. The median duration of pain was 4 years. There were 2 cases with spinal cord injury, 2 with syringomyelia, 2 with spinal tumor, 3 with degenerative disease, 1 with spinal dural arteriovenous fistula and 1 with adhesive arachnoiditis. Among these lesions, 7 were located at the cervical level, 3 at the thoracic and 1 at the conus medullaris. The efficacy of SCS was evaluated using visual analogue scale (VAS) scores.

Results: The mean VAS score before SCS was 89. During the trial stimulation, significant VAS score reduction ($\geq 50\%$) was observed in 7 (63.6%) of 11 patients. Permanent implantation of the SCS system was performed in 6 of these 7 patients. Of the 6 patients, 5 received paddle leads and 1 received percutaneous leads. After a mean follow-up of 1.5 years, SCS was still effective in 5 (83.3%) of 6 patients. In all the five, electrodes were placed distal to the lesion site.

Conclusions: This study clearly shows that our result is more favorable than that in the reported studies. SCS is likely to be suitable treatment for neuropathic pain below the level of spinal cord lesions.

819. IMPACT OF TARGET LOCATION ON THE RESPONSE OF TRIGEMINAL NEURALGIA TO STEREOTACTIC RADIOSURGERY

Zhiyuan Xu, MD; David Schlesinger, PhD; Krisztina Moldovan, MD; Colin Przybylowski; Xingwen Sun; Cheng-Chia Lee, MD; Chun-Po Yen; Jason Sheehan, MD, PhD (Charlottesville, VA)

Introduction: We evaluate the impact of target location on the rate of pain relief (PR) in patients with intractable trigeminal neuralgia (TN) undergoing stereotactic radiosurgery (SRS).

Methods: A retrospective review of 99 idiopathic TN patients identified from a prospectively maintained database treated with SRS targeting the dorsal root entry zone with a maximum dose of 80 Gy was conducted. Targeting the more proximal portion of a trigeminal nerve with the 50% isodose line (IDL) overlapping the brainstem was performed in 36 patients (proximal group). In a matched group, 63 patients received the SRS targeting the 30% IDL tangential to the emergence of brainstem (distal group). The median follow-up time was 33 months (range, 6 to 124 months).

Results: The actuarial rate of maintenance of Barrow Neurological Institute (BNI) Pain Score I-IIIa was attained in 89% of patients at 1 year, 81% at 2 years, and 69% at 4 years, respectively following SRS. Kaplan-Meier analysis revealed that durability of PR was only associated with the proximal location of the radiosurgical target (Log-rank test, $p=0.018$). Radiosurgery-induced facial numbness (BNI II to III) developed in 35 patients, which was significantly more frequent in the proximal group (19 patients (53%) compared to 16 (25%) in distal group ($p=0.015$)).

Conclusions: The radiosurgical target appears to affect the duration of pain relief in idiopathic trigeminal neuralgia patients with the target closer to brainstem affording extended pain relief. However, the proximal SRS target was also associated with an increased risk of mild to moderate facial numbness.

820. Age and Pain Duration as Predictors of Long Term Effectiveness in Spinal Cord Stimulation for Chronic Pain

Ido Strauss, MD; Karim Taha, BS; Vibhor Krishna, MD; Soha Alomar, MD; Mojgan Hodaie, MD (Toronto, Canada)

Introduction: Spinal cord stimulation (SCS) is an accepted surgical treatment for neuropathic pain secondary to failed back syndrome or complex regional pain syndrome. However, in a clinical setting, even in the best-selected cases, there is still discrepancy as to what specific factors can act as potential criteria for adverse outcome or lack of benefit. The aim of the present study was to identify factors predictive of outcome in patients undergoing SCS.

Methods: We performed a retrospective chart review of our neurosurgical database for patients who underwent SCS between 2006 and 2012. We collected data on demographics, etiology of pain, previous spinal surgery profiles, psychiatric assessments, and pre- and post-operative VAS (visual analog scale) outcomes. We also noted the reported outcomes of intra- and post-operative stimulation (qualitative coverage and percentage if charted). Statistical analyses (Chi-squared and T-test measures) were performed to investigate the relationship between patient characteristics and self-reported post-operative pain level.

Results: Forty-one patients underwent implantation of epidural electrodes, 34 patients had a successful stimulation trial and received permanent devices. Nine patients experienced a late failure at a median time of 7.8 months (range 4.5-19 months) after implantation. Age and duration of symptoms prior to SCS therapy were significantly associated with outcome. Older patients had a significantly higher rate of treatment failure, and none of the patients above 65 years had a successful long-term outcome. Patients with a longer duration of pain (greater than 8.15 years) were more likely to have a successful outcome compared to patients with a shorter duration of pain (less than 8.15 years) preoperatively (75% vs. 40% successful outcome, respectively; $p=0.049$).

Conclusions: Age and duration of pain may influence the success of SCS therapy. Older patients may have greater tendency to failure, and patients with longer chronic pain duration may respond more favorably to this procedure.

821. Descending Tractotomy in Cases of Intractable Trigeminal Facial Pain Syndromes

John Anthony Braca III, MD; Giuseppe Toia, MS; Douglas Anderson, MD (Maywood, IL)

Introduction: Trigeminal Neuralgia (TN) is a debilitating source of severe facial pain. TN presents as paroxysmal bouts of lancinating and unilateral pain. Idiopathic TN may originate from aberrant neurovasculature compressing the 5th nerve root entry zone. Intractable TN, refractory to pharmacological intervention, is treated by microvascular decompression (MVD) of the nerve. Some patients do not display robust compression. Descending tractotomy (DT) is a feasible alternative, a method by which the surgeon ablates the descending tract of the trigeminal nerve. DT is less studied and surgical outcome data is scarce.

Methods: A retrospective chart analysis of patients with idiopathic TN who underwent retrosigmoid craniectomy for DT with and without MVD at a single institution by the same surgeon was performed.

Results: Of 101 patients with intractable TN or atypical facial pain, 12% demonstrated no neurovascular compression and 67% showed unimpressive small vessel compression. Patients who

received DT (n = 16) demonstrated at least some pain relief in 100% of cases at hospital discharge, in 100% of cases at first follow-up (median = 0.56 months), and in 89% of cases at long-term follow-up (median=25.9 months). Data from 7 patients are pending future follow-up. Facial numbness was the most common post-operative complaint (n=5).

Conclusions: This cohort reaffirms that overt neurovascular compression is not found in all cases of intractable TN and thus MVD is not possible or as effective. DT was demonstrated to be a possible alternative for pain relief. The inclusion of diffusion tensor imaging may enhance systematic pre-operative planning.

822. Mechanical Allodynia following Disc Herniation requires Autoimmune Intra-neural Macrophage Infiltration and can be Blocked by Supraphysiologic Systemic Selenium Delivery

Mohammed Farid Shamji, MD PhD FAANS (Toronto, Canada); Yu Shan Tu; Michael Salter (Toronto)

Introduction: Disc-herniation induced radiculopathy arises from both mechanical compression and biochemical inflammation of apposed neural elements. This study demonstrated the need for intra-neural macrophage migration after placement heterotopic disc tissue to generate the painful neuropathy phenotype.

Methods: C57BL/6 mice underwent a surgical procedure with mid-thigh exposure of the sciatic nerve. Control animals underwent exposure only (n=12) and experimental animals underwent placement of littermate tail nucleus pulposus (n=12). Animals were evaluated throughout one week for mechanical allodynia by Von Frey testing, thermal hyperalgesia by heat withdrawal latency, cold allodynia by acetone testing, and gait stability by RotaRod testing. At sacrifice, immunohistochemistry was performed to identify perineural and intra-neural macrophage and lymphocyte presence. Necessity of an inflammatory response was tested by attenuating systemic inflammation with intraperitoneal selenium delivery.

Results: Mice exposed to heterotopic NP stimulation demonstrated substantial mechanical allodynia maximal through the first five days and resolving by three weeks after surgery (0.014 ± 0.007 g (NP) vs. 1.0 ± 0.3 g (sham), $p=0.02$). Associated thermal hyperalgesia and cold allodynia also occurred. Substantial intra-neural macrophage infiltration was observed in this group, alongside associated CD3+ IL17+ autoreactive lymphocytes at the disc-nerve interface. Systemic selenium administration blocked this behavioral phenotype in the acute inflammatory phase, also affecting the extent of macrophage extravasation.

Conclusions: Non-compressive disc herniation leads to altered behavior in this animal disease model, with demonstrated need for intra-neural macrophage migration. Strategies to decrease perineural inflammation or maintain integrity of the blood nerve barrier may be effective in treating painful disc-herniation radiculopathy.

823. Neurostimulation for the Treatment of Headache Disorders: A Large, Retrospective Cohort Analysis

Shivanand P. Lad, MD PhD; Jeffrey Hatef, BS; John Gallis; Kevin Huang, BA; Yuliya Lokhnygina, PhD (Durham, NC)

Introduction: Neurostimulation is currently an off-label treatment for several medically refractory headache syndromes. Although the results of neurostimulation for chronic daily headaches (CDH) have been promising, most studies have been small, institutional studies. We designed a retrospective cohort analysis of patients who underwent trials of neurostimulation

for CDH and analyzed the effect of permanent neurostimulation implantation on subsequent healthcare utilization.

Methods: Patients from the Thompson Reuters MarketScan Database who underwent neurostimulation for CDH were included; those with a permanent neurostimulatory system placed within one year were analyzed as the intervention group. Healthcare utilization was compared in terms of median levels of total provider payments, outpatient/inpatient provider payments, number of procedures, and monthly medication costs.

Results: A total of 717 patients were analyzed, 172 (24.0%) converting to a permanent system within one year. Subsequent costs were lower in the intervention group with regard to median total monthly provider payments (\$1,190 vs \$1,883), median yearly number of outpatient procedures (25.2 vs 28.8), and median monthly outpatient provider payments (\$1,006 vs \$1,295). Costs were not always lower in the intervention group: median monthly number of all medications was greater in the intervention cohort (4.7 vs. 4.2), as was median total medication cost (\$322.40 vs. \$229.50). However, median total monthly costs were 20% lower in the intervention group (\$1,871 vs. \$2,388).

Conclusions: Neurostimulation for the treatment of CDH is associated with substantial reductions in overall postoperative healthcare utilization. Further research is needed to investigate both the efficacy and cost-effectiveness of this procedure for debilitating headache syndromes.

824. Thoracic Postherpetic Neuralgia- A Case Series and Proposed Treatment Approach

Jonathan Riley, MD; Lindsey Nicole Urquia; Nicholas Boulis, MD (Atlanta, GA)

Introduction: Thoracic postherpetic neuralgia (TPHN) is a clinically rare complication of herpes zoster. This form of neuropathic pain is commonly refractory to medical interventions and lacks a defined surgical treatment approach. This study explores the surgical experiences of 3 TPHN patients and attempts to identify an approach to surgical intervention.

Methods: A retrospective study of TPHN patients seen by a single surgeon was reviewed over a 5-year period, from 2008-2013. Identified patients received neurosurgical intervention for medically refractory TPHN. Surgical and clinical follow-up data were reviewed.

Results: 3 patients received surgical intervention for medically refractory TPHN. All patients received electrode lead placement and trial stimulation into the neural foramina corresponding to affected dermatomes. One patient experienced substantial pain improvement following stimulation and maintained this improvement on the internalized stimulator for 2 years before becoming refractory to stimulation. All patients ultimately received dorsal rhizotomy. Two of three patients experienced complete pain resolution following rhizotomy, followed for at least 6 months.

Conclusions: One of three patients in this series successfully responded to neurostimulation, maintaining this response for 2 years. Given the irreversible nature of ablative procedures such as dorsal rhizotomy, the results of this small case series support consideration of stimulation-based treatment prior to ablative procedures for this form of neuropathic pain. Dorsal rhizotomy can provide complete pain relief, though the durability of this relief remains to be determined. Finally, the presence of persistent pain following dorsal rhizotomies in a single patient supports that TPHN can result from plasticity in the central and peripheral nervous system.

825. Natural History of Idiopathic Syrx

Jennifer Strahle, MD; Brandon Smith, MD; Jordan Starr, BS; Karim Muraszko, MD; Hugh Garton, MD; Cormac Maher, MD (Ann Arbor, MI)

Introduction: The natural history of idiopathic syrinx (without Chiari, tethered cord or tumor) has not been clearly defined.

Methods: All patients with an intramedullary spinal cord cyst 3mm or greater in width and no associated pathology were identified from 13,928 consecutive patients undergoing MR imaging over an 11-year period.

Results: 76 patients with an isolated syrinx were identified. The majority of patients (n=42, 55%) had associated scoliosis (10 degree Cobb angle or greater). 65 patients had clinical follow-up over an average of 6.0 years and 52 patients had an average imaging (MRI) follow-up of 4.6 years. The majority of syringes remained stable or decreased in width (84%) and length (90%). Of the syringes that increased in length, all but two increased by one level. Five patients presented with neurologic changes; three of whom improved by the time of last follow-up. One patient underwent placement of a syngo-subarachnoid shunt, with no change to his presenting symptoms. 20 patients underwent surgical correction for scoliosis. At the most recent clinical follow-up all patients who did not undergo surgery were stable without any new symptoms. One patient had numbness after scoliosis correction. The average change in degree of maximum curve was 16 for those who ultimately underwent scoliosis correction (n=20), compared with -2 for those who did not (n=20). There was no difference in syrinx characteristics (width, length, cranial or caudal extent) between the groups.

Conclusions: The natural history of idiopathic syrinx is likely benign with little risk of progression.

826. Indwelling intrathecal baclofen trial: Assessment of efficacy and safety in 124 pediatric patients with cerebral palsy and dystonic overlay

Robert F. Keating, MD, FAANS; Seth Butler; Tiffani DeFreitas; Chima Oluigbo, MD; Jeffrey Rabin, DO; Bennett Lavenstein, MD; Suresh Magee, MD; John Myseros, MD (Washington, DC)

Introduction: Intrathecal baclofen trials, using an indwelling catheter for the titrated infusion of baclofen, offers many advantages compared to the administration of a single intrathecal bolus via lumbar puncture. Frequently these patients have mixed movement disorders(spasticity/dystonia) and those with significant dystonia historically require elevated doses of baclofen for meaningful reduction in tone. An indwelling catheter, which can be placed at higher locations in the spine (cervicothoracic), allows for the delivery of escalating doses of intrathecal baclofen in sufficient doses and appropriate localization, to effect meaningful reduction in tone and arrive at useful predictive conclusions.

Methods: Over the past 15 years, 124 patients(72 M/52F), average age of 12.9 years, underwent placement of a percutaneous lumbar catheter for trial administration of intrathecal baclofen for spastic/dystonic quadraparesis. Baclofen dosage was incrementally increased every 12 hours until reduction in tone/dystonia was observed or the patient manifested side effects(sedation/respiratory depression).

Results: 92/124(74%) trial patients proceeded to baclofen pump insertion after 3.9(1-27) months. Five patients(4%) had a trial complication: CSF leak, baclofen OD, wound breakdown, pronounced vomiting(2). Average LOS was 2.76(1- 16) days with average dose of 150 (50-500) ug before significant reduction in

tone. 25 patients(20%) needed doses greater than 200 ug before demonstrating clinical efficacy. Present day doses for this cohort is currently 516ug/day.

Conclusions: The use of an indwelling lumbar catheter for an intrathecal baclofen trial effectively permits identification of dystonic patients requiring a higher dose for a positive trial. The trial also assists in predicting optimal doses for effective clinical response for the dystonic patient with minimal morbidity(4%).

827. Predictors of shunt revision: should the shunt revision rate be used as a quality metric?

Paul Klimo, Jr., MD, FAANS; Nickalus Khan, MD; Nick Rossi, MD; Frederick Boop, MD (Memphis, TN)

Introduction: Hospital readmission rates are now considered a metric for quality of care evaluation of physicians and institutions. Shunting procedures are associated with a readmission rate. The highly publicized US News & World Report has as one of its primary outcome measures the 90-day shunt revision rate. The objective of this study is to identify risk factors, both modifiable and non-modifiable, associated with shunt reoperation.

Methods: A retrospective, single institution review of all CSF shunt procedures performed from January 2010 to mid-2013 was performed. Only shunt systems with an intracranial proximal catheter were included for analysis. A large number of variables were assessed: patient demographics, hydrocephalus history, and operative details.

Results: A total of 762 procedures performed in 463 patients were analyzed. Overall, 27.9% of patients undergoing CSF shunt surgery required revision surgery within 90 days of the procedure, and 33.9% at 180 days. Binary logistic regression analysis demonstrated that the number of proximal catheters (p <0.013) and number of prior shunt related surgeries (p <0.009) were to predictors of shunt failure.

Conclusions: Our preliminary analysis has shown that the only predictive variables were related to the child's hydrocephalus history and thus, non-modifiable. Our findings call into question the use of the 90-day shunt revision rate as a useful indicator of quality of care rendered.

828. Diagnostic and Therapeutic Interventions in Children with Cerebral Venous Sinus Thrombosis: A National Study

Michael Schiraldi, MD PhD; Doniel Drazin, MD, MS; Faris Shweikeh, BS; Miriam Nuno, PhD; Moise Danielpour, MD; Michael Alexander, MD (Los Angeles, CA)

Introduction: Despite available treatment modalities, mortality of pediatric cerebral venous sinus thrombosis(CVST) remains high. Accessing a national inpatient pediatric database, we studied diagnostic and treatment modalities utilized for CVST.

Methods: A cohort of 745 children with CVST was identified from the Kids' Inpatient Database for years 2000, 2003, 2006 and 2009 using International Classification of Diseases-9(ICD-9) codes. Multivariate logistic regression analysis was used to assess mortality.

Results: Diagnostic procedures included: magnetic resonance imaging, 168 patients(22.5%); computed tomography, 50 patients(6.8%); venography with contrast, 57 patients(7.7%); cerebral arteriography, 93 patients(12.5%). Some patients required mechanical ventilation(6.9%). Six patients(0.8%) underwent endovascular embolectomy; their mortality rate was 24.3% versus 2.6% in those not requiring the procedure(p=.008). Both patients

survived who underwent angioplasty. Stents were placed in 3 patients. Infusion of heparin was used for 29 patients (3.8%); this group had mortality of 10.7% ($n=3$, $p=.02$). Infusion of any thrombolytic, excluding heparin, was used for 21 patients (2.8%); their mortality was 28.1% ($n=6$, $p=<.0001$). Hydrocephalus developed in 69 patients (2.4%). Of these, 6 (0.8%) patients underwent ventriculoperitoneal shunting; their mortality rate was 23.1% ($p=.0008$ vs all patients without shunt).

Conclusions: Various modalities are used to diagnose and treat pediatric CVST. The most severely affected patients, and patients who failed standard medical therapy, required interventions such as thrombolytic infusions, embolectomy, and ventricular CSF drainage, and due to their higher acuity, these patients had worse outcomes. Patients with hydrocephalus necessitating drainage have the highest mortality. This study highlights the need for larger trials to establish diagnostic and treatment standards.

829. Bone Morphogenetic Protein-Associated Complications in Pediatric Spinal Fusion: an analysis of 4658 patients and systematic review of the literature

Brandon G. Rocque, MD, MS (Birmingham, AL); Mick Kelly, BS (Madison, WI); Joseph Miller, MD (Birmingham, AL); Yiping Li, MD; Paul Anderson, MD (Madison, WI)

Introduction: Use of recombinant human bone morphogenetic protein-2 (BMP) has risen steadily since its approval by the FDA for use in anterior lumbar interbody fusion. The use of BMP in children has not been approved by the FDA. Age under 18 or lack of evidence of epiphyseal closure are considered contraindications to BMP use by the manufacturer. We performed a query of the database of a large health insurance company to determine the rate of BMP use and complications in pediatric patients undergoing spinal fusion.

Methods: We utilized PearlDiver Technologies private payer database containing all records from United Healthcare from 2005 to 2011 to query all cases of pediatric spinal fusion with or without BMP use. We also performed a systematic review of the literature to examine the complications associated with BMP use in pediatric spinal fusion.

Results: 4658 patients underwent spinal fusion. The majority was female (65.4%), and the vast majority was age 10-19 (94.98%) and underwent thoracolumbar fusion (93.13%). BMP was used in 1752 (37.61%) spinal fusions. There was no difference in the rate of BMP use comparing male to female or age greater than 10 versus less than 10. Anterior cervical fusions were significantly less likely to use BMP (7.25%). Complications occurred in 9.82% of patients with vs. 9.88% of patients without BMP. Complication rate was nearly identical in male vs. female patients and in patients older vs. younger than 10. Comparison of systemic, wound-related, CNS, and other complications showed no difference between groups with and without BMP. Reoperation rate was also nearly identical.

Conclusions: BMP is used in a higher than expected percentage of pediatric spinal fusions. The rate of complications in these operations does not appear to be different with versus without BMP.

830. Health Disparities Impact Outcomes in Children with CNS Malignancies

David I. Sandberg, MD, FAANS (Houston, TX); Mary Austin, MD, MPH; Hoang Nguyen, MD, PhD; Jan Eberth; Andras Heczey; Dennis Hughes, MD, PhD; Linda Elting, PhD (Houston)

Introduction: Our objective was to identify barriers to health

care in children with CNS malignancies and examine their impact on disease presentation and outcome.

Methods: We examined all children (age < 18 years) diagnosed with CNS solid tumors and enrolled in the Texas Cancer Registry between 1995 and 2009 ($n=2,230$). Geocoded information was used to calculate the driving distance between a patient's home and the nearest pediatric cancer treatment center. Socioeconomic status (SES) was determined using the Agency for Healthcare Research and Quality (AHRQ) formula and 2007-2011 US Census block group data. Logistic regression was used to determine factors associated with advanced-stage disease. Survival probability and hazard ratios were estimated using life table methods and Cox regression.

Results: Children with advanced-stage CNS solid tumor malignancies were more likely to be Hispanic or non-Hispanic Blacks (all $p < .05$ years old (OR 1.75, 95%CI 1.07, 2.88), and in Hispanics (OR 1.69, 95%CI 1.29, 2.21) compared to non-Hispanic Whites. Distance to treatment and SES did not impact disease stage at presentation. However, children < 10 years old, Hispanic and non-Hispanic Blacks, and patients in the lowest SES quartile had the worst 1- and 5- year survival probability (all $p < .05$). Adjusted overall survival differed by age, race, SES, and stage, but not distance to the nearest treatment facility.

Conclusions: Socioeconomic and racial disparities are important factors in disease presentation and outcome for children with CNS solid tumors.

831. Pial Synangiosis for Moyamoya Syndrome in Children with Sickle Cell Anemia: A Comprehensive Review of Reported Cases

Benjamin Kennedy, MD; Michael McDowell, BS; Peter Yang, BS; Sida Li; Caroline Wilson (New York, NY); Todd Hankinson, MD (Denver, CO); Neil Feldstein, MD; Richard Anderson, MD (New York, NY)

Introduction: Children with Sickle Cell Anemia (SCA) carry a significant risk of developing Moyamoya Syndrome (MMS). We reviewed the safety and efficacy of pial synangiosis for MMS in children with SCA by performing a comprehensive review of all previously reported cases.

Methods: We retrospectively reviewed the clinical and radiographic records of 17 patients at The Children's Hospital of New York with SCA who developed radiological evidence of MMS and underwent pial synangiosis between 1996-2012. We then added any additional reported cases of pial synangiosis for this population in the literature for a combined analysis of clinical and radiographic outcomes.

Results: The combined data consisted of 48 pial synangiosis procedures performed in 30 patients. 27 patients presented with seizure, stroke, or TIA, while three patients were referred after transcranial doppler screening. 13 (43%) patients had an ischemic stroke while on chronic transfusions. Long-term imaging (MR angiography or catheter angiography) at a mean of 25 months post-operatively was available in 39 (81%) treated hemispheres. In 34 (87%) of those hemispheres with imaging there were demonstrable collateral vessels. There were 4 neurological events in 1575 cumulative months of follow-up, or 1 event per 33 patient-years. In our series, post-operative stroke rate was reduced more than 6-fold from the pre-operative stroke rate ($p=0.0003$).

Conclusions: Pial synangiosis in SCA patients with MMS is a safe and effective treatment option. TCD/MR screening in asymptomatic SCA patients is recommended for the diagnosis of MMS.

832. Pediatric Survivors of Traumatic Atlanto-occipital Dislocation and their Neurosurgical Management: the Loma Linda University Children's Hospital Experience

Joseph Ryan Keen, DO; Joseph Keen, DO; Robert Ayer, MD; Alexander Zouros, MD (Loma Linda, CA)

Introduction: Traumatic atlanto-occipital dislocation (AOD) is rare but often fatal. Children are at high risk given anatomic predispositions at the craniocervical junction; however, they make up the majority of survivors and given an increasing survival rate, reliable and safe fixation is mandatory. The pediatric spine does not easily accommodate adult fixation techniques. Various approaches have been utilized but rates of mechanical failure and non-union are high. Rigid occipitocervical instrumentation, which commonly involves fixation of the occiput to C1-C2 via screw and rod/wire constructs, has evolved but long-term outcomes remain uncertain. We report a series of children (age 8 or less), who survived AOD and underwent instrumented occipitocervical fusion.

Methods: Retrospective review of all surviving pediatric patients diagnosed with traumatic AOD, who underwent instrumented occipitocervical fusion at Loma Linda University Children's Hospital between 2006 and 2014.

Results: Thirteen children suffered traumatic AOD and underwent occipitocervical fusion. All were under the age of 8 and either passengers involved in a motor vehicle collision or pedestrians struck by an automobile. Mean age at surgery was 3.83 years (range, 6 months to 8 years), and all underwent fusion using rod and/or wire constructs anchored to the following screw fixations: C1-2 transarticular (1), C1 lateral mass (4), C2 translaminar (11), subaxial lateral mass (3). All had rib autograft incorporated into the constructs. Postoperative halos were not utilized. Ten children, for whom data was available, achieved fusion at mean follow-up of 21 months. One construct failed but subsequently achieved fusion.

Conclusions: Rigid occipitocervical fixation in children under 8 years of age, and as young as 6 months, was safe and resulted in fusion in every patient (10/13) for whom data was available. Translaminar screws and rib autograft were particularly advantageous given the pediatric anatomy.

833. The Spectrum of Sacral Agenesis and associated Malformations- Two Decades experience.

Natarajan Muthukumar, MD (Madurai, India)

Introduction: To report this author's experience in treating total and partial sacral agenesis (SA) and associated malformations.

Methods: The study is based on a prospective database of SA maintained by this author from 1990. Patients with isolated coccygeal agenesis were excluded. All children underwent neurological examination, plain radiographs, MRI. Surgical intervention was undertaken in appropriate cases. Follow up ranged from 6 months to 10 years.

Results: Between 1990 and 2012, 52 patients were treated. Maternal diabetes mellitus was proved in two patients. 8 patients had total agenesis and 44 had partial agenesis. Among the 8 with total agenesis there were 3 with lumbosacroccygeal agenesis, 3 with sacroccygeal agenesis, 1 each with split notochord syndrome and mermaid malformation. Radiologically, among the total agenesis group Type II was the commonest. Imaging revealed dural sac stenosis in 2, high ending club shaped conus in 4, dural sac stenosis with tethered cord in 1 and thickened filum terminale in 1. Two patients with tethered cord underwent untethering with partial improvement. Among the 44 patients with partial agenesis,

64% had associated anorectal malformations. Associated segmental spinal dysgenesis and Jarcho-Levin syndrome were encountered in one patient each. Radiologically, Type IVc was the commonest type encountered. 39% of the 44 patients had tethering lesions.

Conclusions: In this series, the entire spectrum of anomalies of sacral agenesis was encountered. Maternal diabetes was not a common etiological factor in this series. Anorectal malformations are common in this group. Tethering lesions are more common in partial agenesis group than in total agenesis.

834. Effectiveness and Safety of Independent Pediatric Nurse Practitioners in Evaluating Plagiocephaly

Nathan R. Selden, MD, PhD, FAANS; Curtis Bergquist, BA; Lisa Crupi; Maureen Oliverio, NP; Anna Kuang, MD (Portland, OR)

Introduction: In 2000 the craniofacial disorders (CFD) program at Oregon Health & Science University established a plagiocephaly screening clinic staffed by pediatric nurse practitioners (PNPs).

Methods: Electronic medical records of patients seen in a single accredited CFD clinic from 2005 to 2011 were reviewed retrospectively to identify those patients whom PNPs independently screened for positional plagiocephaly vs. synostosis.

Results: Over a 7-year period, 1228 patients were independently screened in the CFD PNP clinic for plagiocephaly. Over half (638; 52%) were followed through subsequent CFD visits without any direct surgeon input. Of these, 169 (26%) were treated with orthotic consultation for a molding helmet, 385 (60%) received a combination of counseling and/or physical therapy for torticollis, and 84 (13%) were lost to follow-up. No patient independently managed by a PNP was later identified to have cranial synostosis or underwent early or delayed surgery. All returning patients (554; 86%) showed improvement in, or resolution of, their presenting deformity. The remaining 590 patients (48%) were referred at the time of their initial CFD PNP clinic evaluation for surgical consultation. The surgical team ruled out synostosis based on clinical evaluation alone in 325 (55%) of these patients. In 265 patients (45%), CT imaging revealed synostosis in 121 (56%).

Conclusions: PNPs accurately screened over half of patients referred to a high volume CFD program for positional plagiocephaly vs. synostosis, without surgeon input. Only 22% of all patients referred underwent CT imaging. No synostosis diagnosis was overlooked using this approach. With specific training, PNPs in a CFD program can safely screen for positional vs. synostotic plagiocephaly and appropriately management patients with positional deformity.

835. Non-operative pediatric skull fracture: return to system and utility of surveillance imaging

Joshua J. Chern, MD, PhD; Brian Howard, MD; Markus Bookland, MD; David Wrubel, MD; Barun Brahma, MD; Andrew Reisner, MD; William Boydston, MD (Atlanta, GA)

Introduction: Traumatic skull fracture is one of the main non-operative admissions. The clinical outcome is expected to be benign, and it is unclear whether post-injury surveillance imaging contributes to adverse event prevention.

Methods: Patients with skull fractures were identified in a 4-year period. Demographic, socioeconomic, and clinical characteristics were prospectively collected. Clinical events within the 180 days following discharge were reviewed and analyzed. These clinical events included Emergency Department (ED) utilization, clinic visit, and utilization of surveillance CT and skull X-ray.

Results: 937 patients were included. Patients who required operations at the index admission were excluded. The average age of the patients was 5.1 years, and the average length of stay was 1.7 days. Initial imaging was normal (15%), demonstrated skull fracture only (22.6%), brain contusion (10%), or a combination of subdural or epidural hematoma (41.6%). Adverse events in the 4-year period consisted of 34 ED visits that led to 3 surgical procedures. Careful review suggested that better discharge instruction and concussion education could perhaps prevent 13 of the 34 returned ED visits. These preventable cases included scalp swelling, mild nausea, vomiting and headache, and a lack of instruction regarding dried blood in the ear canal. The use of surveillance imaging, either CT or skull x-ray, at the time of follow-up clinic visit varied between 7% to 65% among the 6 pediatric neurosurgeons. The utilization of imaging significantly correlated with the identity of the physicians but not with the severity of injury on the initial imaging. Because adverse events are rare, the use of surveillance imaging could not be statistically shown to decrease the rate of adverse events.

Conclusions: Adverse events after non-operative pediatric skull fracture are rare. It is difficult to determine whether or not there is a beneficial effect from extensive use of post-injury surveillance imaging.

836. Sleep apnea before and after hydrocephalus management and Chiari 2 decompression in spina bifida patients

Daxa Mahendra Patel, MD; Betsy Hopson; Anastasia Arynchyna; E. Ralee' Bishop; Brandon Rocque, MD, MS; Jeffrey Blount (Birmingham, AL)

Introduction: There is a paucity of literature examining sleep apnea in patients with spina bifida, Chiari 2 malformation and related hydrocephalus. Even less is known regarding the effect of hydrocephalus treatment or Chiari 2 decompression on sleep hygiene. The aim of our study is to evaluate the effects of surgical treatment, in particular to see whether Chiari 2 decompression or hydrocephalus management is associated with improvement in sleep organization.

Methods: We performed a retrospective review of patients from a multi-disciplinary spina bifida clinic. Polysomnography results were available for nine children both before and after Chiari 2 decompression and/or shunt placement between August 2005 and February 2013.

Results: Patient age at the time of surgery ranged from 16 days to 8.6 years (median 4.2 ± 4.14 years). 7 patients (78%) received a diagnosis of sleep apnea. After surgery, the mean number of respiratory events decreased from 34.8 to 15.9 ($p = 0.098$); the mean number of obstructive events decreased from 14.67 to 13.89 ($p = 0.85$); and the mean number of central events decreased from 20.11 to 2.25 ($p = 0.15$). Most importantly, the apnea-hypopnea index (AHI: total respiratory events / total hours of sleep) improved for most patients. The mean AHI decreased from 5.05 to 2.03 ($p = 0.038$).

Conclusions: Myelomeningocele patients who have abnormal sleep structure and undergo operative treatment of hydrocephalus and/or Chiari 2 have reduced obstructive and central events and a statistically significant decrease in AHI. These results suggest that polysomnography is useful in the evaluation and management of myelomeningocele patients.

837. Sustained Local Release of Methylprednisolone from a thiol-acrylate poly(ethylene glycol) Hydrogel for Treating Chronic Compressive Radicular Pain

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Introduction: Compressive radiculopathy (CR) can cause costly disability and result in chronic peripheral nerve pain. One leading treatment for this condition involves the epidural injection of steroid to temporarily alleviate pain. This treatment provides only short-term relief of symptoms. Here we describe the engineering and use of a non-swelling, thiol-acrylate PEG hydrogel to locally release methylprednisolone in a controlled and sustained fashion.

Methods: The injectable, biodegradable hydrogel described was engineered using a Michael-type conjugate addition reaction. Its non-swelling property is uncharacteristic of this class of materials and makes this device attractive for use in the nervous system. The rodent sciatic nerve ligation model was used to create CR in injured animals. Mechanical hyperalgesia was assessed using a dynamic plantar aesthesiometer. Allodynia was assessed using a Catwalk automated gait analysis platform. Immunohistochemistry analyses included assessment of macrophage infiltration into injured and control nerves, and quantifying the expression of Monocyte chemoattractant protein-1 (MCP-1).

Results: The use of the hydrogel plus methylprednisolone results in a significant reduction of mechanical hyperalgesia and improvement in the gait pattern of animals with chronic lesions as compared to animals treated with steroid alone. In addition, animals treated with hydrogel plus steroid showed a marked reduction in the number of infiltrating macrophages at the sciatic nerve and significantly reduced expression of the neuro-inflammatory chemokine MCP-1 as compared to animals treated with steroid alone.

Conclusions: Currently, the interventional treatment of choice for CR is bolus epidural injection of methylprednisolone. However, it is evident that a method for sustained, controlled local release would be beneficial. Thiol-acrylate PEG hydrogels for sustained and local release of methylprednisolone could be a potentially effective new treatment for CR. Further study towards human translation of this novel system is ongoing.

838. Comparison of graft repair vs nerve transfer for reconstitution of elbow flexion

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Introduction: Reconstruction of elbow flexion carries high priority in brachial plexus repair. At present nerve reconstruction is the preferred method. Nerve transfers were considered optional in case of root avulsion. We compared the results of the different methods for reconstitution of elbow flexion.

Methods: A retrospective analysis of cases between 01/2002 – 12/2011 was conducted. We identified 108 patients, who underwent surgery for restoration of elbow flexion. Ten patients were lost to follow up. The patients were divided into five groups. Group 1: Reconstruction by autograft to musculocutaneous nerve (MCN) (11 patients) / Group 2: Reconstruction by autograft to

fasciculus lateralis (11 patients) / Group 3: Reconstruction by combination of autograft with nerve transfer to MCN (16 patients) / Group 4: Oberlin transfer (24 patients) / Group 5: transfer of spinal accessory nerve to MCN (36 patients).

Results: Functional elbow flexion (M3) was regained by 49% of the whole collective. Group 1: 54% recovery to M3 / Group 2: M3: 45% / Group 3: M3: 43% / Group 4: M3: 80% / Group 5: M3: 31%. In comparison the outcome of group 4 was significantly better to the other groups.

Conclusion: Contrary to the standard therapy regime of applying autologous graft repair when feasible, the outcome of patients with Oberlin transfer as a stand alone nerve transfer for elbow flexion was significantly better as the outcome of stand alone nerve repair or combined methods. Is there a need to adapt treatment algorithms for brachial plexus repair?

839. A Review of Postoperative Delayed Cervical Palsies: Understanding the Etiology

Grant William Mallory, MD (Rochester, MN); William Clifton, MS; Ross Puffer, MD; Ahmad Nassr, MD; Michelle Clarke, MD (Rochester)

Introduction: Delayed palsy is a well-recognized complication of cervical spine surgery, most commonly occurring at the C5 level. While various theories such as mechanical stretch have been proposed, the true etiology is unknown. The present study reviewed the incidence and previously cited risk factors in a retrospective cohort who developed delayed cervical palsies.

Methods: A retrospective cohort of cervical decompressions with and without fusion at the Mayo from 2008-2012 was studied. Patients who developed delayed cervical palsies (new/worsened upper extremity weakness confined to one or more myotomes not attributable to intraoperative trauma) were included. Established radiographic risk factors such as laminectomy trough width and postoperative cord drift were analyzed in patients with postoperative MRIs. Lordosis angles of pre and postoperative radiographs were compared. Risk factors for post-surgical inflammatory neuropathy such as history of autoimmune disease, diabetes, smoking, and blood transfusions were collected. Overall incidence was calculated, and palsy rates with or without fusion were compared. The prevalence of risk factors was compared to historical controls.

Results: Thirty four patients developed delayed palsies over the study during which 1,330 cases were performed. The overall incidence was 2.5%. The risk was significantly higher after instrumented fusion ($p=0.0014$). While the majority involved C5 (74%), 52% involved more than one myotome, and 29% were bilateral. No difference between mean pre and postoperative lordosis was found ($p=0.8$). Both cord drift (mean = 5.3 mm, $N=9$) and laminectomy trough width (mean = 23.5 mm, $N=9$) were greater than controls reported by Radcliff et al, 2012 ($p=0.0003$ and $p=0.008$). Sixty percent had risk factors for post-surgical inflammatory neuropathy.

Conclusions: The incidence of delayed cervical palsy is higher after instrumented fusions. While mechanical risk factors were present in our cohort, the high prevalence of autoimmune risk factors supports an autoimmune response as a potential etiology.

840. Peripheral Nerve Stimulation for Chronic Lower Extremity Pain – A Retrospective Case Series Analysis

Sukreet Raju; Jonathan Riley, MD, MS; Nicholas Boulis, MD (Atlanta, GA)

Introduction: Management of medically refractory lower extremity (LE) pain presents a therapeutic challenge. This study evaluates the role of implanted peripheral nerve stimulators (PNS) for LE pain in the distribution of a major peripheral nerve.

Methods: A retrospective review of patients with medically refractory chronic LE pain, seen by a single surgeon from 2008-2013, was completed. All patients received peripheral neurostimulation for pain in the distribution of a major peripheral nerve. The sandwich method of sewing together the lead netting of two on-point Medtronic PNS, placed deep and superficial to the nerve was used in all cases. Surgical and clinical follow-up data were reviewed.

Results: 11 patients received intervention. Mean age at first surgery was 37.9 years and mean pain duration at presentation was 10.3 months. 4 patients received de novo implantation, 7 received electrode implant with an externalized trial (mean trial duration 4.7 days). Nerves stimulated were: Sciatic 7; Tibial 2; Common Peroneal 2; Superficial Peroneal 1. 5 of 7 externalized trial patients proceeded to internalization. In the 9 patients who received chronic neurostimulation, hardware explantation was required for a surgical site infection in one. 8 of 11 patients continue to receive stimulation.

Conclusions: 8 of 11 patients that received de novo implantation ($n=4$) or a stimulation trial ($n=7$) continue to receive chronic stimulation. Each of these patients had failed medical management and a varying combination of nerve blocks and other surgical treatments. These results support consideration of neurostimulation for chronic, treatment refractory lower extremity pain.

841. Long term results of DREZ operation for brachial plexus avulsion. An institutional case series, and patient reported outcome

Ahmed Raslan, MD (Portland, OR); Jeffrey Raskin, MD, MS; Kim Burchiel, MD; (Portland, OR)

Introduction: DREZ procedure is an effective treatment of brachial plexus avulsion pain. Long term results are scarce and therefore we conducted a patient reported outcome study to evaluate our long term results of DREZ procedure.

Methods: Retrospective review of the institutional data base of patients who have undergone brachial plexus DREZ procedure since 1995. A phone interview was conducted to assess the long term pain outcome.

Results: Between 1995 and 2012, 26 male and 3 female patients ($n=29$) had a cervical DREZ procedure for brachial plexus avulsion. The mean age was 47 $\pm$ 12. The median symptom duration preoperatively was 87 months. Prior to a DREZ procedure, many patients needed reconstructive or salvage surgery including amputation (13), muscle transfer (3), nerve reconstruction (6), arterial reconstruction (1), previous DREZ (2), pain surgery (3) and cervical fusion (1). On average, each DREZ procedure was 4.8 $\pm$ 2 levels. Of the 29 patients with neuropathic pain, 12 had pre-procedure amputation and 17 had a non-functioning arm. Immediately 2 weeks after surgery, 16/29 (55.1%) had complete pain relief, 7/29 (24.1%) had partial but satisfactory pain relief and 6/29 (20.6%) had no pain relief. The average follow-up duration was 5.7 years, ranging from 2-180 months. At last follow-up, 10/29 (34.4%) continued to have

complete pain relief, 13/29 (44.8%) had partial but satisfactory pain relief and used supplementary medical therapy. All secondary partial pain recurrence occurred within 6 months of surgery. Of the remaining 6 patients who failed DREZ immediately, four had previous interventions involving reconstruction of the brachial plexus, muscle or nerve transfer or previously failed DREZ.

Conclusion: DREZ thermoablation has a 79.2% efficacy in achieving complete or partial but satisfactory pain relief at long-term follow up. Previous interventions prior to DREZ may predict poor outcome.

842. Re-operation After Progression: Safety/Efficacy from AVAglio, a Phase III Study in Newly Diagnosed Glioblastoma

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Introduction: Bevacizumab (BEV) prolonged PFS in patients with newly diagnosed glioblastoma in AVAglio. We report safety/efficacy outcomes of patients undergoing post-progression surgery.

Methods: Patients (≥ 18 years/histologically confirmed glioblastoma) received BEV+RT/TMZ or Plb+RT/TMZ (6wks). After a 28-day break, patients received BEV+TMZ or Plb+TMZ (x6), then BEV or Plb until progression/unacceptable toxicity. Statistical analyses: exploratory, non-protocol specified.

Results: Post-progression surgery rates: 16% (73/458; BEV+RT/TMZ) and 23% (107/463; Plb+RT/TMZ). In this non-randomized comparison, baseline characteristics were balanced, and similar to the ITT population. Median PFS for re-surgery patients (11.8 [BEV+RT/TMZ] vs 6.7 [Plb+RT/TMZ] months) was comparable to the ITT population (10.6 vs 6.2 months). At progression, most patients had local tumors: 80.3% (BEV+RT/TMZ), 77.8% (Plb+RT/TMZ), mainly with an infiltrating pattern. Most re-surgeries were partial resection: 75.3% (BEV+RT/TMZ); 70.1% (Plb+RT/TMZ). Median time from last study dose to re-surgery was 2.1 (BEV+RT/TMZ) and 1.5 months (Plb+RT/TMZ). Most re-surgery patients received subsequent therapies (70% both arms). Median OS (re-surgery patients): 22.6 (BEV+RT/TMZ) and 21.3 months (Plb+RT/TMZ), compared with 16.8 and 16.7 months, respectively, ITT population. Adverse events (AEs) after surgery (BEV+RT/TMZ versus Plb+RT/TMZ, respectively): AEs, 16.4% vs 29.9%; AEs of special interest for BEV (AESI), 5.5% vs 11.2%. Grade ≥ 3 AESI (BEV+RT/TMZ versus Plb+RT/TMZ) included: wound-healing complications, 0.0% vs 2.8%; venous thromboembolic events 1.4% vs 3.7%; arterial thromboembolic events 1.4% vs 1.9%. No post-operative hemorrhages were reported.

Conclusions: Patients who underwent post-progression surgery had similar tumor patterns/surgical treatment, independent of study arm. This subset had longer median OS than the ITT population. BEV+RT/TMZ-treated patients had fewer post-surgery AEs/AESIs, than Plb+RT/TMZ.

843. The Capacity of Glioblastoma-Released Exosomes to Stimulate Peripheral Immune Effectors

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Introduction: Recent evidence suggests that exosomes may play a role in the pathogenesis of many tumor types by enabling intercellular communication between tumor cells and both the local environment and peripherally through the circulation. Glioblastoma (GBM)-released exosomes circulating in the blood have been shown to contain the protein and transcript signatures of their parent tumors. We thus investigated GBM-released exosomes' ability to interact with peripheral immune effectors by antigen-presentation machinery, co-stimulatory signals, or mediators of immunosuppression.

Methods: GBM-released exosomes from established and patient-derived GBM cultures were concentrated by serial ultracentrifugations. Western blot analysis determined protein levels of exosome-specific markers, antigen-presentation machinery, costimulatory molecules, and a putative mediator of peripheral immunosuppression (B7H1). Patient peripheral blood leukocytes were separated and treated with varying doses of autologous and non-autologous GBM-released exosomes and controls. Flowcytometry quantified T-cell and monocyte subpopulations, as previously described.

Results: Exosome-specific markers are concentrated in GBM-released exosome samples. Furthermore, exosome samples reflected the antigen-presenting protein signatures expressed by their parent GBM cells, in particular, MHC I and HSP70. However, exosomes lacked co-stimulatory CD80/CD86/CTLA-4 and B7H1 expression, regardless of expression by parent cells. Patient T-lymphocytes treated with autologous GBM-released exosomes failed to differ in either CD3/CD4/CD8 subpopulations or interferon expression, as compared to controls. Patient monocytes treated with autologous GBM-derived exosomes neither activated nor altered their B7H1 expression.

Conclusions: There is growing evidence that tumor-released exosomes can contribute to interactions with immune effectors, heralding the promise of new vaccination strategies and insight into mechanisms of immunosuppression. However, our results suggest that despite exhibiting the antigen-presenting machinery of their parent cells, GBM-released exosomes were restricted in their capacity to directly prime or guide a T-cell response. Further investigation is imperative to understand what roles, if any, do GBM-released exosomes play in GBM pathogenesis, or whether they represent an artifact without physiological relevance.

844. Recurrence in Atypical Meningiomas: Analysis of Predictive Factors and the Role of Adjuvant Radiation Therapy

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Introduction: Predicting progression after atypical meningioma resection remains challenging without consensus regarding adjuvant radiation therapy (RT). This study examines predictors of progression and impact of RT.

Methods: Cox regression and Kaplan-Meier analysis of newly

diagnosed AM patients (excluding neurofibromatosis type 2) were performed to assess risk factors for progression and impact of external beam RT (EBRT) or stereotactic radiosurgery (SRS).

Results: 215 patients [1996-2012, median age 55 (10-80), 41% male, median follow-up 48 months (range, 6-195)] were identified. Gross and subtotal resection (GTR and STR) were achieved in 151 (70%) and 64 (30%). 36% and 53% of patients had adjuvant RT (median EBRT dose 54 Gy, median SRS dose 17 Gy) after GTR (36 EBRT) and STR (25 EBRT, 9 SRS). After GTR, 13 patients (9%) had recurrence (median 47 months [range, 15-140]). After STR, 28 patients (44%) had progression (median 30 months [range, 7-137]). STR (HR=4.3, $p < 0.001$), higher mitotic index (HR=1.1, $p < 0.05$), and brain invasion (HR=2.9, $p < 0.01$) predicted progression in univariate and multivariate analyses. Non-convexity location predicted recurrence or progression in univariate analysis likely due to correlation with extent of resection (EOR). EBRT ($p = 0.03$) and SRS ($p = 0.03$) increased median time-to-progression following STR but not time-to-recurrence after GTR ($p = 0.8$). Necrosis decreased time-to-progression after STR and adjuvant EBRT/SRS ($p < 0.001$).

Conclusions: In the largest single-institution series of AMs undergoing first-time resection, EOR, mitotic index, and brain invasion independently predicted progression. EBRT or SRS improves progression-free survival after STR.

845. Extent of resection as a predictor of survival in a modern series of low-grade gliomas: a volumetric analysis

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Introduction: Current guidelines offer numerous options for treatment of low-grade gliomas including observation, surgical resection, and chemoradiation. Recent data suggest that maximal surgical resection at the time of diagnosis may lead to improved survival. To further investigate the role of surgery in this patient population, we conducted a volumetric analysis of outcomes in patients with intracranial low-grade gliomas.

Methods: Clinical data from adult patients with newly-diagnosed low-grade gliomas evaluated at Mayo Clinic, Rochester 1998-2011 were retrospectively reviewed. Pre-operative tumor volume, post-operative tumor volume, and extent of resection were calculated from magnetic resonance imaging. The Kaplan Meier method was used to calculate survival. Variables potentially associated with survival were assessed via univariate and multivariate analysis.

Results: 193 patients were included. Median follow-up was 73 months. Peri-operative neurological complication rate was 8%. OS was significantly associated with extent of resection (HR, 0.98; 95% CI, 0.97-0.99; P5- and 10-year OS was greatest in patients

with 90-100% resection (98%, 89%) compared to 70-89% (83%, 56%) and 0-69% (68%, 36%) ($P < .001$).

Conclusions: Greater extent of resection as a continuous variable is associated with improved survival in adult low-grade gliomas. For every 1% increase in tumor resection, there was a 2% decreased risk of death.

846. Characterization of brain tumor mutations from cell-free DNA in cerebrospinal fluid

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Introduction: The molecular diagnosis of brain tumors remains a challenging task, but has clear implications for patient treatment and outcomes. Brain biopsy carries a corresponding significant risk of morbidity. We hypothesized that cell-free DNA in cerebrospinal fluid (CSF) may provide a window to characterize the somatic mutations of brain tumor in a less invasive way.

Methods: As little study has been done related to the cell-free DNA in the CSF, we first set out to characterize its landscape. Using digital PCR and qPCR, we quantified the amount of cell-free DNA, which varies from 100 – 10000 genomic copies per milliliter of CSF. According to whole genome sequencing and microfluidic gel electrophoresis analysis, the average size of the cell-free DNA in CSF is around 300bp. To prove that brain tumor DNA could be detected in CSF, we sequenced the CSF, serum, and tissue of a patient with a metastatic melanoma. CSF distal from the resection cavity was collected through an external ventricular drain.

Results: We identified the somatic mutations by applying Exome sequencing analysis on the matched brain tumor tissue and normal tissue (blood cells) samples. Ten of the identified point mutations in tumor were detected in CSF using Tagged Amplicon Deep Sequencing. 5 of these tumor mutations were detectable in CSF, with the allele frequency ranging from 0.03% to 4%.

Conclusions: This result shows the great potential of using the tumor's cell-free DNA in CSF for diagnosis and to monitor disease progression or response to treatment. This technique holds promise for directed cancer therapy, and monitoring for recurrence.

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