Oral Presentations

2020 AANS Annual Scientific Meeting

Boston, Massachusetts • April 25–29, 2020

(DOI: 10.3171/2020.4.JNS.AANS2020abstracts)

Disclaimer: *The Journal of Neurosurgery Publishing Group (JNSPG) acknowledges that the preceding abstracts are published as submitted and did not go through JNSPG's peer-review or editing process.*

100: Gum Chewing to Expedite Return of Bowel Function after Anterior Lumbar Surgery

Alexandra Richards, DNP (Phoenix, AZ); JoDee Winter, PA-C; Naresh Patel, MD; Matthew Neal, MD; Chandan Krishna, MD; Pelagia Kouloumberis; Maziyar Kalani, MD

Introduction: Anterior lumbar interbody fusion (ALIF) is used to treat lumbar spondylosis and spondylolisthesis. The operation involves an anterior, retroperitoneal approach to the spine. Patients frequently experience a slow return of bowel function secondary to anesthetic time, opioid use, and primarily due to the bowel displacement intraoperatively; however, this operation is amenable to outpatient surgery. Gum chewing decreases the time for return to bowel function (RBF) in postoperative colorectal and gynecology patients. Despite this data, the association between gum chewing and RBF has only been studied in posterior spine patients.

Methods: Preoperative patients needing one or two level ALIF were recruited at a single institution. Patients were selected based on inclusion criteria and randomized by a random number generator; a blinded research assistant assisted with randomization. The experimental group (gum-chewing) and control group (hospital standard management) were compared with the endpoints of length of stay, length to return of bowel function via the passing of flatus and passing of stool. Medical care was standardized with regard to pain control, diet, ambulation, and deep venous thrombus prophylactic and perioperative antibiotic prophylaxis. The experimental group received standard hospital management but were told chew gum for 30 minutes every two hours during waking hours. At the 24-hour mark, participants are examined for bowel sounds and completed a survey regarding flatus, distention, comfort level, and pain. At two-week follow-up visit, all participants completed the same survey.

Results: Results revealed that gum-chewing promotes return to bowel function sooner than observation alone. It also decreases patient pain scores and discomfort. Patients randomized to gum-chewing discharged home sooner with fewer gastrointestinal complications.

Conclusion: Gum-chewing after ALIF may aid in discharging patients the same day of surgery with a decreased risk of complications related to bowel function.

102: Intra-wound Liposomal Bupivacaine in Pediatric Chiari Decompression

Melissa Ann LoPresti, MD (Houston, TX); Nathan Harrell; Eric Goethe, MD; Samuel McClugage, III, MD; Karla Wyatt, MD; Sandi Lam, MD, MBA

Introduction: Intra-wound liposomal bupivacaine is a long-acting local anesthetic used to decrease postoperative pain in a variety of procedures. While it is used in posterior cervical and suboccipital approaches in the adult population, it is currently off-label for pediatrics. In this study we examine intra-wound liposomal bupivacaine for pediatric Chiari decompression and evaluate its role in postoperative opioid consumption.

Methods: A retrospective analysis was performed on all patients aged 0-18 years-old who underwent Chiari decompression from January 2017 to July 2019 at our tertiary care hospital. Demographic as well as clinical data regarding postoperative opioid use, subjective and objective pain control, length of stay, discharge medications, and comorbid conditions were collected.

Results: Forty-three patients were included in this study: 28 females and 15 males. Of these patients, six received local injection of liposomal bupivacaine. Patients treated with liposomal bupivacaine were found to require less opioids in hospital (83.3% vs. 29.7% $p < 0.04$). There was no difference in pain control immediately postoperatively, pain control at clinical follow-up, or inpatient length of stay between each group. Patients who received liposomal bupivacaine did not require opioid analgesics at time of discharge from hospital.

Conclusion: The use of intra-wound liposomal bupivacaine can decrease inpatient and outpatient postoperative opioid consumption amongst pediatric patients following Chiari decompression, while providing adequate pain control. We highlight liposomal bupivacaine perioperative blockade as a viable option for opioid-sparing pain control in the postoperative setting for the pediatric population.

103: Variability in Reversal of Anti-Coagulation in Patients With Mild TBI

Christopher J Whiting (Falmouth, ME); Bruce Chung, MD; Jesse Ritch, PA; Anand Rughani, MD

Introduction: With the recent introduction of novel oral anticoagulants (NOACs) and some evolution of reversal agents, the authors have hypothesized that there has been increased variability in methods of reversal.

Methods: At a single 637-bed Level 1 trauma center, we queried the medical records of all patients admitted with a minor TBI (GCS 14-15) and positive head CT. We limited the search to those taking any oral anticoagulant medication (warfarin, rivaroxaban, dabigatran and apixaban). We excluded those on an anti-platelet medication. Manual chart review was performed to document presenting INR, whether reversal was performed, reversal agent, post-reversal INR and stability on follow-up CT.

Results: We identified 66 anti-coagulated patients with mild TBI admitted from 2013-2018 under the care of 13 attending trauma surgeons and 10 consulting neurosurgeons. The indication for anti-coagulation was atrial fibrillation in 82% of patients. The most common medication used was warfarin in 65% of patients, with 35% taking a NOAC. Reversal of INR was performed in 50% of patients, and the method of reversal in 69% of cases was with prothrombin complex concentrate (PCC). While 60% of patients on warfarin were reversed, only 33% on a NOAC were reversed. The INR on presentation averaged 2.7 in those on warfarin, 1.7 on rivaroxaban, and 1.3 on apixaban. Average INR in those on coumadin, not reversed, was 1.8. Radiographic progression on CT was similar in those reversed versus not (17% vs 13%). Seven patients ultimately required neurosurgical intervention.

Conclusion: The emergence of NOACs in tandem with the use of warfarin has increased the complexity of management of anti-coagulation in patients with intracranial trauma. Notwithstanding the complexity of the indications for anti-coagulation and the severity of trauma, there appears to be high variability in acute management.

104: Social Media, a Powerful Platform in Neurosurgery

Leslie Schlachter, PA (New York, NY)

Introduction: The use of social media is a fast-growing and relevant platform to engage diverse participants in the global neurosurgical community. Physicians, APPs, medical students, patients and industry are all active users of neurosurgery-specific social media platforms. This represents a paradigm shift from prior generation's access to neurosurgery information. Unlike peer-reviewed medical journals, social media pages are unsupervised and not fact-checked. Social media influencers work to directly affect product sales, this method has quickly become a most effective means of information-gathering for millennials, our future doctors and patients.

Methods: In July 2017 we initiated a neurosurgery Instagram account @Brainyleslie representing an experienced Neurosurgery PA, Leslie Schlachter. The goal of @Brainyleslie was to raise awareness of neurosurgical medicine and physician assistant practices. On average, two posts and two Instagram stories are posted each week covering pathology pictures, videos, medical team images, patient stories, and personal tidbits of Leslie's life. @Brainyleslie has access to 3D virtual reality surgical representations to educate the social media community.

Results: @Brainyleslie has over 17,700 followers. Follower demographics: 90% ages of 18-34, 53% men, 47% women. Location: United States (32%), Brazil (7%), and India (6%). Engagement is tracked and ranked based on likes, comments, impressions, views, profile visits, shares and direct contact. The most well-liked posts show how our team works together, as well as patient interest stories. The most commented posts are when @Brainyleslie offers her thoughts on cases or pathologies. Followers are a good mix of members of the medical community, future members, patients and lay people seeking collaboration or medical information.

Conclusion: If consumers of neurosurgical clinicians are looking for information on social media, it is our obligation to provide an accurate representation of this complex field we have worked so hard to be a part of.

105: Intrathecal Baclofen Infusion Trials: Outcomes and Costs

Elizabeth C. Tyler-Kabara, MD, PhD, FAANS (Pittsburgh, PA); Kristen Stabingas, MD; Jenna Turnley, PA-C

Introduction: Intrathecal baclofen is utilized to treat patients with generalized spasticity and dystonia. Screening tests include bolus trials and multi-day infusions. Bolus trials may not predict long term outcomes particularly in patients with dystonia or other hyperkinetic movements. Preimplant trials have been increasingly mandated by insurance. At our institution, intrathecal hospital stays: placement of an intrathecal catheter and a second admission for a multiday infusion followed by placement of the pump. The purpose of this retrospective analysis is to determine if there is a need for intrathecal baclofen infusion trials, and to explore the safety, cost, and differences in outcome based on patient population.

Methods: We identified all patients undergoing intrathecal baclofen infusion trials or new baclofen pump placement between January 1, 2008 and December 31, 2017. Patient demographics, type of movement disorder, complications, reason for trials and cost were determined.

Results: 95 patients underwent either new pump placement or infusion trial. Seventy-one patients did not require a trial. Of the 24 patients who had an infusion trial, 23 patients underwent pump placement. Eleven of these patients underwent trials for insurance purposes, all of which went on to have a pump implanted. All of these patients had generalized spasticity and dystonia. All remaining patients underwent a trial as part of our multidisciplinary team's recommendations. Of the 24 patients who underwent trials, 5 reported complication during their immediate postoperative admission. One patient developed infection of the intrathecal catheter prior to baclofen pump placement. A single patient's port was unable to be accessed. The average total hospital cost for patient who required a trial followed by implantation was \$45,242.66, compared to \$22,385 for new pump.

Conclusion: Intrathecal baclofen infusion trials are safe. However, in patients with a disease processes known to respond well to intrathecal baclofen, an infusion trial is an unnecessary step that carries an increased cost and delay in treatment.

106: An Atlas of Multifunctional Cortical Networks for Language

Kiefer Forseth, BS (Houston, TX); Nora Maerean; Patrick Rollo, BA; Nitin Tandon, MD

Introduction: Language comprises manifold processes that arise from a shared cortical architecture. The operant modulation of these conserved networks for distinct linguistic functions is central to understanding the neurobiology of language. To resolve the functional architecture of such networks and evaluate their changing behavior, we used large-scale electrocorticography of two essential and categorically dissociated tasks — visually-cued noun and verb naming — to generate the first complete atlas of multifunctional cortical dynamics in humans.

Methods: Intracranial electrodes (n=27074, 151 patients) implanted for the evaluation of epilepsy, including both surface grid and penetrating stereotactic depth electrodes, yielded complete cortical coverage. Surface-based mixed-effects multilevel analysis of broadband gamma activity with narrow overlapping time windows produced a time-varying map of relative cortical engagement in noun and verb naming. The state dynamics and inter-regional connectivity were subsequently captured by an autoregressive hidden Markov model (ARHMM) that integrated network activity across patients and tasks.

Results: We identified a parallel sequence of network state dynamics in noun and verb naming involving a conserved set of distributed neural substrates spanning the language dominant hemisphere. Both tasks evoked a convergent network state for visual recognition immediately following picture presentation. The cortical response subsequently diverged — while the same architecture was engaged, the intranodal connections were unique. Concurrent with articulation, these distinct streams fused in network states corresponding to production and self-monitoring. With this analysis, we identify underappreciated roles in language production for middle fusiform gyrus, supplementary motor area, dorsomedial prefrontal cortex, and posterior middle temporal gyrus.

Conclusion: This work characterizes the divergent behavior of conserved cortical language networks, forming the foundation of closed-loop multi-site stimulation designs for the modulation of evoked behavior. In addition to answering long-standing questions regarding the neurobiology of language, we present a powerful analytic framework that may be used in the future to study generalized human cognition.

107: A Functional Circuit for Executive Control

David Bonda, MD (Port Washington, NY); Michael Wulf; Adam Kepecs, PhD

Introduction: The ability to overcome reflexive or instinctive behavior requires executive control. Dysfunctions in such cognitive suppression characterize numerous neuropsychiatric disorders, for which targeted therapies remain elusive. Current evidence implicates the prefrontal cortex as a core region in overcoming reflexive behavior, many of which are orchestrated by midbrain nuclei. To gain further insight into such top-down control, we mapped the connectivity between the prefrontal cortex and the midbrain, developed a novel rodent assay modeling the suppression of instinctive drive, and performed in vivo neural recordings in mice engaged in this task.

Methods: We utilized retrograde viral and chemical tracing methods, in combination with confocal microscopy, to delineate anatomic projections from medial prefrontal cortex (mPFC) to midbrain nuclei. We then developed a behavioral assay that puts into conflict the pursuit of reward and reflexive escape. Specifically, mice trained to gather a reward were intermittently exposed to varying intensities of an innately threatening auditory stimulus. To record from the mPFC-midbrain circuit in these mice, we performed targeted cell type- and projection-specific intraparenchymal calcium imaging during the stimulus/reward conflict.

Results: Tracing studies revealed a long-range circuit in which glutamatergic neurons from the mPFC synapse onto interneurons in the midbrain regions known to orchestrate escape. Neurons in the latter were also found to be modulated by inhibitory projections from thalamic areas that encode contextual fear information and working memory. Interestingly, calcium recordings from the mPFC revealed markedly increased activity when mice withheld their escape response in pursuit of reward.

Conclusion: Cognitive control over instinctive behavior enables flexibility in the face of uncertainty. We combined neuroanatomic tracing, rodent psychophysics, and cellular-resolution optical imaging to identify a novel prefrontal-midbrain executive control circuit. Ongoing experiments will enable causal interrogation of this circuit via optogenetic activation and inhibition. As many psychiatric disorders involve deficits in executive control, insight into its precise neurophysiology will be crucial to the development of targeted therapies.

108: A Biomechanical Paradigm of Carotid Plaque Disruption Based On Histopathological Analysis, High Definition Imaging With Next-Generation Platforms, Computational Flow Dynamics and Mechanical Testing Of Atheromas

Luis E. Savastano, MD (Cambridge, MA); Hossein Mousavi, MD; Siri Khalsa, MD; Evan Davis, MS; Yihao Zhang, PhD; Yang Liu, PhD; Adithya Reddy, MSc; Joshua Cockrum, MSc; Aditya Pandey, MD; B Thompson, MD; David Gordon, MD; Howard Yonas, MD

Introduction: Although strokes due to carotid artery disease (CAD) are typically thromboembolic, clinical management is guided by the degree of stenosis, largely because of limited understanding of the plaque disruption mechanism. This study provides a mechanistic paradigm of plaque degradation supported by morphological, hemodynamic and mechanical analyses.

Methods: 345 carotid endarterectomy specimens (CES) were serially sectioned for morphological analysis. All lesions were categorized and matched to preoperative symptomatology. Morphological patterns were analyzed in 25 intact CES with laser angioscopy and micro-CT. Hemodynamic conditions in each lesion type were analyzed by computational flow dynamics (CFD). Needle penetration in 5 CES and 5 uncomplicated cadaveric atheromas tested mechanical strength.

Results: Ulceration (fibrous cap disruption) was observed in 82% of plaques and 91% occurred upstream to the point of maximal stenosis (POMS). Intra-plaque hemorrhage (IPH) occurred in 68% of specimens and 93% in continuity to the upstream ulceration, with necrotic core (NC) exposed to ICA lumen in 62%. Intra-plaque false luminal formation was observed in 48%. In our cohort, patients had symptomatic CAD in 12% of plaques without ulceration, 43% of plaques with ulceration, 64% of plaques with ulceration and IPH, 88% of plaques with false lumens. In CFD, hemodynamic stress was the highest upstream to POMS, and upon ulceration the inflow stream excavates the NC cranially and then recirculates into the true lumen. In mechanical testing, NC offers minimal resistance to penetrating forces compared to fibrous cap and tunica media.

Conclusion: Carotid plaque disruption is a hemodynamically driven phenomenon triggered by fibrous cap ulceration proximal to POMS followed by penetration of blood into the NC. Under pro-occlusive conditions, IPH forms with plaque expansion and luminal thrombus extension resulting in arterial narrowing. Under pro-excavatory conditions, the necrotic core is chiseled with downstream embolization resulting in false luminal formation.

109: Development of Normal Pediatric Growth Curves for Cerebral Ventricular Volume

Noah Cutler (Ann Arbor, MI); Sudharsan Srinivasan; Siri Khalsa, MD; Bryan Aaron, BS; Michael Kang; Cormac Maher, MD

Introduction: Normal percentile growth charts for head circumference, length, and weight are well-established tools for clinicians to detect abnormal growth patterns. Currently, no standard chart exists describing normal growth for cerebral ventricular volume. Standard practice is to rely on clinical experience for a subjective assessment of cerebral ventricular size in order to diagnose hydrocephalus. A growth curve of normal ventricular volumes would facilitate a more data-driven diagnostic process. Previous work has described normal volumes on smaller cohorts. We sought to develop a growth curve of cerebral ventricular volumes using a large number of normal pediatric brain MRIs.

Methods: We performed a retrospective analysis of patients aged 0 to 18 years, who were evaluated at our institution between 2009-2019 with a brain MRI obtained for headaches, convulsions, or head injury. Patients were excluded for diagnoses of hydrocephalus, congenital brain malformations, intracranial hemorrhage, meningitis, or intracranial mass lesions established at any time during a 6-month to 10-year follow-up. The 3D volume of the cerebral ventricles for each T2-weighted MRI sequence was calculated with a semi-automated segmentation program written in MATLAB. Normal percentile curves were calculated using the Lambda-Mu-Sigma smoothing method.

Results: 3D ventricular volume was calculated for a total of 687 normal brain MRIs for 598 different patients. A chart with standardized growth curves was developed from this set of normal ventricular volumes representing the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles. The charted data was binned by age at scan date by 3-month intervals for ages 0-1 year, 6-month intervals for ages 1-3 years, and 12-month intervals for ages 3-18 years.

Conclusion: We developed a centile estimation growth chart of normal 3D ventricular volumes measured on brain MRI for pediatric patients. This chart may serve as a quantitative clinical reference to help discern normal variance from pathologic ventriculomegaly.

110: Spinal Cord Injury in the United States Army Special Forces

Remi A. Kessler (New York, NY); Raj Shrivastava, MD; Ansh Bhammar, BS; Jonathan Rasouli, MD; Joshua Bederson, MD; Deborah Benzil, MD; Constantinos Hadjipanayis, MD, PhD

Introduction: Spinal cord injury (SCI) is high priority in military medicine, as reports indicate SCI occurred in >11% of wounded soldiers in the Iraq/Afghanistan Wars and that it may be present in 38% of all war-related casualties. Despite the fact that the US Army Special Forces (SF) soldiers, known as Green Berets, constitute 60% of all Special Operations casualties, the demographics and ramifications of SCI specifically among SF have never been investigated. The objective of this study was to determine the incidence/etiologies of SCI affecting this population, given their highest-risk military operations globally and closest proximity to combat.

Methods: A 162-question study was formulated via collaboration of US board-certified neurosurgeons, retired SF members, and operational staff of Green Beret Foundation (GBF). Data on military background, demographics, medical history, and exposures in training/deployment were collected. This study was disseminated to thousands of SF soldiers via the GBF's military network. Inclusion criteria mandated 18-Series qualification (SF-designation). Descriptive statistics were employed to present a composite of the incidence/etiologies of SCI.

Results: 529 participants met inclusion criteria. SCI diagnosis was reported by >18% of SF soldiers, of whom 84% were involved in combat operations and 51% are Military Free-Fall-qualified. 69% are currently receiving SCI disability benefits with a mean Veterans Administration (VA) disability rating of 82/100. Most common causes were Parachute Jump/Fast-roping/Airborne-Operations (61%). Over 88% were wearing headgear and only 36% were wearing body armor at time of injury. Only 21% of SF soldiers with SCI were Medevac'ed.

Conclusion: Our results demonstrate high incidence of SCI among US Army SF soldiers, with most receiving VA disability benefits and high disability ratings. Airborne operations landings were the leading cause. That a majority of SCIs occurred with headgear and no body armor may reflect inadequate shock absorption in protective equipment that is not optimized for airborne landings. Low rate of Medevac rescue may suggest that tertiary medical care was not attainable or that SCIs were deemed minor at time of injury.

111: Early versus Late Decompression: Does it Affect Neurological Outcome, Complications and Survival in Metastatic Spinal Cord Compression?

Nida Fatima, MBBS (Boston, MA); John Shin, MD

Introduction: Metastatic spinal cord compression (MSCC) is an oncological emergency, and requires expeditious treatment to prevent permanent neurological impairment. The ideal surgical timing in patients with MSCC is still debated, therefore, we aimed to discern the optimal timing of DS by determining its influence on clinical outcomes.

Methods: Patients undergoing DS for MSCC were extracted from prospectively maintained database at an academic tertiary care hospital (2011-2018). The Analysis of variance (ANOVA) and Kaplan Meier Estimate (KPM) using Log-rank Mantel Cox test was used to evaluate the association of DS with neurological outcome, complications and survival.

Results: With a median age of 67 years (range, 33-84 years), there were 75 male patients (63%) and 44 female patients (37%) in our cohort. Among 119 patients, 40 patients (33.6%) underwent DS within 24 hours (Group 1), 28 patients (23.5%) within 24-48 hours (Group 2), and 51 patients (42.9%) >48 hours (Group 3), from the onset of acute neurological deterioration. Greatest improvement in postoperative neurology was observed in patients under Group 1 [2 grades (n=16, 40.0%) and 3 grades (n=1, 2.5%)] compared to patients under Group 2 [2 grades (n=4, 14.3%)] and Group 3 [2 grades (n=5, 9.8%)], with statistically significant difference ($p=0.004$). The overall median survival was 345 days (95% CI: 91.77-658.2 days) in our cohort, with no statistically significant difference among the three groups ($p=0.15$). Thirty-two patients (26.8%) developed complications postoperatively, however, with no statistically significant difference among the groups ($p=0.99$).

Conclusion: Direct DS within 24 hours, improves the neurology, however the timing of DS does not influence the rate of complications and survival at 6-months.

112: MR-Guided Focused Ultrasound Thalamotomy of the Central Lateral Nucleus for Neuropathic Pain: Early Phase I Trial

Abdul-Kareem H. Ahmed, MD (Baltimore, MD); Jiachen Zhuo, PhD; Joel Greenspan, PhD; Timothy Miller, MD; Howard Eisenberg, MD; James Russell; Elias Melhem, MD; Rao Gullapalli; Dheeraj Gandhi, MD

Introduction: Neuropathic pain (NP) is a chronic pain syndrome resulting from damage to the central or peripheral somatosensory nervous system. For medically-refractory NP, the clinical utility of stereotactic central lateral nucleus thalamotomy (CL) has been demonstrated in afflicted patients. This early phase I trial aimed to determine the safety and efficacy of MR-guided focused ultrasound (MRgFUS) thalamotomy for NP in five patients.

Methods: Five patients were enrolled with medically-refractory NP, all with at least 6 months of symptoms and with an eligible skull density ratio (SDR0.40). Brief Pain Inventory (BPI) severity, interference, and disability index baseline scores were collected. Patients were treated with bilateral MRgFUS thalamotomy of the CL nucleus. Similar pain scores were collected at 3-months of follow-up.

Results: Four men and one woman were treated (mean age 53.611.0 years). No serious adverse events were noted, all mild adverse events resolved within two weeks. Four patients underwent bilateral CL thalamotomy with MRgFUS, one unilateral. The average SDR was 0.490.03 (range 0.45-0.53). Average treatment time was 135.430.7 minutes. At 3 months, mean reduction in pain severity was 44.4 percent ($p=0.025$), mean reduction in pain interference 58.5 percent ($p=0.003$), and mean reduction in pain disability 42.6 percent ($p=0.045$).

Conclusion: MRgFUS thalamotomy of the CL nucleus caused no serious adverse events. All participants experienced reduction in NP symptoms measured by validated pain scales. Long-term data is needed to assess durability of response.

113: De Novo Mutations in TRIM71 Cause a Novel Syndrome of Human Congenital Hydrocephalus with Consistent Clinical and Radiographic Findings

Adam Kundishora, MD (New Haven, CT); Andres Moreno de Luca, MD; Hannah Smith; Duy Phan, BA; Sheng Jin, PhD; Charuta Furey, MD; August Allocco, BA; Tyrone DeSpenza, BA; Xue Zeng; Richard Lifton; Kristopher Kahle

Introduction: Recently, next-generation whole exome sequencing (WES) has identified multiple genes as being associated with congenital hydrocephalus (CH), including TRIM71. In the wake of these discoveries, genotype-phenotype correlation within cohorts harboring the same mutation has yet to be undertaken. Herein, we describe the clinical-radiographic associations amongst a cohort of TRIM71 associated CH patients which seemingly defines a discrete syndrome.

Methods: WES was performed on 381 CH probands, including 232 parent-offspring trios. 1798 control trios comprising unaffected siblings from the Simons simplex autism cohort were analyzed in parallel. De novo variants were called using the Genome Analysis Toolkit Haplotype Caller. Full medical records and cranial imaging of probands with TRIM71 mutations were obtained. Imaging was independently reviewed for congenital malformations by two sources, one neurosurgeon and one neuroradiologist.

Results: TRIM71 De novo mutations were identified in 9 probands, including three p.R608H mutations, three p.R796H mutations, two p.R336Q mutations and one p.N701K mutations. Adequate records were obtained for 7 of 9 probands. Clinical traits shared across >50% of probands included developmental delay, epilepsy, and cranial nerve abnormalities. Hearing loss was present in 3 out of the 7. Adequate imaging was obtained for 6 of 9 probands. Independent review of radiographs yielded a >90% concordance of findings. 100% of probands displayed communicating forms of hydrocephalus with corpus callosum abnormalities and significant white matter volume loss. 5 of 6 probands displayed anterior commissure and forniceal abnormality as well as dehiscence or agenesis of the septum pellucidum. Other radiographic features shared amongst >50% of probands included cerebellar tonsillar ectopia qualifying as Chiari I malformation, interhemispheric cyst, and anterior/posterior cingulate abnormalities.

Conclusion: TRIM71 associated CH is a unique form of hydrocephalus with a distinct set of clinical and radiographic features. These findings underscore the importance of genetic testing for all congenital hydrocephalus patients.

114: Intraventricular Delivery and CRISPR-Cas9 Disruption of PD-1 is required for CAR T-cell Efficacy in Glioblastoma

Bryan Choi, MD (Boston, MA); Xiaoling Yu; Anna Castano; Amanda Bouffard; Matthew Frigault; Andrea Schmidts; William Curry; Bob Carter; Marcela Maus

Introduction: Signaling through programmed cell death ligand 1 (PD-L1) has been implicated as a central mechanism of glioma-mediated immune suppression. In our recent trial of EGFRvIII CAR T cells in patients with GBM, we observed intense upregulation of PD-L1 in post-infusion tumor samples, resulting in eventual T-cell dysfunction and disease progression. Moreover, several logistical challenges regarding clinical translation of CAR T cells for glioma remain. Autologous CAR T-cell manufacturing, is both costly and time consuming, and the development of "off-the-shelf," allogeneic CAR T cells could have meaningful benefit. Lastly, with regard to route-of-administration, the advantages of loco-regional administration of glioma-targeted CAR T cells remain unclear.

Methods: Using CRISPR-Cas9 gene-editing, we created universal CAR T cells resistant to PD-1 inhibition through multiplexed gene disruption of endogenous T-cell receptor (TRAC), beta-2 microglobulin (B2M) and PD-1 (PDCD1). Triple gene-edited CAR T cells were tested for efficacy against human glioma cell lines in vitro and in murine models of orthotopic, human GBM. Following tumor engraftment, CAR T cells were administered via either intravenous or intracranial infusion.

Results: EGFRvIII CAR T cells were triple-edited at high efficiency rates (>80%). PD-1 disruption led to enhanced CAR T-cell efficacy against PD-L1-expressing glioma. Prolonged survival in mice bearing intracranial tumors was achieved after intraventricular, but not intravenous administration ($p < 0.001$).

Conclusion: CRISPR-Cas9 gene-editing can be used to generate universal, EGFRvIII-targeted CAR T cells resistant to PD-L1 checkpoint inhibition. This strategy warrants further investigation in patients with GBM. These findings contribute to mounting data suggesting that route-of-administration may play a critical role in achieving optimal CAR T-cell activity against tumors in the brain.

115: A Multidisciplinary Spine Clinic Model Significantly Reduces Lead Times for Appropriate Specialist Visit and Appropriate Intervention

Michael Longo (Bronx, NY); Yaroslav Gelfand, MD; Joshua Benton, BA; Andrew Gitkind, MD; Reza Yassari; Vijay Yanamadala

Introduction: Streamlining the route to specialist consultation and/or intervention can mitigate healthcare costs and improve patient outcomes and satisfaction. We instituted a multidisciplinary spine clinic (MSC) with physicians from neurosurgery, orthopaedics, pain medicine, and physiatry, where patients are simultaneously seen by providers from all these specialties, as appropriate. We hypothesized that patients from an underserved population initially seen in the MSC would experience reduced lead times to specialist visits and appropriate interventions compared to similar patients seen in a traditional unidisciplinary neurosurgery clinic (UDC).

Methods: Records from 150 consecutive outpatients seen by a spine-specialized neurosurgeon either in the MSC or UDC from April 2018 — July 2018 were abstracted. Multiple linear regression was used to determine if utilization of a MSC led to shorter lead times from initial visit with a spine surgeon (IV) to pain specialist visit (SV) and/or intervention.

Results: The analytic sample consisted of 150 patients (n=49 UDC, n=101 MSC). Median time to SV and intervention in the UDC were 49 days (IQR 32-111) and 63 days (IQR 42-172). In the MSC, median time to SV was 20 days (IQR 0-38) and median time to intervention was 43 days (IQR 22-79). After controlling for differences between the two groups, multivariate analysis showed that the time to SV was reduced by 45 days (coef. -45.9, 95%-CI [-69.5,-22.2], $p<0.001$) and time to intervention was reduced by 60 days (coef. -55.0, 95%-CI [-94.1,-15.8], $p=0.007$) for patients seen in the MSC.

Conclusion: By centralizing providers in a MSC, outpatients with degenerative spinal conditions experienced shorter lead times to specialist consultation and intervention. As the direct and indirect costs of caring for spinal diseases balloon, implementation of MSCs can improve care coordination for patients.

116: Assessing the Predictive Value of Primary ImPACT Testing Following Head Injury

Nickolas Dreher (New York, NY); Theodore Hannah; Adam Li; Dhruv Shankar; Ryan Adams; Mark Lovell; Tanvir Choudhri

Introduction: Concussions are a major public health concern especially for high school and college student athletes. However, there are few prognostic metrics that can accurately quantify concussion severity in order to anticipate recovery time and symptom regression. The Immediate Post-Concussion Assessment and Cognitive Test (ImPACT) is a widely-used neurocognitive assessment that can diagnose and track recovery from concussions. This study assesses whether initial ImPACT scores, collected within 48 hours of the injury, can predict persistence of concussion at follow-up.

Methods: Results from 6,912 ImPACT tests were compiled from 2,161 unique student athletes, ages 12-22. We defined a novel metric, Severity Index (SI), which is a summation of the number of standard deviations from baseline at the 80% confidence interval for each of the five composite scores reported by ImPACT. Patients were binned into groups based on SI (0-4, 4-8, 8-12, 12-16, 16+) and the relationships between SI groups, composite scores, symptom profiles, and recovery time were characterized using one-way and two-way ANOVAs and Kaplan-Meier plots. A logistic regression assessed the value of SI for predicting concussion at follow-up.

Results: Patients with higher SI at diagnosis were more likely to still be concussed at their first follow-up ($F(4,2299)=70.90$; $p<0.0001$). Higher SI groups also displayed consistently slower recovery over a 42-day period and were more likely to report symptoms in all four symptom clusters (Migraines, Cognition, Sleep, and Neuropsychiatric). When controlling for sex, age, number of previous concussions, days between assessments, and location, SI significantly increased the odds of being concussed at follow-up (OR=1.122, 95% CI=1.088 — 1.142, $p<0.001$). This model showed good discrimination with AUC=0.74.

Conclusion: SI is a useful prognostic tool for assessing head injury severity. Concussions with higher initial SI tend to last longer and have broader symptomatic profiles. These findings can help patients and providers estimate recovery based on similar ImPACT score profiles.

117: Creation of a Novel Mouse Model of Sporadic Cerebral Arteriovenous Malformations

Keyan Peterson (Madison, NC); Zhidan Xiang, PhD; Anthony Anzalone, MS; Christine Tschoe, MD; Stacey Wolfe, MD

Introduction: Recent studies have found that sporadic cerebral arteriovenous malformations (AVMs) carry endothelial mutations in the Mitogen Activated Protein Kinase signaling pathway, notably in the KRAS and BRAF oncogenes, in up to 87% patients. Given this newly discovered mosaicism, an appropriate pre-clinical model is needed to assess the contribution of these mutations to the pathogenesis of cerebral AVMs and to test therapeutic targets.

Methods: To create a model of cerebral AVMs, a newly discovered AAV2 serotype labeled AAV2-BR1 was selected for its tropism for the brain endothelium. To confirm delivery of the vector and titrate the minimum dose required for optimal penetrance, AAV2-BR1-CAG-luc was packaged and injected retro-orbitally into 8-week-old male FVB mice, at low (2.5×10^{10}), medium (5.0×10^{10}), and high (7.5×10^{10}) doses at Day 0. At day 7, 14 and 21, IVIS bioluminescence recorded luciferase reporter activity.

Results: At day 7, 14, and 21 following AAV injection, IVIS revealed high-intensity luciferase reporter activity in the cranial region, even in the low and medium dose groups, with appropriate absence of signal in control animals.

Conclusion: A lower dose of AAV2-BR1 than previously reported (2.5×10^{10}) appears to be sufficient for delivery to the cerebral endothelium. Ongoing studies include injection of FVB mice with AAV2-BR1-CAG-KRASG12V, a virus harboring the most common MAPK pathway mutation recently discovered in human cerebral AVMs. Delivery of this mutation and the effect on angiogenesis and proliferation will be assayed using Western Blot, mRNA analysis, wet-mount IHC, and whole-brain latex perfusion. Future directions include testing existing BRAF inhibitors, currently used as well-tolerated chemotherapeutic agents, with and without radiosurgery to hasten time to AVM obliteration.

118: Evaluating Surgical Resection Extent and Adjuvant Therapy in the Management of Gliosarcoma

Elisa Liu (New York, NY); Michael Jin, BS; Siyu Shi, BS; Iris Gibbs, MD; Reena Thomas, MD; Lawrence Recht, MD; Scott Soltys, MD; Erqi Pollom, MD, MS; Steven Chang, MD; Melanie Hayden Gephart, MD, MAS; Seema Nappal, MD; Gordon Li, MD

Introduction: Gliosarcomas are aggressive, biphasic tumors with glial and sarcomatous components histologically distinct from glioblastoma. However, the impact of resection extent and post-operative therapy on gliosarcoma outcomes is not well understood.

Methods: Patients with histologically-confirmed gliosarcoma diagnosed between 1999 and 2019 were identified. Clinical, molecular, and radiographic data were assembled based on historical records. Comparisons of categorical variables used Pearson's Chi-square and Fisher's exact test while continuous values were compared using the Wilcoxon signed-rank test. Survival comparisons were assessed using Kaplan-Meier statistics and Cox regressions.

Results: Seventy-one gliosarcoma patients were identified. Secondary gliosarcoma was not associated with worse survival when compared to recurrent primary gliosarcoma when landmarked at time of transformation and recurrence, respectively (median survival 9.8 months vs 7.6, $p = 0.7493$). On multivariable analysis, receipt of temozolomide (HR = 0.02, 95% CI 0.001 to 0.21) and achievement of gross total resection (GTR; aHR = 0.13, 95% CI 0.02 to 0.77) were independently prognostic for improved progression-free survival (PFS) while only receipt of temozolomide was independently associated with extended overall survival (OS) (HR = 0.03, 95% CI 0.001 to 0.89). In patients receiving surgical resection followed by radiotherapy and concomitant and adjuvant temozolomide, achievement of GTR was significantly associated with improved PFS (median 32.97 months vs 5.45, $p = 0.0092$) and OS (median 56.73 months vs 14.83, $p = 0.0252$). During the course of treatment, 45.7% of patients reported treatment-related adverse effects.

Conclusion: Multimodal therapy is associated with improved survival in gliosarcoma. Even in patients receiving aggressive post-operative multimodal management, total surgical removal of macroscopic disease remains important for optimal outcomes.

119: Medical Malpractice Following Traumatic Brain Injury*Adam Khan, MD (Minneapolis, MN); Uzma Samadani*

Introduction: There has been a large uptick in the number of public health laws addressing concussion management by healthcare providers, with all fifty states in the United States of America enacting one or more traumatic brain injury (TBI) laws over the past decade. Litigation concerns have been cited in multiple surveys as a factor in deriving medical decision-making. This study aims to characterize the cases and unique circumstances in which patients suffering from TBI proceeded with litigation alleging medical malpractice.

Methods: The Westlaw online legal database (Thomson Reuters, New York, NY) and LexisNexis database (LexisNexis, New York, NY) were searched for jury verdict and settlement reports pertaining to TBI from 1980 to 2018. Data was collected regarding patient age and gender, outcome, award, alleged cause of malpractice and factors involved in the plaintiff's decision to file. Initial search queried 614 cases, after which exclusion criteria were applied to eliminate duplicates, cases that failed as a matter of law, and cases involving non-physicians, yielding twenty-seven cases for analysis.

Results: Of the twenty-seven cases reviewed, twenty-two involved the initial diagnosis of concussion. The verdict was in favor of the defendant in ten cases out of twenty (50%). The average jury verdict award for the plaintiff was \$4,515,712.36 (ten cases, adjusted for inflation). A smaller number of cases (6) involved post-concussion management.

Conclusion: A factual understanding of previous litigation history is of substantial interest to those in the medical community concerned about a medical malpractice suit. A strict adherence to observation guidelines was a strong common factor in cases where defendants won the verdict. A strong commitment to guidelines and documentation may help reduce concerns over increased healthcare costs and excessive medical decision-making costs in this vulnerable patient population.

120: Medicare Reimbursement of Implantable Spinal Cord Stimulators from 2000-2019*Kent Richter (Mesa, AZ); Jack Haglin, BS; Jordan Pollock, BS; Naresh Patel, MD*

Introduction: Chronic back pain is one of the most common ailments of individuals within the United States. There are a variety of procedures and devices designed to improve back pain depending on the etiology of the pathologic process. One such device is the implantable spinal cord stimulator. Currently, there is no literature evaluating procedural reimbursement for implantation of spinal cord stimulators. The purpose of this study is to evaluate monetary trends in Medicare reimbursement for implantable spinal cord stimulators between 2000 and 2019.

Methods: CPT reimbursement codes 63650, 63655, 63680 for spinal cord stimulation were identified using Reimbursement Services. Subsequently, reimbursement of these CPT codes was identified using the Physician Fee Schedule Look-Up Tool from the Centers for Medicare & Medicaid Services. The raw percent change in Medicare reimbursement rate from 2000 and 2019 was calculated for each procedure and averaged. This was then compared to the percent change in consumer price index over the same time. Using data adjusted for inflation, trend analysis was performed for all included procedures.

Results: After adjusting all reimbursement data for inflation, the average reimbursement for included procedures decreased by an average of -36.71% between 2000 and 2019. Code 63650 (percutaneous implantation of neurostimulator electrode array) decreased by -35.99%. Code 63655 (Laminectomy for implantation of neurostimulator electrodes, plate/paddle) decreased by -24.87%. Code 63685 (Insertion or replacement of spinal neurostimulator pulse generator or receiver, direct or inductive coupling) decreased by -49.27%.

Conclusion: This is the first study to evaluate trends in procedural Medicare reimbursement for Implantable Spine Stimulation devices. When adjusted for inflation, Medicare reimbursement for included procedures has decreased significantly from 2000 to 2019. Increased awareness and consideration of these trends will be important as hospitals and physicians continue to provide palliative care for patients who suffer from chronic back pain.

121: Socioeconomics and Insurance Type Affect Opioid Consumption Due To Lumbar Degenerative Disease and Lumbar Spinal Fusion

Corey Walker, MD (Phoenix, AZ); Corey Walker, MD; Christopher Louie, BS; Arpan Patel, MD; Santiago Angel, BS; Juan Giraldo, BS; Alexander Whiting, MD; Juan Uribe, MD; Jay Turner, MD, PhD

Introduction: Opioid prescription remains a change in the pre- and post-operative setting for patients with lumbar degenerative disease. It remains unclear how socioeconomic status and insurance type affect opioid usage in this area of neurosurgery.

Methods: A retrospective evaluation of consecutive patients receiving posterior open lumbar spinal fusion for degenerative etiologies between July 2017 and June 2018 at a single institution was performed. Pre-operative opioid intake was recorded using a state prescribing database. Peri-operative variables were recorded for all patients, including opioid consumption in the first 72 hours after surgery. Patient's zip codes were used as a proxy for determining their socioeconomic status by using median income data from the US Census Bureau.

Results: A total of 237 patients met inclusion criteria. 31 (13%) patients had Medicaid, 104 (44%) Medicare, 88 (37%) Private and 14 (6%) Veteran's insurance. Patients with Private insurance (mean age 58.8 yrs.) and Medicare (mean age 71.4 yrs.) lived in higher income zip codes (mean \$82,679 and \$79,664) compared to those with Medicaid (mean age 52.9 yrs.) and Veteran's (mean age 66.7 yrs.) insurances (mean \$51,892 and \$53,909, $p < 0.01$). Similarly, patient's with Private insurance and Medicare compared to Medicaid and Veteran's had lower pre-operative opioid intake (27 and 25 vs 46 and 50 MME daily, $p < 0.05$) and 72-hr post-operative opioid consumption (109 and 89 vs 134 and 151 MME, $p < 0.05$). There was no difference in operative duration, number of levels fused or length of stay between groups (all $p > 0.05$).

Conclusion: Socioeconomics and insurance type impact patient's opioid consumption in the setting of lumbar degenerative disease and spinal fusion surgery. Patients with Private insurance and Medicare tend to consume less opioids than patients with Medicaid and Veteran's plans.

122: First Flight of Neurosurgery: Report of a Decompressive Craniectomy in 1908

Nirali Patel, MD (Washington, DC); Nirali Patel, MD; Kelsi Chesney, MD; Joseph Watson, MD

The first person to suffer death from a mechanical flight first endured a neurosurgical attempt to save his life at a field hospital in Northern Virginia. With this report, we describe the decompressive craniectomy performed on Lieutenant Thomas E. Selfridge. He gained the unfortunate distinction of being both the first to die in a motorized plane crash and the first military airplane fatality. Lieut. Selfridge was the lone passenger in an experimental flight with Orville Wright on September 17, 1908 when the aircraft's propeller split and the plane crashed. Selfridge was found unconscious with a head laceration and rushed to a nearby field hospital at Northern Virginia's Fort Myer military base, where the flight demonstration was taking place. Orville Wright was badly injured, but recovered. Selfridge apparently struck the suspension wires and frame of the plane with his head on impact and was unconscious at the scene and groaning. He appeared to have a compound fracture of the left frontal skull base and was immediately taken to surgery by several physicians who were in attendance, Majors Crosby, Ireland, and McCaw and a Dr. Watters of New York City. At the time of surgery, Selfridge was convulsing. The surgery, performed primarily by Major Crosby, took 40 minutes. It involved a 6 inch incision in the left frontal region and a frontal craniectomy and evacuation of hemorrhage. Lieutenant Selfridge died some five minutes after the conclusion of surgery. This is the first report of the neurosurgical aspects of this historically morbid event and provides some insight into the surgical specialty in its infancy striking some parallels to the primitive and developing specialty of motorized air travel. It was also thereafter that pilots wore head gear for protection.

200: Complications of femoral vs. radial access in neuroendovascular procedures with propensity adjustment**Cerebrovascular Section Best Clinical Scientific Paper Abstract Award**

Joshua Catapano, MD (Phoenix, AZ); Vance Fredrickson, MD; Tatsuhiro Fujii, MD; Tyler Cole, MD; Jacob Baranoski, MD; Daniel Cavalcanti, MD; Andrew Wilkinson, MD; Neil Majmundar, MD; Michael Lang, MD; Michael Lawton, MD; Andrew Ducruet, MD; Felipe Albuquerque, MD

Introduction: The transradial artery (TRA) approach for neuroendovascular procedures continues to gain popularity, but neurointerventionalists still lag behind interventional cardiologists in the adoption of a TRA-first approach. This study compares the complications and efficiency of the TRA to the standard transfemoral artery (TFA) approach at our institution during our initial phase of adopting a TRA-first approach.

Methods: A retrospective analysis was performed on all consecutive neuroangiographic procedures performed at a large cerebrovascular center from October 1, 2018 to June 30, 2019. The standard TFA approach was compared to TRA access, with the primary outcome of complications analyzed via a propensity adjusted analysis.

Results: A total of 1,050 consecutive procedures were performed on 877 patients during this 9-month period; 206 (20%) procedures were performed via TRA and 844 (80%) via TFA. The overall complication rate was significantly higher in the TFA versus the TRA procedures (7% [60/844] vs. 2% [4/206], respectively; $P=0.003$). A propensity adjusted analysis showed that the TFA approach was a significant risk factor for a complication (OR 3.6, 95% CI 1.3 — 10.2, $P=0.01$). However, the propensity analysis showed that fluoroscopy times were on average 4 minutes less in TFA relative to TRA procedures ($P=0.003$).

Conclusion: The TRA approach for neuroendovascular procedures appears to be safer than the TFA approach. Although a steep learning curve is initially encountered when adopting the TRA approach, the transition to a TRA-first practice can be performed safely for neurointerventional procedures and may reduce complications.

201: Exosomes Derived from Human Neural Stem Cell Improve Recovery in a Cynomolgus Monkey Model of Ischemic Stroke**Best International Abstract Award**

Lukui Chen, MD, PhD (Nanjing, China)

Introduction: Recent work from our group suggested that human neural stem cell (hNSC) — derived exosomes treatment improves both tissue and sensorimotor function in a MCAO rat model of stroke. In this study, hNSC exosomes were evaluated in a Cynomolgus monkey ischemic stroke model, where clinically relevant end points were used to assess recovery in a more translational primate model.

Methods: Ischemic stroke was induced by permanent middle cerebral artery occlusion (MCAO), and either hNSC exosomes or PBS treatment was administered intravenously at 6, 12 and 24 hours post-MCAO. hNSC exosomes effects on tissue level recovery were evaluated via magnetic resonance imaging at 1, 3, 7, 14, 21 and 28 days post-MCAO. Effects on functional recovery were also assessed through the modified KITO non-human primate neurological deficit scale and the PrimateScan behavior analysis system.

Results: hNSC exosomes treatment was neuroprotective and led to significant improvements at the tissue and functional levels in stroked monkeys. hNSC exosomes — treated monkeys exhibited a significant decrease in cerebral lesion volume and brain swelling relative to control monkeys 7-day post-MCAO. hNSC exosomes significantly reduced edema in treated monkeys relative to control monkeys, as assessed by improved diffusivity through apparent diffusion coefficient maps. hNSC exosomes preserved white matter integrity with increased corpus callosum fractional anisotropy values 28 days post-MCAO. Behavior and mobility improvements paralleled structural changes as hNSC exosomes — treated monkeys exhibited improved outcomes, including increased exploratory behavior and faster restoration of spatiotemporal gait parameters.

Conclusion: This study demonstrated for the first time that in a more translational primate model, novel hNSC exosomes significantly improved neural tissue preservation and functional levels post-MCAO, suggesting hNSC exosomes may be a paradigm changing stroke therapeutic.

202: Early Detection of Medulloblastoma Relapse by Genomic Profiling of CSF-Derived Circulating Tumor DNA**James T. Rutka Pediatric Brain Tumor Award***Rahul Kumar (Memphis, TN); Anthony Liu; Kyle Smith; Leena Paul; Amar Gajjar; Giles Robinson; Paul Northcott*

Introduction: Medulloblastoma progression or recurrence occurs in 30% of patients and confers dismal prognosis. Despite incremental advances in multi-modal management and identification of relevant molecular subgroups, suboptimal outcomes in MB is partly due to the lack of sensitive biomarkers for relapse detection and response-adapted treatment personalization. Cell-free circulating tumor DNA (cf/ctDNA) has emerged as a robust platform for tumor detection and characterization through liquid biopsy of the cerebrospinal fluid (CSF).

Methods: CSF from MB patients was collected by lumbar puncture prior to therapy, during therapy, and at 3-month interval follow-up as part of institutional clinical trials. cfDNA was isolated and quantified for yield and fragment size from approximately 1 mL of frozen CSF. After construction of next-generation sequencing libraries, low-pass whole-genome sequencing enabled detection of genome-wide chromosomal and focal copy number alterations (CNAs). CNAs detected in cfDNA were compared against known somatic changes in corresponding tumor-tissue. Detectability of tumor-specific CNAs in cfDNA was then correlated with tumor burden, disease course, and patient outcome.

Results: In preliminary analysis, tumor-specific CNAs were identified in at least one post-resection timepoint in 22/23 (96%) relapsing patients. Of patients with CSF available at or 3 months prior to clinicoradiographic progression, tumor-specific CNAs were identifiable in 16/17 (94%). Presence of tumor-specific CNAs at the end of therapy alone predicted future relapse in 8/12 (67%). A subset of genomic alterations were divergent from tissue-derived primary tumor profiles, suggesting potential tumor evolution and oncogenic mechanisms underlying treatment failure and relapse.

Conclusion: The feasibility and applicability of CSF liquid biopsy for detection and characterization of tumor-derived cfDNA in MB patients is established. With continued expansion of the clinical cohort, we anticipate the broad applicability of CSF-derived cfDNA as an adjunct to clinicoradiographic surveillance while enabling response-adapted treatment.

203: Engineering T Cell Receptors to Target H3.3G34 Mutant Glioblastoma**Preuss Research Award***Anthony C. Wang, MD (Los Angeles, CA); Geoffrey Owens; Matthew Sun; Alexander Lee; Joey Orpilla; Erick Contreras; Janet Treger; Linda Liao; Robert Prins*

Introduction: The two main subtypes of pediatric glioblastoma (GBM) are marked by highly conserved somatic H3F3A gene mutations. H3.3G34 alterations appear to affect K36 residue methylation, which regulates alternative splicing events, including intron retention. We hypothesize that the H3.3G34R mutation in GBM results in tumor-specific neoantigens, derived from dysregulated alternative splicing, targetable by T cell receptor (TCR)-engineered cytotoxic T lymphocytes.

Methods: We created an H3.3G34R GBM PDX. Next-generation exome sequencing was performed on tumor and blood, and RNA-Seq was performed on tumor. Data were analyzed using IRIS, an algorithm that predicts neoantigens derived from alternative splicing variants. To identify and isolate the TCRs mediating HLA-specific binding of the peptides encompassing the H3.3G34R mutation predicted to bind with strong affinity, HLA-specific oligomeric class I MHC molecules were designed for high-value predicted peptides encompassing the H3.3G34R mutation.

Results: Two high-value splice variant-derived targets were identified. Clonal expansion of populations of antigen-specific T cells was observed with PBMC re-stimulation. These T cells demonstrated high binding affinity for the two neoantigen targets, and activation in response to H3.3G34R GBM cells in vitro. To test for TCR-specific peptide binding, we expanded naive donor CD3+ T cells in the presence of synthetic peptides encompassing candidates, and sorted for CD8+ populations. To validate these candidates, peptides were synthesized and used in an indirect HLA binding assay. Oligomeric MHC molecules were designed, and T cell binding was tested. Serial oligomer selection expanded the T cell population selectively binding the target. TCR sequencing was performed to synthesize and clone TCRab chains into a retroviral expression vector. Jurkat cells were transfected and tested for antigen-specific binding.

Conclusion: We identified two high-value candidate neoantigens confirmed to be present within H3.3G34R GBM. T cells expanded against these peptides demonstrated high binding affinity and activation in response to H3.3G34R GBM cells.

204: Distinct Regional Activity and Ontogeny of Tumor Associated Macrophages in Human Glioblastoma Suggests Parallel Recruitment Processes

American Brain Tumor Association Young Investigator Award

Zsolt Zador, MD, PhD (Manchester, United Kingdom); Alexander Landry; Michael Balas; Saira Ali, MD; Julian Spears

Introduction: Tumor-associated macrophages (TAMs) constitute upto 30% of tumor bulk in glioblastoma and play an important role in tumor maintenance and progression. TAMs may be recruited from circulating bone marrow derived monocytes (BMDM) and resident microglia. Microglia derived TAMs are more abundant in the tumor periphery (leading/infiltrative edge) while TAMs originating from BMDM mostly occupy the tumor bulk. In this pilot study we tested if such regional differences in the TAM ontogeny are due to distinct recruitment mechanisms, which becomes highly relevant to targeting immunomodulatory treatments.

Methods: We leveraged single cell gene expression data from 3 glioblastomas (total of 3100 cells). We inferred cell identity and ontogeny (BMDM vs microglia) based on verified expression signatures. TAM activity was represented as a function of cell maturity and degree on inflammation using the technique MacSpectrum. We considered TAM in pre-activation state (M0) to be newly recruited from either microglia or BMDM pool. We utilized the Ivy bulk gene expression database for external verification of our results.

Results: In keeping with previous studies, TAM's originating from BMDM were more abundant in tumor bulk (64%-85% of TAMs) while microglia derived TAMs dominated the tumor periphery (70%-100% of TAMs). In tumor periphery 84.4%-100% of TAMs in pre-activation state were derived from microglia. While tumor core had 77%-92% of pre-activation TAMs originating from BMDM. Differentially expressed genes of peripheral microglia M0 TAM enriched in lipopolysaccharide-mediated signaling pathway and neutrophil chemotaxis. TAMs originating from BMDM in tumor core annotated to cell adherence and glycolysis. Above TAM geographical pattern validated in the Ivy dataset based on top 30 differentially expressed genes.

Conclusion: Our preliminary analysis suggests nearly exclusive regional differences in TAMs origin with distinct recruitment mechanisms. Our research yields important insight and can inform targeting immunomodulatory mechanisms.

205: Sex-Associated Analysis of MGMT Promoter Site Methylation in Newly Diagnosed Glioblastoma

Journal of Neuro-Oncology Award

Addison Barnett, MS (Gates Mills, OH); Justin Lathia, PhD; Hong Li, MS; Gabrielle Yeane, MD; David Bosler, MD; Assad Ali, MS; Anas Saeed Bamashmos, MD; Manmeet Ahluwalia, MD

Introduction: GBM and MGMT have a sexual dimorphism wherein females have higher rates of MGMT methylation and improved methylation-associated overall survival (OS) compared to males. Here, we further characterize this relationship by comparing the degree of methylation at each of five cysteine-phosphate-guanine (CpG) MGMT promoter sites.

Methods: 304 adult patients with CpG data who underwent surgery for newly diagnosed GBM at a single tertiary care institution between 2015 and 2018 were reviewed. MGMT was defined as methylated if the mean of CpG 1-5 ≥ 12 . CpG methylation values were compared using a generalized linear model and Wilcoxon signed-rank test. OS by MGMT methylation status and sex were compared before and after propensity score matching for age, surgery type, and mean CpG methylation using a Kaplan-Meier method and Cox proportional hazard model.

Results: Overall (mean age 63.8, 34.2% female), 39.5% of patients were MGMT methylated and the median (IQR) of CpG mean methylation was 3.0% (2.0, 30.5). More females were MGMT methylated than males (50.0 vs 34.0%) and had greater mean CpG methylation than males (11.0 vs 3.0), $p < 0.002$. Females had increased methylation at each CpG site, with a significant difference at CPG 1, 2, and 4 ($p < 0.008$). Before PS matching ($n=304$), MGMT methylated versus un-methylated females had significantly increased median and 1-year survival (18.9 vs 9.5 months, 68.0 vs 35.9%, $p=0.0004$) compared to males (12.4 vs 11.0 months, 53.3 vs 45.3%, $p=0.27$), $p=0.03$. After PS matching ($n=76$ each), females maintained a significant survival benefit (18.7 vs 10.0 months, 78.4 vs 37.4%, $p=0.004$) compared to males (13.0 vs 13.6 months, 56.0 vs 56.7%, $p=0.76$), $p=0.048$.

Conclusion: Females had higher mean and individual CpG site methylation and conferred a significant OS benefit by MGMT methylation that was not seen in males even with equal degrees of CpG methylation.

206: The Safety and Feasibility of Brain Tumor Resection in the Outpatient Setting – A Pilot Study

Nikita Lakomkin (New York, NY); Blaine Stannard, BA; Constantinos Hadjipanayis, MD, PhD

Introduction: Ambulatory surgery centers (ASCs) have recently seen a substantial increase in neurosurgical volume, particularly in the areas of functional and spine. Outpatient surgery offers the advantages of significant cost savings and increased patient satisfaction. However, the safety and feasibility of brain tumor operations in this setting remains unexplored.

Methods: A large prospectively collected, multicenter surgical registry was employed to identify all patients undergoing craniotomy for resection of meningioma and low/high grade glioma. Patients with skull base tumors, including acoustic neuromas, were excluded. The Charlson Comorbidity Index (CCI) was computed for all patients in order to assess preoperative comorbidity burden. Additional demographics (age, BMI), smoking status, operative time, and postoperative complications were extracted for each patient. These included death, venous thromboembolism, sepsis, and stroke. Minor complications consisted of wound infections, dehiscence, and urinary tract infection. Chi-squared or Fisher's exact tests were employed to explore the differences between inpatient and outpatient cohorts. A binary, multivariable logistic regression was used to assess outpatient surgery as an independent risk factor for adverse events. ROC curve analysis was performed to identify the CCI score beyond which ASC patients experienced increased complications.

Results: A total of 3,671 patients were included, 148 (4%) of whom were operated on as outpatients. Brain tumor patients treated as outpatients had decreased rates of mortality (0.7% vs. 3.3%), major complications (1.2% vs. 16.6%), and minor complications (4.7% vs. 8.6%) when compared to inpatients. After controlling for comorbidities, smoking status, operative time, and age, outpatient surgery was not significantly associated with increased mortality (OR=0.83, 95%CI: 0.78-0.88, P=0.89) or adverse events (OR=0.49, 95%CI: 0.15-1.56, P=0.221). A CCI of 3 or greater was the ideal cutoff predictive of increased complications in the ASC group.

Conclusion: These preliminary data demonstrate that carefully selected brain tumor patients can safely undergo resection as outpatients. Patients with a CCI below 3 may be most suitable for outpatient treatment.

207: Navigated Repetitive Transcranial Magnetic Stimulation Improves the Outcome of Postsurgical Ischemia-related Paresis in Glioma Patients – A Randomized, Sham-controlled Double-blinded Trial**Brainlab Community Neurosurgery Award**

Sebastian Ille, MD (Munich, Germany); Anna Kelm, MD; Axel Schroeder; Lucia Albers, PhD; Chiara Negwer, MD; Vicki Butenschoen, MD; Nico Sollmann, MD; Thomas Picht, MD; Peter Vajkoczy, MD; Bernhard Meyer, MD; Sandro Krieg, MD

Introduction: Navigated repetitive transcranial magnetic stimulation (nrTMS) is effective therapy for stroke patients. Neurorehabilitation could be supported by low-frequency stimulation of the non-damaged hemisphere to reduce transcallosal inhibition. The present study examines the effect of postoperative nrTMS therapy of the unaffected hemisphere in glioma patients suffering from acute surgery-related paresis of the upper extremity (UE) due to subcortical ischemia.

Methods: We performed a randomized, sham-controlled, double-blinded trial on patients suffering from acute surgery-related paresis of the UE after glioma resection. Patients were randomly assigned to receive either low-frequency nrTMS (1 Hz, 15 minutes) or sham stimulation directly before physical therapy for 7 consecutive days. We performed primary and secondary outcome measures on day 1, on day 7, and at a 3-month follow-up (FU). The primary endpoint was the change in Fugl-Meyer Assessment (FMA) at FU.

Results: Compared to the sham stimulation, nrTMS significantly improved outcomes between day 1 and FU based on the FMA (mean [95% CI] +31.9 [22.6, 41.3] vs. +4.2 [-4.1, 12.5]; P=0.001) and the National Institutes of Health Stroke Scale (NIHSS) (-5.6 [-7.5, -3.6] vs. -2.4 [-3.6, -1.2]; P=0.02). To achieve a minimal clinically important difference of 10 points on the FMA scale, the number needed to treat is 2.19.

Conclusion: The present results show that patients suffering from acute surgery-related paresis of the UE due to subcortical ischemia after glioma resection significantly benefit from low-frequency nrTMS stimulation therapy of the unaffected hemisphere.

208: Circulating Serum MicroRNA for Monitoring in Glioma*Jordan J Jones (Melbourn, Australia); Andrew Morokoff; Kate Drummond*

Introduction: Although magnetic resonance imaging (MRI) gives good anatomic and spatial details about gliomas, it is not reliable at predicting their biological behaviour, cannot accurately differentiate between pseudo-progression and true progression, and is inconvenient and expensive. Repeated biopsies are not generally feasible and are subject to sampling error. A circulating biomarker has the potential to aid in these challenges and can be easily obtained by a blood test at multiple timepoints. Micro-RNA are small non-coding RNA fragments that show promise as biomarkers in cancer. We aimed to discover a longitudinal monitoring test for both low-grade-glioma (LGG) and glioblastoma (GBM), based on a serum miRNA biomarker using widescale profiling.

Methods: A prospectively collected cohort of 91 glioma patients underwent pre and post-operative serum miRNA profiling using a next generation sequencing platform (Nanosting®) and was compared to profiling of 17 healthy controls (HC). 11 patients with multiple follow up samples (3-11) underwent droplet digital PCR and was compared to blinded volumetric MRI assessment.

Results: Using a machine learning algorithm we identified a 9-gene miRNA signature that could distinguish between glioma and HC with 99.8% accuracy, 100% sensitivity and 97.8% specificity. From this signature two miRNA's, miR-223 for LGG and miR-320e for GBM demonstrated dynamic changes that correlated best with follow-up MRI appearances and were reduced following surgery suggesting a direct relationship to intracranial tumour load. Whilst, two GBM patients with MRI features of pseudo-progression showed no changes in miRNA expression.

Conclusion: We have identified a highly accurate 9-miRNA signature that can differentiate between HC and glioma patients. Additionally, we observed dynamic-changes in specific miRNAs correlating with tumor status over long term follow up in patients with both HGG and LGG. These results support a large prospective validation study of the serum miRNA biomarkers in glioma patients.

209: Useful Hearing Preservation Is Improved in Vestibular Schwannoma Patients Who Undergo Stereotactic Radiosurgery Before Further Hearing Deterioration Ensues**Leksell Radiosurgery Award***Akiyoshi Ogino (kawagoe-shi, Japan); Hideyuki Kano, MD, PhD; Hao Long, MD; Stephen Johnson, MD; Andrew Faramand, MD; Ajay Niranjani; John Flickinger, MD; L. Dade Lunsford, MD*

Introduction: The present study evaluates whether hearing deterioration during observation reduces serviceable hearing preservation rates after stereotactic radiosurgery (SRS) in vestibular schwannoma (VS) patients with normal hearing.

Methods: We retrospectively analyzed 1447 VS patients who underwent SRS at our center between 1992 to 2017. We identified 119 VS patients who had Grade I Gardner- Robertson (GR) hearing at initial diagnosis but were observed without surgery or SRS (median follow up 13.6 months). We compared hearing after SRS in 84 patients who had GR grade I at initial diagnosis (the hearing maintenance or HM group) to 35 patients whose hearing had worsened from GR grade I to grade II at the time of SRS (the hearing deterioration or HD group). Sex, Koos class, target volume, margin dose, maximum dose, and interval between initial diagnosis and SRS were not significantly different between these groups. Patients in HM group were significantly younger than patients in HD group ($p=0.036$).

Results: The overall serviceable HM hearing preservation rate was 87% at 1 year, 77% at 3 years, and 58% at 5 years. The overall serviceable HD hearing preservation rate was 67% at 1 year, 32% at 3 years, and 24% at 5 years. In univariate analysis, younger age (<55 years) and HM group improved serviceable hearing preservation rates (<55 years, $p<0.001$. HM group, $p<0.001$), and in multivariate analysis, younger age and HM group improved serviceable hearing preservation rates, too (<55 years, $p=0.003$, HR 2.36, 95% CI 1.34-4.16. HM group, $p<0.001$, HR 3.03, 95% CI 1.77-5.18). But sex, Koos class, target volume, margin dose, and maximum dose were not associated with serviceable hearing preservation rates.

Conclusion: SRS before hearing deterioration improved serviceable hearing preservation in VS patients with GR grade I at initial diagnosis. SRS before hearing deterioration ensues can optimize hearing preservation.

210: Differential Methylation Patterns Are Associated With Variable Vestibular Schwannoma Clinical Phenotypes**Columbia Softball Skull Base Award**

Avital Perry, MD (Rochester, MN); Christopher Graffeo, MD; Lucas Carlstrom; Amanda Munoz Casabella, MD; Colin Driscoll, MD; Michael Link, MD

Introduction: Vestibular schwannoma (VS) is a benign nerve sheath tumor, with an incompletely characterized genomic and epigenomic profile. Phenotypic behavior of VS is unpredictable: some rapidly growing while others are essentially indolent; similarly, following resection, some tumor remnants involute or remain stable over years, while others recur rapidly. VS genomic profiling has provided some preliminary insights into predicting tumor behavior; however, VS epigenetics such as methylation status has not been thoroughly investigated to date.

Methods: 45 sporadic VS treated with primary resection and greater than 24 months of clinical and radiographic follow-up, were included. VS phenotypes were characterized, and were tested for associations with methylation abnormalities. Tumor tissue specimens underwent DNA extraction followed by reduced representation bisulfite sequencing (RRBS), for high-throughput genome-wide single-nucleotide-level methylation profiling. The primary statistical technique was differential analysis, using a negative binomial logistic regression.

Results: Rapidly growing VS (>2mm/y prior to resection), or those demonstrating postoperative recurrence/progression, were associated with characteristic patterns of increased CpG density. Areas of methylation enrichment included immune regions, neural crest regions, and others. Hypomethylation was inconsistently noted in a variety of gene promoter regions, including those associated with growth factor receptors. Rapid preoperative growth and/or postoperative recurrence/progression were not consistently correlated with significant abnormalities in the MERLIN gene. Cross-referencing with whole-exome sequencing is under active investigation, with additional results anticipated for presentation in tandem with these data.

Conclusion: VS methylation patterns are associated with characteristic behavioral phenotypes. These relationships are preserved in both the preoperative and postoperative settings. Correlation with whole-exome sequencing is pending at time of submission, but may provide additional insights into critical gene loci for future targeted adjuvant therapies in rapidly growing or recurring VS.

211: Serum-Extracted Epigenetic Signatures for the Detection and Classification of Pituitary Adenomas by a Blood Draw

Karam Asmaro, MD (Detroit, MI); Michael Wells; Thais Sabedot; Maritza Mosella; Tathiane Malta; Kevin Nelson; James Snyder; Adam Robin; Steven Kalkanis; Jack Rock; Houtan Noushmehr; Ana Valeria Castro

Introduction: Molecular profiling of circulating biomarkers released by tumors has a relevant clinical value in central nervous system (CNS) tumors, but its feasibility has not been investigated in pituitary tumors (PT) despite being the second common intraaxial tumors of the CNS (15%). Although usually benign and slow-growing, they can be nonfunctioning and invade surrounding structures resulting in significant comorbidities. DNA methylation aberrations distinguish PT according to their functional status but their role in invasiveness is still unclear. Pre-surgical detection of clinically relevant molecular markers associated with tumor behavior can address current diagnostic and therapeutic challenges. We hypothesized that PT release cell-free DNA (cfDNA) into the bloodstream allowing for the profiling of epigenetic markers associated with relevant clinicopathological features.

Methods: Genome-wide methylome profiling of paired serum cfDNA (EPIC array) and tissue from 13 patients with pituitary macroadenomas (9 males; median age: 62; 9 NFPT, 6 invasive) and 3 control serum samples (patients with epilepsy).

Results: Unsupervised analysis of the serum methylome from patients harboring PT was distinct from controls and other diseases (hypopituitarism, glioma and colorectal cancer). Supervised analysis (Wilcoxon rank-sum test) identified significant differentially methylated probes (DMPs) that segregated PT from control serum specimens. Nonfunctioning and invasive-specific DMPs identified in the serum also defined functional, and less prominently invasive status in the tissue of an independent cohort of PT.

Conclusion: This analysis revealed previously unappreciated means to detect the serum methylome profile of cfDNA derived from adenomas of the pituitary gland. This demonstrated unique methylation signatures that distinguished PT according to functional and invasive subtypes. These results underpin the potential role of epigenomic profiling and liquid biopsy as a noninvasive approach to assess clinically relevant molecular features in the serum of patients with pituitary adenomas.

212: Evading Death: NOXA in Cushing's disease Pituitary Adenomas

Reinier Alvarez (Miami, FL); Konstantinos Floros, PhD; Abhik Ray-Chaudhury, MD; Kory Johnson, PhD; Abdel El-Kahloun, PhD; Weiwei Wu, PhD; Prashant Chittiboina, MD, MPH

Introduction: Treatment failure or recurrence of Cushing's disease (CD) caused by benign pituitary microadenomas are challenging clinical problems. Mechanisms underlying adenoma formation and proliferation remain unknown. Malignant and benign tumors in humans often have dysregulated apoptosis. NOXA is a BH3 proapoptotic protein frequently downregulated in malignant human tumors. Malignant tumors often gain drug resistance by downregulating NOXA via proteasomal degradation. The role of dysregulated apoptosis remains largely unknown in benign tumors and in CD. We hypothesized that altered expression of NOXA protein is a pro-survival adaptation employed by CD adenomas.

Methods: Syngeneic human pituitary adenoma and adjacent normal gland pairs (n=2), and an additional CD adenoma were analyzed with RNAseq. Immunohistochemical (IHC) analysis of 12 surgically resected adenomas (10 CD) for NOXA expression was interpreted by a neuropathologist as 0=none, 1=light, 2=medium, 3=strong. Staining grade represents relative protein expression.

Results: NOXA gene (PMAIP1) mRNA (n = 3) showed a 3.76 linear-fold increase in adenomas vs. normal. However, NOXA IHC showed greater staining in normal pituitary vs. adenoma in 8 of 10 CD patients (3:2, respectively). Equal staining noted in 2 of 10 CD patients (2:2 and 2-3:2-3). In a non-functioning adenoma, NOXA expression was elevated in adjacent normal gland, while no difference was seen in a growth hormone producing adenoma.

Conclusion: We found elevated PMAIP1 (NOXA) gene expression in adenomas compared to adjacent normal gland in CD. However, we also found that adenomas downregulated NOXA protein expression significantly, likely contributing to dysregulated apoptosis. These findings suggest that CD adenomas gain pro-survival advantage by downregulating NOXA protein at post-transcriptional or post-translational level.

213: Predictors of Postoperative Diabetes Insipidus (DI) in Over 1000 Patients Undergoing Transsphenoidal Surgery: A Single Institution Experience

Rushikesh Sanjeev Joshi (San Diego, CA); Taemin Oh, MD; Seunggu Han, MD; Alexander Haddad, BS; Matheus Pereira, BS; John Rolston, MD, PhD; Arman Jahangiri, MD, PhD; Ashley Chopra, BA; Jeffrey Wagner, MD; Lewis Blevins, MD; Sandeep Kunwar, MD; Manish Aghi, MD, PhD

Introduction: Diabetes Insipidus (DI) is a known complication following pituitary surgery and can be difficult to manage, often imposing a significant burden on patient quality of life. Here, we aim to characterize preoperative risk factors that may predispose patients to developing DI after pituitary surgery.

Methods: A retrospective review of consecutive patients treated at a single institution from 2007-2016 was conducted. DI was defined as postoperative sodium >145mEq and urine output >300 cc/hour; patients who received desmopressin (DDAVP) in their postoperative course were also considered to have DI. Univariate and multivariate analyses were performed to determine which patient and surgical variables were associated with postoperative DI.

Results: We identified 1,172 patients treated for the following pathologies: apoplexy (3.8%), craniopharyngioma (3.8%), functioning adenoma (36.3%), non-functioning adenoma (27.6%), Rathke's cleft cyst (10.8%), and other (14.2%). Overall, DI was observed in 192/1172 patients (16.4%). On univariate analysis, redo pituitary surgery, surgical approach (microscopic), postop hyponatremia, intra-op CSF leak, and pathology of adenoma (including both macro/micro and functioning/non-functioning) were significantly associated with postoperative DI. On multivariate analysis controlling for both patient characteristics and surgical parameters, redo surgery (OR=4.14, p<0.001) and intra-op CSF leak (OR 8.31, p<0.001) significantly increased the risk of DI; in contrast, adenomas (functioning: OR =0.09, p=0.017; non-functioning: OR 0.12, p=0.036) were associated with lower risk of DI. Among patients with DI, a plot of postoperative sodium values reflected peak values on post-operative day 9.

Conclusion: In over 1000 patients treated at a single institution, our analysis shows that CSF encountered intra-operatively and redo operations had higher occurrence of postoperative DI. Thus, greater vigilance should be maintained in such patients following pituitary surgeries to ensure adequate symptomatic and clinical management. Functioning or non-functioning adenoma exhibited lower rates of postoperative DI. The results also suggest a peak elevation in serum sodium more delayed than previously reported.

214: Characterization of Rathke's Cleft Cyst (RCCs) by 1H-MRS: Differential Diagnosis of Pituitary Adenomas and RCCs

Integra Foundation Award

David S. Baskin, MD, FAANS, FACS (Houston, TX); Martyn Sharpe; Kumar Pichumani; Omkar Ijare

Introduction: Rathke's Cleft Cyst (RCC) is a rare epithelial cyst arising from remnants of the Rathke pouch in the pituitary gland. RCCs are benign and vast majority of them are asymptomatic. A subset of RCCs enlarge and produce mass effect with consequent hypopituitarism and/or visual loss. Moreover, an RCC with a high intra-cystic protein content may mimic cystic pituitary adenoma. Both cystic pituitary adenoma and RCC may show similar MRI characteristics making their differential diagnosis difficult. The goal of this study is to identify molecular markers in RCCs using ex vivo proton magnetic resonance spectroscopy (1H-MRS) of surgically resected cysts.

Methods: RCCs (n=5) and pituitary adenomas (n=5) were collected from patients undergoing transsphenoidal selective lesionectomy/hypophysectomy at the Houston Methodist Hospital. Pituitary adenoma/RCC tissue specimens were extracted in methanol:chloroform:water (2:2:1 ratio, v/v/v). Aqueous methanol layer was separated and vacuum-dried. The residues were reconstituted in D2O containing 1.0 mM DSS-d6 (internal standard). 1D and 2D (TOCSY) 1H-MRS data of these samples were collected on 600/800 MHz spectrometer.

Results: RCCs exclusively showed the presence of glycosaminoglycans (GAGs, the mucopolysaccharides containing disaccharide units made up of an aminosugar and an uronic sugar) when compared to the pituitary adenomas. The presence of GAGs in RCCs was confirmed by observing their characteristic 1H-MRS signals at 2.02 ppm and 3.35 – 4.0 ppm region. 2D TOCSY experiments also confirmed the presence of GAGs. Intraoperative clinical pathology reports showed features of acellular mucoid/proteinaceous debris in the collected RCCs which further corroborates our findings. These current ex vivo findings can be translated to in vivo methodology for the non-invasive diagnosis of RCCs using MRI scanners.

Conclusion: Preoperative confirmation of RCCs would be helpful to neurosurgeons in the surgical treatment planning. Augmenting 1H-MRS with pituitary MRI protocol would be valuable in the differential diagnosis of RCCs and pituitary adenomas.

215: Epigenetic Modulation as a Novel Treatment Strategy for Chordoma

Brian D. Silber Award

Sakibul Huq (Baltimore, MD); Jayanidhi Kedda; Tianna Zhao; Riccardo Serra; Andy Ding; Manuel Morales; Jeffrey Ehresman; Henry Brem; Gary Gallia; Daniel Sciubba; Betty Tyler (Baltimore, MD)

Introduction: Recent efforts to characterize the epigenetic landscape of chordoma have implicated a distinct histone code and DNA methylation profile that may contribute to chordoma tumorigenesis. Epigenetic reprogramming strategies using inhibitors of histone and DNA methylation have demonstrated promise in multiple cancers but have not been explored in chordoma. We investigated the therapeutic potential of epigenetic modulation with 3-deazaneplanocin-A (DZNep), an inhibitor of global histone methylation, and decitabine, an inhibitor of DNA methyltransferase, on two models of chordoma.

Methods: Multiple in vitro assays were performed using DZNep and decitabine in sacral (UCH1) and clival (UMChor1) chordoma cell lines. Cell growth was evaluated via Cell Counting Kit 8 assay. Proliferation assays were performed to quantify cellular growth over three time points. Clonogenic potential was determined via colony formation assays. Cell death was assessed via flow cytometry with AnnexinV (AnnV) and Propidium Iodide (PI) staining.

Results: DZNep inhibited cell growth with an IC50 of 1.3uM in both UCH1 and UMChor1 cells. DZNep and decitabine independently decreased cellular proliferation at multiple time points in both cell lines. DZNep diminished clonogenic potential in both cell lines, including complete elimination of colony formation in UMChor1 cells. DZNep promoted apoptosis in UMChor1 cells, indicated by an increase in AnnV+/PI- and AnnV+/PI+ cells. The combination of DZNep and decitabine led to significantly decreased cell growth compared to either drug alone in UMChor1 cells.

Conclusion: Treatment of chordoma with a global inhibitor of histone methylation decreased cell growth, proliferation, and clonogenic potential and increased cell death. The combination of inhibiting both histone and DNA methylation led to greater cell growth inhibition than either strategy alone. Our ongoing work is further investigating this combination in chordoma in vitro and in vivo. Epigenetic modulation may be a promising new treatment strategy for chordoma.

216: Effect of Ultra-early (<12 hours) Surgery on Recovery after Cervical Spinal Cord Injury: A TRACK-SCI Study**Stewart Dunsker Award for Best Clinical Spine Abstract**

John Fredrick Burke, MD (San Francisco, CA); Michael Beattie, PhD; Jacqueline Bresnahan, PhD; Adam Ferguson, PhD; Jason Talbott, MD, PhD; Leigh Thomas, BA; Xuan Fernandez, BA; Lisa Pascual, MD; Adam Ferguson, PhD; William Whetstone, MD; Sanjay Dhall, MD

Introduction: Surgical timing after spinal cord injury (SCI) remains a controversial topic. Although several studies have shown that early surgery after SCI is beneficial, it is unclear exactly when patients should be taken to surgery. Previously, retrospective data from our institution demonstrated a recovery benefit for ultra-early surgery (< 12 hours) after injury. We have since adopted this ultra-early protocol, and report here the first results from this prospective trial.

Methods: Patients presented to the emergency department of San Francisco General Hospital with acute spinal cord injury. All patients in the current study were evaluated and determined to require surgical decompression based on their injury. Exclusion criteria consisted of (1) death while admitted to the hospital, (2) inability to participate in regular examinations while admitted, and (3) unknown time of injury. Motor scores were taken daily while patients were admitted, and the difference in motor scores between admission and discharge was recorded.

Results: Clinical and radiographic data from 35 patients with cervical SCI were prospectively collected. The mean time to surgery in this group was 15.4 hours. We grouped patients based on whether they went to the operating room within 12 hours of injury (ultra-early group; 20 patients) or after 12 hours of injury (early group; 15 patients). The average motor score improvement for the ultra-early group was 13.8 and for the early group was 2.47 (t-test; $p=0.06$).

Conclusion: Preliminary data from our prospective trial of time to surgery after spinal cord injury is consistent with our earlier retrospective data, as well as previous published studies. Collectively, these results suggest that faster time to surgery after cervical SCI can improve motor outcome.

217: A Novel Target for Neuromodulation in Spinal Cord Injury: Dorsal Root Ganglion-Stimulation Can Evoke Weight-Bearing Motor Responses in Patients with Chronic Motor Complete Spinal Cord Injury

Sadaf Soloukey (Rotterdam, Netherlands); Judith de Rooij; Rutger Osterthun, MD, PhD; Judith Drenthen, MD; Chris De Zeeuw, MD, PhD; Frank Huygen, MD, PhD; Biswadjit Harhangi, MD, PhD

Introduction: Current strategies for motor recovery after Spinal Cord Injury (SCI) aim to facilitate motor performance through modulation of afferent input to the spinal cord using epidural electrical stimulation (EES). The Dorsal Root Ganglion (DRG) itself, the first relay station of these afferent inputs to the spinal cord, has not yet been targeted for this purpose. This while DRG-stimulation has established itself as a unique target for neuromodulation in chronic pain, leading to more selective and posture-independent stimulation. The current study is the first to explore the possibility to evoke motor response in motor complete SCI using commercially available DRG-stimulators.

Methods: Five patients with chronic motor complete SCI (ASIA A/B) were implanted with DRG-leads placed bilaterally on level L4 during 5 days. Based on a personalized stimulation protocol, we aimed to evoke both isokinetic as well as isotonic motor responses in the bilateral quadriceps muscles, leading to knee extension. On day 1 and 5, EMG- and clinical muscle force measurements (MRC-scoring) were used to objectify motor responses and their reproducibility. In addition, the ability for the patient to come to a weight-bearing position was assessed on day 5 with bilateral DRG-stimulators activated on an isotonic level, using parallel bars and a patient lift system.

Results: For all patients, DRG-stimulation evoked isokinetic and isotonic motor responses with an MRC ≥ 4 in the upper leg, both on day 1 and day 5 of the study, indicating that motor responses were strong and reproducible.

Conclusion: The current proof-of-principle study provides first evidence that bilateral L4 DRG-stimulation can evoke reproducible motor responses in the upper leg, sufficient to facilitate assisted weight-bearing in patients with chronic motor complete SCI. As such, a new target for SCI treatment has surfaced, using existing stimulation devices, making the technique directly clinically accessible.

218: The Change in Inpatient Opioid Use and Pain Scores After Elective Lumbar Fusion Surgery Following Implementation of an Enhanced Recovery after Surgery Protocol

Robert Winkelman (Cleveland, OH); Vikram Chakravarthy, MD; Shiv Dewan; Vineeth Satta; Hana Yokoi; Mariel Manlapaz, MD; Ajit Krishnaney, MD

Introduction: Although opioids are a staple in the management of postoperative pain, excessive utilization of inpatient opioids postoperatively has been associated with prolonged lengths of stay and poor patient outcomes. Recently, Enhanced Recovery After Surgery (ERAS) protocols have gained popularity in many surgical subspecialties by optimizing patient postoperative recovery and minimizing opioid exposure. The goal of the present study was to assess how the recent implementation of an ERAS protocol for spine surgery impacted inpatient opioid use, adjunct pain medication utilization, and patient-reported pain following lumbar fusion surgery.

Methods: This study is a retrospective review of 632 patients who underwent elective posterior lumbar fusion surgery in the year prior (2016) and the year after (2018) the introduction of an ERAS protocol for spine surgery at a single academic medical center. Inpatient opioid medications, adjunct analgesic medications (oral/IV NSAIDs, gabapentinoids, and local anesthetic agents), and daily visual analog scale (VAS) pain scores were obtained by querying the electronic medical record. All opioid medications were converted to oral morphine equivalent doses (MEDs) and totaled according to day of admission (DoA). The average daily MEDs, overall adjunct pain medication utilization, and daily pain scores were compared between the patients from the two years.

Results: Patients in the year after the implementation of the ERAS protocol had significantly lower opioid use over the first three DoAs and overall significantly higher utilization of all four adjunct pain medications. VAS pain scores on the day of surgery were found to be significantly lower in the year after ERAS.

Conclusion: After the implementation of an ERAS protocol for spine surgery, lumbar fusion patients received less opioids, more adjunct pain medications, and reported lower pain scores during their inpatient admission. This study demonstrates that ERAS following spine surgery may help to mitigate perioperative opioid use without adversely impacting patient pain control.

219: Trends in Spine Surgery Training during Neurological and Orthopedic Surgery Residency: A Ten-Year Analysis of ACGME Case Log Data

Martin Huy Pham, MD (La Jolla, CA); Andre Jakoi, MD; Arvin Wali, MD; Lawrence Lenke, MD

Introduction: Spine surgery training in the United States currently involves residency training in neurological or orthopedic surgery. Due to different core residency surgical requirements, volume of spine surgery procedures may vary between the two residencies.

Methods: The Accreditation Council of Graduate Medical Education resident case logs for both orthopedic surgery and neurological surgery were reviewed for exposure to spine surgery procedures for the graduating years of 2009-2018.

Results: The average number of spine surgery procedures performed during that 10-year period was 433.8 for neurosurgery residents and 119.5 orthopedic surgery residents ($p < 0.01$). From 2009 to 2018, neurosurgery residents saw an increase of 26.5% in spine surgery procedures from 389.6 to 492.9 procedures whereas orthopedic surgery residents saw a decrease of 41.3% from 141.1 to 82.8 procedures. The 10-year average percentage of total spine procedures of all total surgical cases was 33.5% for neurosurgery residents compared to 6.2% for orthopedic surgery residents ($p < 0.01$). This percentage decreased both for neurosurgery residents (35.8% in 2009 to 31.3% in 2018) and orthopedic surgery residents (7.2% in 2009 to 4.9% in 2018). Neurosurgical residents performed on average 3.6 times more total spine procedures than orthopedic surgery residents, a number that increased from 2.8 fold in 2009 to 6.0 fold in 2018.

Conclusion: Case volume of spine surgery procedures vary greatly with higher rates for neurological and lower for orthopedic surgery residencies, with an enlarging increasing discrepancy over time. Although case volume alone cannot solely determine quality of training, it is one measure to assess opportunities to develop optimal spine education around a certain accepted volume of surgical patient care. The results found here may help to explore various needs and differences between residents seeking to pursue careers in spine, and the role of spine surgery fellowships currently and in the future.

220: A Comparison of Complications, Clinical and Radiologic Outcome between the Mini-open Prepsoas and Mini-open Transpsoas Approach for Lumbar Interbody Fusion

Alexander Spiessberger, MD (Manhasset, NY); Varun Arvind; Basil Gruter; Florian Huber; Roman Guggenberger; Vikas Varma; Samuel Cho

Introduction: To compare complication rates, clinical and radiologic outcome between the mini-open prepsoas and mini-open transpsoas approach for lateral lumbar interbody fusion.

Methods: A systematic review of literature was performed. Data was extracted from original publications and sorted in two groups, the prepsoas and transpsoas approach group. A random effects model meta-analysis was performed including Fisher exact test.

Results: A total of 115 studies included data of 13260 patients, 2450 in the prepsoas and 10810 in the transpsoas group. Demographics for prepsoas vs transpsoas group were, weighted mean average: age 61.9 vs 60.9 years; female sex 0.53 vs 0.63, levels fused 1.4 vs 2.6, blood loss 52.4 vs 122.3ml, operating time 125.1 vs 200.7min. The following statistically significant differences in complication rates between prepsoas vs transpsoas approach were found: transient psoas weakness or thigh/groin numbness 0.05 vs 0.26 (95%CI 0.11—;0.17), motor neural injury 0.004 vs 0.01 (95%CI 0.16-0.623), major vascular injury 0.018 vs 0.012 (95%CI 1.04-2.31); no statistically significant differences were found for: kidney or ureter injury 0.0004 vs 0.0008, injury pleural/peritoneal structures 0.005 vs 0.002, cage subsidence 0.05 vs 0.04, surgical site infection 0.01 vs 0.01, abdominal wall pseudo-hernia 0 vs 0.01, sympathetic chain injury 0.05 vs 0, Ogilvie syndrome 0.0024 vs 0.0022, directly procedure related death 0.0004 vs 0. Pooled mean perioperative change between prepsoas and transpsoas approach were: segmental sagittal cobb angle 3.07 vs 1.99deg; foraminal height 2 vs 6.96mm;

Conclusion: The prepsoas had fewer complications than the transpsoas approach. Furthermore the prepsoas approach showed superior restoration of segmental lordosis, whereas foraminal height restoration was superior with the transpsoas approach. This could be explained by the different location of the interbody device in relation to the center-of-rotation line between the two surgical techniques.

221: Predicting Tumor Specific Survival in Patients with Metastatic Renal Cell Carcinoma: Which Scoring System Is Most Accurate?

Elie Massaad (Boston, MA); Nida Fatima, MD; Muhamed Hadzipasic, MD, PhD; Christopher Alvarez-Breckenridge, MD; Ganesh Shankar, MD, PhD; Andrew Schoenfeld, MD; Joseph Schwab, MD; John Shin, MD

Introduction: Renal cell carcinoma (RCC) is one of the most commonly diagnosed malignancies, with an estimated 74,000 new cases in 2019. Approximately 40% of bony metastasis occurs in the spine. This study aims to assess the performance of previously validated prediction models for spine metastatic disease to predict the survival of RCC patients.

Methods: A multi-centric retrospective study, included n=86 patients with spinal metastatic RCC. Preoperative scores were calculated using: (1) Tomita, (2) original Tokunashi, (3) revised Tokunashi, (4) original Bauer, (5) modified Bauer, (6) Katagiri, (7) Van Der Linden, (8) SORG classic algorithm, (9) SORG nomogram, (10) New England spinal metastasis score (NESMS). Univariate Cox proportional hazard models were calculated to assess the association of patient variables with 1-year survival. The time-dependent ROC was performed for each model. Cut-offs for (AUC) are as follows: excellent (AUC $\geq$ 0.90), good (AUC $\geq$ 0.80 and 0.90), fair (AUC $\geq$ 0.70 and 0.80), and poor performance (AUC 0.70).

Results: N=86 patients (60.90 $\pm$ 11.36 years, 73.25% male) undergoing spine surgery for spinal metastatic RCC. Univariate analysis showed that patient and tumor factors were strongly associated with 1-year survival: (1) Poor KPS (HR:6.78 [95% CI:1.96—;23.48]), (2) ECOG grade 3-4 (HR:3.52 [1.57-7.91]), (3) Frankel grade A-D (HR:2.54 [1.01-6.46]), (4) albumin <3.5 g/dL (HR:4.05 [1.67-9.80]). NESMS had the best performance in predicting survival at t=3 months (AUC= 0.83 [95% CI:0.63-1]), t=6 months (AUC=0.84 [0.70-0.98]), t=12 months (AUC=0.88 [0.77-0.99]). All other prognostic scores had a poor or fair performance at t=3 months (AUC range: 0.61-0.78), t=6months (AUC= 0.59-0.73), t=12months (AUC=0.60-0.76).

Conclusion: Most validated prognostic scores have a poor or fair performance in predicting the survival of RCC surgical patients with spinal metastatic disease. Tumor-specific factors and newer treatment modalities affect the survival of RCC patients and should be evaluated in future prognostic studies.

222: Decompression and Fusion versus Decompression Alone For Grade I Degenerative Lumbar Spondylolisthesis: 24-Month Results From The Prospective, Multicenter QOD Spondylolisthesis Study Group

Andrew K. Chan, MD (San Francisco, CA); Erica F. Bisson MD, MPH, Mohamad Bydon MD, Kevin T. Foley MD, Steven D. Glassman MD, Christopher I. Shaffrey MD, Eric A. Potts MD, Mark E. Shaffrey MD, Domagoj Coric MD, John J. Knightly MD, Michael Y. Wang MD, Paul Park MD, Kai-Ming Fu MD, PhD, Jonathan R. Slotkin MD, Anthony L. Asher MD, Michael S. Virk MD, PhD, Panagiotis Kerezoudis MD, MS, Mohammed A. Alvi MBBS, Jian Guan MD, Regis W. Haid MD, and Praveen V. Mummaneni MD

Introduction: Prior studies—including two recent randomized clinical trials—have not revealed the ideal surgical management strategy for degenerative lumbar spondylolisthesis. Using the multicenter, prospectively-collected Quality Outcomes Database (QOD) registry, we compared 24-month outcomes for patients undergoing decompression alone versus decompression and fusion for grade 1 degenerative lumbar spondylolisthesis.

Methods: Twelve, top-enrolling QOD sites formed a spondylolisthesis study group to investigate the effectiveness of fusion for grade 1 degenerative lumbar spondylolisthesis. From 7/2014 through 6/2016, 608 patients underwent single-segment surgery for grade 1 degenerative lumbar spondylolisthesis at these sites. Demographics, clinical characteristics, surgical variables, and radiographic parameters were collected. The primary outcome, 24-month Oswestry Disability Index (ODI) change, was analyzed with multivariable linear regression. Other secondary outcomes included the proportion reaching ODI minimal clinically important difference (MCID; 12.8 point change), Numeric Rating Scale (NRS) Back Pain (NRS-BP), NRS Leg Pain (NRS-LP), EuroQoL-5D (EQ-5D), NASS Satisfaction, and reoperation rates.

Results: Of the 608 patients (85.5% 24-month follow-up rate), 140 (23.0%) underwent decompression alone and 468 (77.0%) underwent decompression and fusion. The 24-month ODI change was significantly greater in the fusion group (25.8 ± 20.0 vs. 15.2 ± 19.8 , $p < 0.001$). Fusions were significantly more likely to reach ODI MCID at 24 months (73.3% vs. 56.0%, $p \leq 0.001$). Reoperation rates were similar for fusion and decompression-only groups (6.2% vs. 9.3%, respectively, $p = 0.206$). In multivariable analyses, the addition of fusion was independently associated with superior ODI change ($B = 7.05$, 95%CI(3.39-10.70), $p < 0.001$), ability to achieve ODI MCID ($OR = 1.77$, 95%CI(1.06-2.94), $p = 0.03$), NRS-BP change ($B = 1.18$, 95%CI(0.61-1.76), $p < 0.001$), and NASS satisfaction ($OR = 2.22$, 95%CI(1.41-3.45), $p < 0.001$) at 24 months. Type of procedure was not associated with NRS-LP or EQ-5D change ($p > 0.05$).

Conclusion: The results of our study suggest that decompression with fusion may offer superior outcomes compared to decompression alone in patients with grade 1 degenerative lumbar spondylolisthesis at 24 months.

223: Development Of A Prediction Model For Central Cord Syndrome: An Evaluation Of Motor Recovery And The Effectiveness Of Early Surgery in a Prospective, Multicentre Cohort of 211 Patients

Michael G. Fehlings, MD, PhD, FAANS, FRCS (Toronto, Canada); Jetan Badhiwala, MD; Jefferson Wilson, MD, PhD

Introduction: There remains a paucity of data on the prediction of outcomes of central cord syndrome (CCS). Further, the efficacy of early surgical decompression for CCS remains unclear. In patients with CCS, we therefore sought to: 1) develop a clinical prediction model for neurological outcome; and 2) evaluate the effect of early surgery (<24hrs) on neurological recovery.

Methods: Patients with CCS (AIS grade C/D; LEMS — UEMS ≥ 5) were identified from two prospective, multi-center SCI datasets (NACTN; STASCIS). A clinical prediction model was developed by multiple linear regression; the outcome was change in ASIA motor score (AMS) at 1-year. Covariates were chosen a priori: 1) age; 2) baseline AMS; 3) baseline AIS grade; 4) time to surgery (early [< 24 hrs] vs. late [≥ 24 hrs]); and 5) time to surgery $\times$ AIS grade. Effect sizes were summarized by β coefficients. Internal validation was performed by bootstrapping. The model was externally validated in the NASCIS III cohort.

Results: Two-hundred and eleven patients were eligible (mean age, 52.1yrs; 21.3% female; 79.1% AIS D). β coefficients were significant for all variables in the model: age (-0.12, $P = 0.04$); baseline AMS (-0.71, $P < 0.01$); AIS grade (9.69, $P = 0.01$); time to surgery (12.67, $P < 0.01$); AIS grade $\times$ time to surgery (-13.18, $P < 0.01$). The mean R^2 across bootstraps was 0.66. In patients with AIS C injury, early surgery resulted in significantly improved motor recovery (marginal mean: 12.7, 95% CI 5.8-19.6); there was no difference in recovery with early surgery in patients with AIS D injury (marginal mean: -0.5, 95% CI -4.4-3.3). The model showed good external validity ($R^2 = 0.65$ in validation cohort).

Conclusions: Motor recovery after CCS may be predicted by age, AMS, AIS grade, and time to surgery. Early surgery improves recovery, particularly in patients presenting as AIS grade C. These data support early surgical decompression in AIS C central cord injury patients.

224: Feasibility of Using Computerized Adaptive Testing To Capture Patient Reported Outcomes in an Outpatient Setting: A Pilot Evaluation of PROMIS-CAT in Neurosurgery

Mohamad Bydon, MD, FAANS (Rochester, MN) ; Anshit Goyal, MBBS; Kelsey Wolff, MBA; Allie Canoy Illies, MPH; Mohammed Alvi, MBBS; Sandy Goncalves, MS; Atul Dhanoerkar, MBA; Aaron Biedermann, MBA; Travis Paul, MBA; Andrea Cheville, MD; Mark Nyman, MD

Introduction: Current challenges around Patient Reported Outcomes (PRO) administration include redundant and uncoordinated PRO collection leading to excessive patient burden and diminished response rates. In this pilot, we aimed to improve completion rate of the baseline PROMIS (Patient-Reported Outcomes Measurement Information System) questionnaire among patients presenting for outpatient evaluation in our department, while reducing patient burden, using a computerized adaptive testing (CAT) format.

Methods: PROMIS-CAT was selected as the tool for capturing PROs using our institutional patient online services (POS) portal, linked directly to the electronic health record (EHR). Prior to the pilot, PROMIS-29 administered online via an iPad (Qualtrics) was the main PRO collected during outpatient visits. With PROMIS-CAT, participant responses guide the computer's choice of subsequent items from the full item bank, thereby reducing the question burden. Moreover, it is available for providers' reference within the medical record.

Results: Prior to the pilot, PROMIS responses were not available within the Epic electronic health record. The completion rate of the questionnaire was at 30%. During the two month pilot, 1943 patients were assigned PROMIS-CAT, of which 1330 or 68.4% of patients completed the questionnaire. The average number of questions answered by each patient was 45.2. The pilot did not significantly alter outpatient satisfaction as measured by top box scoring in the patient movement and access questions on the Press-Ganey survey (Patient access post vs pre-pilot: 55.4% and 49.7%; patient movement post vs pre-pilot: 68.4% vs 64.9%)

Conclusion: Computerized adaptive testing is a viable PRO collection mechanism in the outpatient setting that does not significantly alter outpatient satisfaction. EHR integration may bypass common patient-provider communication barriers by collecting pre-visit ePROs and delivering results in real time at the point of care

225: Effect on the Regional Metabolic Information in the Brain of Awake Rats after Short-term or Long-term Spinal Cord Injury

Liang Wu (Yin Chuan, China); Hechun Xia; Jie Wang

Introduction: Spinal cord injury (SCI) is a common cause of disability in the world, which often leads to motor and sensory dysfunction below the spinal injury site. However, the regional effects on the metabolic information in the brain after spinal cord injury have been little studied, such as metabolite concentrations and metabolic kinetics of amino acid neurotransmitters.

Methods: Female SD rats (8w, 200±10g) were divided into short-term (3 day), long-term (8 weeks) groups and sham group for each treated group (n = 10 to 12 in every group). Animals in the sham groups were doing the same surgery without damaging the spinal cord, and the animals in the treated groups were completed injured the spinal cord following the modified Allen's method. Method of BBB (Basso, Beatti and Bresnahan Scores) score was used to evaluate the behaviors on the 1st, 7th, 14th, 21st and 28th day after surgery. All animals were infused with [1-13C] glucose through the tail vein catheterization in the awake state, and euthanized with head focused on microwave method. Then different brain regions were divided and the metabolites were measured with 1H-observed/13C-edited NMR method.

Results: The total concentrations of metabolites in every region of different groups were almost similar. However, SCI altered metabolic kinetics in most regions in the short-term group ($p < 0.05$), particularly in the cortical area, medulla and midbrain ($p < 0.01$). After long-term recovery, most metabolic kinetics were recovered and the GABAergic system was even increased in some region, such as MID ($p < 0.05$).

Conclusion: The metabolic kinetic changes have revealed the alteration of metabolism and neurotransmission in different brain regions after SCI, which present an evidence for the alternation of brain glucose oxidation. SCI has significantly influent the cerebral function, especially for short-term intervention.

226: Does Interbody Fusion Protect against Rod Fracture in the Lower Lumbar Spine after Long Fusions to the Sacrum: A Comparative Analysis of Adult Spinal Deformity Patients

Owoicho Adogwa, MD, MPH (St. Louis, MO); Mostafa El Dafrawy, MD; Keith Bridwell, MD; Owoicho Adogwa; Max Shlykov; Jonathan Kosco, MD; Lawrence Lenke, MD; Thamrong Lertudomphonwanit, MD; Michael Kelly, MD; Munish Gupta, MD

Introduction: Several strategies have been proposed to decrease pseudarthrosis rates across the lumbosacral junction. The aim of this study is to compare the rate of rod fractures in patients undergoing surgery for correction of ASD with or without the use of interbody fusions.

Methods: We reviewed clinical records of patients that underwent surgery for correction of ASD. All cases were primary surgeries with long fusion to the sacrum and bilateral spinopelvic fixation. Patients were dichotomized into one of two groups based on whether an interbody fusion was performed at the caudal levels of the fusion construct. All patients had a minimum 2-year follow-up.

Results: 230 patients were enrolled in the study with a mean follow-up of 55 months. 117 patients had an interbody fusion while 113 patients did not. Both groups were similar at baseline. The severity of the sagittal plane deformity was similar between both groups. At last follow-up, there was no statistically significant difference in the rate of rod fractures between the cohort of patients that had an interbody fusion and the cohort that did not (interbody fusion cohort: 17.94% vs. no interbody fusion cohort: 14.15%, $p=0.49$). The rate of bilateral rod fractures was low [IBF $n=10$ (8.54%) vs NIF $n=6$ (5.3%) $p=0.33$]. The location of RF was different between the two groups; RF above L4 was most common location in IF group (85%) compared to NIF group where the most common location for RF was L4-S1 (73%).

Conclusion: The use of interbody fusions during correction of ASD may not be associated with a decrease in the incidence of rod fractures. Interbody fusion does not protect against rod failure in the lumbar spine in ASD patients with long posterior spinal fusion and may encourage failure at the level above the interbody fusion.

227: Outcomes and Complications with Age in Spondylolisthesis: An Evaluation of the Elderly from the Quality Outcomes Database

Michael Karsy, MD, PhD (Salt Lake City, UT); Andrew Chan, MD; Praveen Mummaneni, MD; Erica Bisson, MD, MPH

Introduction: Degenerative lumbar spondylolisthesis affects 3 — 20% of the population and up to 30% of the elderly. There is not yet consensus on whether age is a contraindication for surgical treatment of elderly patients. The purpose of this study was to assess the effect of age on patient-reported outcomes (PROs) and complication rates after surgical treatment for spondylolisthesis.

Methods: The Quality Outcomes Database multicenter, prospective registry was used to evaluate patients from 12 U.S. centers, including academic and private institutions, who underwent surgical treatment for grade 1 lumbar spondylolisthesis between July 2014 and June 2016.

Results: A total of 608 patients who fit the inclusion criteria were categorized by age <60 ($n=239$), 60–70 ($n=209$), 71–80 ($n=128$), and >80 ($n=32$) years. Older patients showed lower mean body mass index ($p=0.00001$) and higher rates of diabetes ($p=0.007$), coronary artery disease ($p=0.0001$), and osteoporosis ($p=0.005$). A lower likelihood for home disposition was seen with higher age (89.1% in <60-year-old vs. 75% in >80-year-old patients; $p=0.002$). There were no baseline differences in PROs (Oswestry Disability Index, EQ-5D, Numeric Rating Scale for leg pain and back pain) among age categories. A significant improvement for all PROs was seen regardless of age ($p<0.05$), and most patients met minimal clinically important differences (MCIDs) for improvement in postoperative PROs. No differences in hospital readmissions or reoperations were seen among age groups ($p<0.05$). Multivariate analysis demonstrated that, after controlling other variables, a higher age did not decrease the odds of achieving MCID at 12 months for the PROs.

Conclusion: Our results indicate that well-selected elderly patients undergoing surgical treatment of grade 1 spondylolisthesis can achieve meaningful outcomes. This modern, multicenter U.S. study reflects the current use and limitation of spondylolisthesis treatment in the elderly, which may be informative to patients and providers.

228: Pain Outcomes in Single-Dose versus Fractionated Stereotactic Body Radiation Therapy for Spinal Metastases

Christine Park (Las Vegas, NV); Vikram Mehta, MD, MPH; Luis Ramirez, MPH; Elizabeth Howell, BS; Meghan Price, BS; John Kirkpatrick, MD, PhD; Scott Floyd, MD, PhD; Muhammad Abd-El-Barr, MD, PhD; Isaac Karikari, MD; Jordan Torok, MD; Rory Goodwin, MD, PhD

Introduction: Spinal stereotactic body radiation therapy (SBRT) offers a non-invasive treatment modality for the control of spinal neoplasms. High radiation doses can cause adverse outcomes, fractionated delivery of SBRT may improve its safety profile while maintaining its efficacy. This study aims to examine whether 3-fraction SBRT improves pain outcomes compared to single-fraction SBRT.

Methods: A single-institution retrospective study was performed of 156 adult patients with spinal metastases treated with single- or 3-fraction SBRT from 2008 to 2019. Demographics and baseline characteristics, radiographic data, and minimum 3-month follow-up post-treatment outcomes — including patient-reported pain scores, tumor progression, performance status, and morphine equivalent dosing — were recorded.

Results: Of the 156 patients included in the study, 70 (44.9%) underwent single fraction SBRT and 86 (55.1%) underwent 3-fraction SBRT. At baseline, higher proportion of patients in the 3-fraction group had previous non-SBRT radiotherapy ($p<0.0001$), had prior resection to the site of SBRT ($p<0.001$), presented with greater severity of pain ($p<0.05$), and exercised greater pain medication use on average ($p<0.001$) compared to that in the single-dose fraction cohort. At 3-month follow-up, although there was no significant difference in the mean pain medication usage both between and within the two groups, the 3-fraction cohort experienced a greater frequency of improved pain outcomes compared to the single-fraction group ($p<0.05$).

Conclusion: A greater frequency of patients who received fractionated delivery of spinal SBRT achieved significant pain relief compared to those treated with single-fraction. Future work is needed to further establish the relationship between fractionation schedule and clinical outcomes including consideration of primary tumor type and effect on health-related quality of life metrics.

229: The Impact of Smoking on Outcomes Following Surgery for Grade 1 Lumbar Spondylolisthesis.

Arati Patel, MD (San Francisco, CA); Andrew K. Chan MD, Erica F. Bisson MD, MPH, Mohamad Bydon MD, Kevin T. Foley MD, Steven D. Glassman MD, Christopher I. Shaffrey MD, Eric A. Potts MD, Mark E. Shaffrey MD, Domagoj Coric MD, John J. Knightly MD, Michael Y. Wang MD, Paul Park MD, Kai-Ming Fu MD, PhD, Jonathan R. Slotkin MD, Anthony L. Asher MD, Michael S. Virk MD, PhD, Panagiotis Kerezoudis MD, MS, Mohammed A. Alvi MBBS, Jian Guan MD, Regis W. Haid MD, and Praveen V. Mummaneni MD

Introduction: Studies have demonstrated higher rates of perioperative complications and non-union in smokers undergoing spinal fusion surgery. Yet, few studies have investigated the impact of smoking on outcomes in patients undergoing surgery for degenerative lumbar spondylolisthesis. Here, we assess the impact of smoking on patient reported outcomes (PROs) and radiographic fusion in patients undergoing surgery for grade 1 degenerative lumbar spondylolisthesis.

Methods: We analyzed patients undergoing single-segment surgery for grade 1 lumbar spondylolisthesis in the prospective Quality Outcomes Database (QOD) registry. Multivariable linear regression was performed to assess for associations between smoking status and PROs. Repeated measures ANOVA was performed to assess for differences in baseline and 24-month PRO scores. Binary logistic regression was performed to assess for association between smoking and Oswestry Disability Index Minimal Clinically Important Difference (ODI MCID) and radiographic fusion at 24 months, respectively. Radiographic fusion was assessed by an independent neuroradiologist.

Results: This study included 531 non-smokers and 71 smokers. On univariate analysis, smokers and non-smokers significantly differed in age, gender and BMI ($p<0.05$). The two groups had significant differences in mean baseline ODI (non-smokers: 45.53 ± 16.99 vs. smokers: 56.82 ± 15.17 , $p<0.001$). Both smoking and non-smoking groups demonstrated significant improvement in ODI from baseline ($p<0.00$). In multivariable analysis, non-smokers were more likely to achieve a minimum clinically important difference (MCID) in ODI (OR=7.30, 95%CI[2.32-12.28], $p=0.004$). There was no significant difference in radiographic fusion between the smoking and non-smoking groups (smokers: 100% fusion rate vs. non-smokers: 95.5%; adjusted OR=1.45, 95%CI[0.16-12.95], $p=0.74$).

Conclusion: Though both smokers and non-smokers benefit from surgery, non-smokers demonstrated greater improvement in disability. There was no negative association between smoking and radiographic fusion.

230: Autologous Bone Marrow-Derived Cell Therapy Combined With Physical Therapy Induces Functional Improvement in Chronic Spinal Cord Injury Patients

Wael Abou Elkheir Kamel, MD (Cairo, Egypt, Arab Rep.); Osama El-Ghannam; Hala Gabr; Samer Mounir

Introduction: Spinal cord injuries (SCI) cause sensory loss and motor paralysis and are treated with physical therapy, but most patients fail to recover due to limited neural regeneration. Here we describe a strategy in which treatment with autologous adherent bone marrow cells is combined with physical therapy to improve motor and sensory functions in early-stage chronic SCI patients.

Methods: In a phase I/II controlled single-blind clinical trial (clinicaltrials.gov identifier: NCT00816803), 70 chronic cervical and thoracic SCI patients with injury durations of at least 6 months were treated with either intrathecal injection(s) of autologous adherent bone marrow cells combined with physical therapy, or with physical therapy alone. Patients were evaluated with clinical examinations, electrophysiological somatosensory evoked potential, MRI imaging, and functional independence measurements.

Results: Chronic cervical and thoracic SCI patients treated with autologous adherent bone marrow cells combined with physical therapy showed functional improvements over patients in the control group treated with physical therapy alone, and there were no cell therapy-related side effects. At 18 months posttreatment, 23 of the 50 cell therapy-treated cases (46 percent) showed sustained improvement using the American Spinal Injury Association (ASIA) Impairment Scale (AIS). Compared to those patients with cervical injuries, a higher rate of functional improvement was achieved in thoracic SCI patients with shorter durations of injury and smaller cord lesions.

Conclusion: Therefore, when combined with physical therapy, autologous adherent bone marrow cell therapy appears to be a safe and promising therapy for patients with chronic spinal cord injuries. Randomized controlled multicenter trials are warranted.

231: Reducing Opioid Utilization for Pain Management in Postoperative Spine Surgeries with Long-acting Local Anesthetic Exparel

Abby York (Columbia, MO; Endrit Ziu, MD, PhD; Mesfin Fassil, MD, PhD)

Introduction: Patients undergoing spine surgeries experience a significant amount of pain in the immediate postoperative period of recovery. Traditionally, patients undergoing these procedures have their pain managed with the use of opioid analgesics. The heavy use of opiates to treat post-operative pain puts patients at an elevated risk for opioid tolerance and reliance. Liposomal bupivacaine (Exparel) is a long-acting local anesthetic that is safe and effective to use in the immediate postoperative management of pain. Its benefit to postoperative spine patients is yet to be determined. This study hypothesizes that the administration of Exparel in postoperative spine patients results in a reduction of opioid utilization, without compromising pain management.

Methods: This study utilizes a retrospective chart review of patients who have undergone spine surgery, utilizing a posterior approach, between 2014 to 2019. The primary outcome measured was opioid medications administered within the first 72 hours postoperatively. The 2018 Medicare Part D Program Policies & Procedures guidelines were used to standardize dosing into morphine milligram equivalents (MME). The secondary outcomes measured were visual analog pain scale and length of stay.

Results: Results showed that the average opioid utilization (in MME) for patients who did not receive Exparel was 93mg postop day 1, 59mg postop day 2, and 56mg postop day 3, whereas patients who received Exparel used on average 70mg, 39mg, and 53mg respectively. These results demonstrated a significant reduction ($p < 0.01$) in opiate utilization in patients who were given Exparel. Additionally, most patients were discharged home after an overnight stay in the hospital for the Exparel group, compared to an average of 3 days for non-Exparel group.

Conclusion: Exparel reduces opiate utilization for pain management in postoperative spine patients. Furthermore, Exparel can promote the current national trend of moving toward the idea of outpatient-based spine surgery.

232: Variation in Outcome Measures in Lumbar Spondylolisthesis Patient Registries and the Need for Harmonization

Michelle Leavy (Boston, MA); Richard Gliklich, MD; Robert Harbaugh, MD; Elise Berliner, PhD

Introduction: Lumbar spondylolisthesis (LS) is a common cause of low back pain. Many questions exist regarding the comparative effectiveness of different treatment approaches, pain management strategies, and long-term patient outcomes. New, efficient research approaches are necessary to address these questions. Connecting data across registries and other data collection efforts would yield a robust national data infrastructure to help address these questions, but a lack of harmonization in the outcome measures currently collected in registries, quality improvement efforts, and clinical practice hinders the ability to connect these data sources. The purpose of this effort was to collect and categorize outcome measures used in LS registries and clinical practice and to identify measures for which harmonization is needed.

Methods: LS patient registries were invited to join the workgroup and submit outcome measures. Additional measures were identified through literature searches and reviews of consensus statements. Outcome measures were categorized using the Agency for Healthcare Research and Quality's Outcome Measures Framework (OMF), a conceptual model for classifying outcomes that are relevant to patients and providers across most conditions.

Results: Nine LS registries participated and submitted 57 outcome measures. Measures of clinical response (37%) and patient-reported outcomes (37%), such as pain intensity, pain interference, and physical function, were most common, followed by events of interest (16%), such as surgical complications. The remaining measures were categorized as resource utilization (5%), survival (4%), and experience of care (2%). Several measures, such as pain, were captured using different instruments and at different timepoints.

Conclusion: Many LS registries measure the same concepts but use different instruments or different timeframes. Collection of a standardized set of outcome measures at consistent intervals in registries and in other systems would support the creation of a national research infrastructure to efficiently address new questions and improve patient outcomes.

233: Timing of Neurological Recovery in Patients with Acute Thoracic AIS A SCI Implanted with an Investigational Neuro-Spinal Scaffold™: Results of the INSPIRE Study

Kee D. Kim, MD, FAANS (Sacramento, CA); K. Stuart Lee, MD; James S. Harrop, MD; Domagoj Coric, MD; Nicholas Theodore, MD; Richard M. Toselli, MD

Introduction: Limited data exist regarding the timing of AIS conversions among traumatic SCI patients. The investigational Neuro-Spinal Scaffold(TM) (NSS) is a biodegradable device developed to facilitate spinal cord repair following intraparenchymal implantation. Per FDA guidance for Humanitarian Device Exemption applications, the INSPIRE study (NCT02138110) was conducted to investigate the safety and probable benefit of NSS implantation in acute, thoracic complete SCI patients. This analysis evaluated the timing of AIS conversions in patients who achieved improvement in neurological function.

Methods: This open-label, prospective, single-arm multicenter study enrolled patients with non-penetrating, T2 — T12, AIS A SCI requiring open stabilization surgery ≤96 hours of injury. Safety and neurological outcomes through 24-months post implantation are reported.

Results: Sixteen of 19 patients (84%) implanted with the NSS completed the 6-month follow-up examination. Three early deaths were deemed by investigators to be unrelated to the NSS or its implantation procedure. Seven of 16 patients (44%) had ≥ 1 AIS grade improvement by 6-months post implantation: 2 converted to AIS C by 1 month and were AIS C at 24 months, 3 had initial conversion to AIS B (by 1, 2, and 3 months, respectively) with further neurological improvement to AIS C by 12 (n=2) and 24 (n=1) months, and 2 converted to AIS B by 2 and 6 months, respectively, but were lost to follow-up by 24 and 12 months, respectively. There were no unanticipated or serious adverse device effects, or serious adverse events related to the NSS or its implantation procedure as determined by investigators.

Conclusion: In this small group of patients with acute thoracic AIS A SCI implanted with the NSS, 43% of patients with early AIS conversion had additional improvement in neurological function by 12 (n=2) and 24 (n=1) months post implantation. This analysis supports the safety and probable benefit of NSS implantation in this patient population.

234: Cerebral Structural Alterations and Functional Reorganization Associated with Cervical Spondylosis by Diffusion Weighted Imaging

Azim Laiwalla, MD, PhD (Los Angeles, CA); Chencai Wang, PhD; Noriko Salamon, MD; Langston Holly, MD; Benjamin Ellingson, PhD

Introduction: Cervical spondylosis (CS) is the most common cause of spinal cord impairment, occurring in up to eighty percent of the total population, and can lead to debilitating functional impairments. Studies have demonstrated microstructural spinal cord changes, and more recently, cerebral structural and functional alterations. We hypothesized that neurological function is preserved in CS patients through upstream cerebral reorganization, particularly localized to sensorimotor and pain modulatory regions.

Methods: Prospective, observational analysis were performed on twenty-six CS patients and thirty-two neurologically intact healthy volunteers. Diffusion tensor imaging and probabilistic tractography by seeding of the brainstem were utilized to compare cohorts, and associated with severity of CS, as measured by the modified Japanese Orthopedic Association scale.

Results: CS patients had significantly lower fractional anisotropy (FA) and higher mean diffusivity (MD) along somatosensory and motor tracts ($p < 0.05$), and these alterations were correlated with worsening neurological function (i.e. corona radiata; $r = 0.1528$, $p = 0.0024$ - FA measurement; $r = 0.1144$, $p = 0.0094$ - MD measurement). Conversely, higher FA and lower MD values were observed in CS patients in a portion of the basal ganglia and internal capsule. Probabilistic tractography by seeding the brainstem identified significant differences in the corticospinal tract ($p < 0.0001$) between CS patients and healthy controls, including regions extending through the corona radiata and internal capsule.

Conclusion: CS patients undergo cortical reorganization, particularly in sensorimotor and pain modulatory regions, which may serve as a compensatory mechanism to preserve neurological function.

235: Management And Survival In Patients With Spinal Cord Astrocytomas: A Consecutive 108 Patients At A Single-Institution

Wen qing Jia (Beijing, China); Yongzhi Wang; Yaowu Zhang; Rui-Chao Chai

Introduction: Spinal cord gliomas are rare and have no established treatment guidelines. We determined the clinical characteristics and prognostic factors of spinal cord astrocytomas based on the 2016 World Health Organization (WHO) classification to improve the management and survival of patients with these rare neoplasms.

Methods: We retrospectively analyzed 108 consecutive patients with spinal cord astrocytomas in our institution from 2011 to 2018. Clinical characteristics were analyzed using descriptive statistics, and prognostic factors and survival using Kaplan-Meier and Cox regression analyses.

Results: The median age was 30 years; 82 of 108 patients (75.9%) were adults. The positive rate of H3 K27M mutation was 38%, and 31 histological grade II/III tumors were defined as grade IV diffuse midline gliomas according to the 2016 WHO classification. Low-grade astrocytomas (WHO grade I/II) accounted for 50% of cases and occurred in younger patients than did high-grade astrocytomas (27.0 vs. 35.5 years, $P = 0.001$). All patients underwent open surgical resection within the safe range. For high-grade tumors, only 42.6% of patients underwent gross total resection while nearly 40% had open biopsy. Surgical resection improved the survival of low-grade astrocytoma patients ($P = 0.014$), but not of high-grade astrocytoma patients ($P = 0.119$). Adjuvant chemo- and radiotherapy showed no significant effect on the median survival time of low- and high-grade tumors ($P > 0.05$).

Conclusion: We summarized the characteristics and prognostic factors of spinal cord astrocytomas based on the 2016 WHO classification. The findings could help with evidence-based management of spinal cord astrocytomas.

236: Improving Risk Management in Spine Surgery Patients through Cost Burden Prediction

Joseph Zabinski (Boston, MA); Richard Gliklich, MD; Costas Boussios, PhD; Jigar Bandaria, PhD; Cameron Jones, PhD

Introduction: Value-based care program management requires preoperative identification of patients at greatest risk of high postsurgical resource utilization. Identifying these patients allows clinicians to focus resources on risk reduction, particularly if contributing risk factors are also surfaced. Preoperative risk stratification is relevant for spine surgeries, as similar procedures are characterized by significant variation in cost (Ugiliweneza et al., *Spine*, 2014). This stratification is especially important in spine surgery-focused bundled payment programs, including the CMS' Bundled Payments for Care Improvement (BPCI) initiative.

Methods: We developed a machine learning model to predict future resource utilization for patients undergoing spine surgeries, trained using a patient-level dataset. Patients were selected using CPT codes in their histories associated with common spine procedures (e.g., spinal fusions). These criteria captured 578,442 patients. One year of each patient's preoperative medical history data was used to generate a single individualized risk score for each patient. Scores' ability to predict postsurgical resource utilization was assessed. The prediction system also generated key risk factors from patients' medical history with greatest contribution to assessed risk.

Results: The preoperative risk score was highly predictive of future resource utilization, including identification of highest utilizers (area under the receiver operating characteristic curve = 0.82 for presence in the top 1% of utilization). The model's use of patients' medical histories enabled isolation of key risk factors at both granular and organ system-category levels.

Conclusion: We report a pre-operative risk score for spine surgery patients that is highly predictive of future postoperative resource utilization. This performance has specific utility for predicting financial outcomes in spine surgery contexts, including risk of bundle-breaking. The model's ability to identify key risk factors may also enable better preoperative risk management. To test potential applicability, the model is undergoing trial implementation at a major spine surgery center to better inform preoperative risk management.

237: Replay of Cortical Spiking Sequences Mediates Human Memory Retrieval**Young Neurosurgeon Abstract Award**

Alex Vaz (NC); John Wittig, Jr., PhD; Sara Inati, MD; Kareem Zaghloul, MD, PhD

Introduction: Episodic memory retrieval is thought to rely on the replay of past experiences. This has been demonstrated robustly in rodent models where spatial memories are replayed and consolidated concomitant to fast frequency oscillations known as ripples. Strikingly, these memory representations take the form of highly stereotyped sequences of neural activity that are replayed with variable speeds. However, it remains unknown how neural spiking activity in humans is organized during episodic memory encoding and retrieval.

Methods: We simultaneously recorded intracranial macro-iEEG, micro-LFP, and single unit data in 6 patients with medically refractory epilepsy during monitoring for potential resective surgery. To accomplish this, we implanted subdural macro-iEEG contacts over clinically relevant brain areas and Utah micro-electrode arrays (MEAs) in the anterior temporal lobe of each patient. In order to examine temporal patterns of spiking activity during memory, the participants completed a paired associates verbal memory task during electrophysiological monitoring.

Results: We found that ripple oscillations in the human cortex reflect bursting of local spiking activity. During memory formation, this spiking activity organized into repeated memory-specific sequences for correct but not incorrect trials. Consequent successful memory retrieval involved the replay of the respective spiking sequence from the memory formation period, and this cortical spiking replay was preferentially observed following ripples in the medial temporal lobe (MTL).

Conclusion: Our findings demonstrate that episodic memories in humans are encoded by specific sequences of neural activity and memory recall involves reinstating this temporal order of activity. In a broader sense, this data connects recent findings of coupled ripple oscillations between the human MTL and neocortex to a general mechanistic understanding of how information is represented in the human brain.

238: Frameless MLC-based Linear Accelerator Radiosurgical Thalamotomies are Safe and Effective - Early Results of Prospective Phase I/II Clinical Trial

Evan Thomas (Birmingham, AL); Barton Guthrie, MD; Erik Middlebrooks, MD; Harrison Walker, MD; Richard Popple, PhD; Markus Bredel, MD, PhD

Introduction: Stereotactic radiosurgery (SRS) to the ventral intermediate nucleus (VIM) of the thalamus has been used with success to manage tremor in select patients. Because of the high doses, small target, & required precision, Gamma Knife (GK) has been the historical choice platform. Our institution recently developed a technique to replicate functional SRS GK dose distributions on a multi-leaf collimator (MLC)-equipped linear accelerator (LINAC) without cumbersome, inefficient cones. We deployed this technique & tested it in a prospective clinical trial of safety & efficacy of SRS thalamotomy for non-DBS candidate patients with medically refractory essential or Parkinsonian tremor.

Methods: We quantified pre-treatment tremor according to FTM/PROMIS scores. We generated MPRAGE, FGATIR, diffusion-weighted tractographic, & resting-state fMRI sequences with Phillips 3T Prisma MRI. We identified the VIM via both thalamic parcellation & classical stereotactic reference location, & targeted it to 130Gy dmax in a fashion dosimetrically equivalent to 4.5mm GK shot. We adjusted each target such that the 25Gy isodose line did not overlap the posterior limb of the capsule. We immobilized patients in a highly rigid thermoplastic mask (Qfix Encompass). We delivered treatment with Varian Edge LINAC with high-definition HDMLC & intrafraction optical surface monitoring (OSMS) to ensure patient immobility. We surveilled post-treatment imaging and tremor scores.

Results: We accrued 20 patients over 18 months. One withdrew, & one elected to pursue previously declined DBS. At submission, 11 of the 18 patients had ≥6 month follow-up. 10/11 (91%) exhibited clinically meaningful tremor reduction. Median tremor reduction was 59.4% (range: 11 - 100%). Time to patient-reported tremor improvement ranged from 0.3 to 15 months. No patients experienced ≥ Grade 2 toxicity.

Conclusion: Frameless, coneless MLC-based SRS thalamotomy on the LINAC is a safe, effective treatment. Proper implementation requires attentive involvement by an experienced movement disorder radiosurgery team. Data continue to mature, but current results anticipate congruence to historical GK controls. We have expanded the trial to allow 20 additional patients.

239: Hippocampal RNA Expression Gene Sets and Biological Pathways with Prognostic Value for Seizure Outcome Following Anterior Temporal Lobectomy with Amygdalohippocampectomy

Albert Alan (Tucson, AZ); Martin Weinand, MD; Ryan Sprissler, PhD; Michael Hammer, PhD

Introduction: Approximately 1% of the U. S. population suffers from epilepsy. Among these patients, 30% are defined as medically intractable and thus potential candidates for epilepsy surgery, most commonly amygdalohippocampectomy (AH) with or without anterior temporal lobectomy (ATL) in temporal lobe epilepsy (TLE). Approximately 65% of patients treated with AH will be seizure-free. Therefore, there is need to improve prognostic value of selection criteria for AH surgical candidates. Thus, we pursue an approach known as neurosurgical genomics, where the identification of RNA-Seg biomarkers will establish gene expression profiles in patients with different seizure outcomes.

Methods: Whole transcriptome analyses were performed to test the hypothesis that hippocampal tissue RNA expression differs between patients rendered seizure-free (SF) and non-seizure-free (NSF) to establish predictive prognostic biomarkers. A total of 14 patients (mean age: 33.1 years, range 16-56 years; 10 males, 4 females) with intractable TLE have undergone AH/ATL with 1-year minimum follow-up dichotomized into SF and NSF. Logistic regression analysis of Next Generation Sequencing reveals sufficient statistical power for hippocampal RNA expression data.

Results: Comprehensive analysis of hippocampal RNA expression revealed an upregulation in biological pathways consisting of glucuronidation, reproduction, and activation of matrix metalloproteinases prognostic for SF group. Likewise, an upregulation in biological pathways encompassing the innate and adaptive immune system prognostic for NSF group.

Conclusion: Hippocampal tissue RNA expression is expected to enhance selection of TLE surgery candidates by establishing predictive prognostic biomarkers for successful outcome from operative AH/ATL. This research seeks to improve our understanding of pathophysiological TLE over-activation of the innate and adaptive immune system. This increases the transcription of pro-inflammatory genes perpetuating hippocampal neuroinflammation by damaging endothelial cell tight junctions breaching the blood-brain barrier to transcellular leukocyte diapedesis influencing epileptogenicity and seizure onset.

240: Deep Brain Stimulation of the Mesencephalic Locomotor Region Acutely Enhances Locomotion in a Large Animal Model of Incomplete Spinal Cord Injury

Stephano Chang, MD (Vancouver, Canada); Andrea Santamaria, MD; Francisco Sanchez, DVM; Luz Villamil, MD; Pedro Saraiva, MSc; Yohjan Nunez-Gomez, BS; Ioan Opris, PhD; Juan Solano, MD; James Guest, MD, PhD; Brian Noga, PhD

Introduction: The mesencephalic locomotor region (MLR) is a region of the midbrain that when electrically stimulated, can elicit locomotion in small animal models and enhance locomotion in small animal models of incomplete spinal cord injury (SCI). Assessing the effect of MLR deep brain stimulation (DBS) in a freely moving large animal model of SCI is a major step in determining the feasibility of using MLR DBS to augment gait clinically for gait disorders (i.e. SCI, Parkinson's disease). We hypothesized that DBS of putative MLR sites in awake and freely moving Yucatan micropigs would augment locomotion parameters after SCI.

Methods: DBS electrodes were chronically implanted into putative MLR sites of Yucatan micropigs using MRI-guided stereotactic targeting. Intraoperative stimulation was used to evoke locomotor-like activity and confirm our stereotactic targeting. The ability to initiate and augment locomotion with MLR DBS was confirmed in intact animals before they received incomplete T9 contusive SCI by weight drop. Patterns of muscle activation in agonist/antagonist muscles of all four limbs were recorded during locomotion with and without stimulation using intramuscular EMG electrodes. Kinematics data during locomotion was collected using a motion capture system.

Results: We demonstrate that in addition to initiating and augmenting locomotion in the intact micropig, MLR DBS can be used after SCI to increase hindlimb EMG amplitudes, limb excursion, stepping frequency, weight-support, and to enhance coordination of limbs during locomotion.

Conclusion: Electrode location and stimulation parameters are crucial to eliciting specific locomotor outputs in the intact Yucatan micropig. These findings of optimal electrode position and stimulation parameters allowed us to effectively evaluate the acute locomotor effects of MLR DBS after SCI in this animal model. Our research may have direct translation to DBS trials targeting this region. Supported by DOD Award # SCI140238 and NINDS Grant 1R01 NS089972

241: Spectral Organization of Focal Seizures within the Thalamotemporal Network

Adeel Ilyas, MD (Birmingham, AL) Andrew Romeo, MD; Kristen Riley, MD; Sandipan Pati, MD

Introduction: Thalamocortical connectivity has been hypothesized to regulate temporal lobe seizures, and the presence of temporothalamic connectivity is an independent predictor of poor surgical outcome. Therefore, the objective of this study is to investigate dynamic changes in neural activity between the anterior nucleus of the thalamus (ANT) and the seizure onset zone (SOZ) in patients with drug-resistant temporal lobe epilepsy (TLE).

Methods: Eleven patients undergoing stereoelectroencephalography for seizure localization were recruited prospectively for local field potential (LFP) recording directly from the ANT. The SOZ was identified using line length and epileptogenicity index. Changes in power spectral density (PSD) were compared between the two anatomic sites as seizures (N = 53) transitioned from interictal baseline to the post termination stage.

Results: At baseline, the thalamic LFPs were significantly lower and distinct from the SOZ with the presence of higher power in the fast ripple band ($P < 0.001$). Temporal changes in ictal power of neural activity within ANT mimic those of the SOZ, are increased significantly at seizure onset ($P < 0.05$), and are distinct for seizures that impaired awareness or that secondarily generalized ($P < 0.05$). The onset of seizure was preceded by a decrease in the mean power spectral density (PSD) in ANT and SOZ ($P < 0.05$).

Conclusion: The ANT can be recruited at the onset of mesial temporal lobe seizures, and the recruitment pattern differs with seizure subtypes. Furthermore, changes in neural dynamics precede seizure onset and are widespread to involve temporothalamic regions, thereby providing an opportunity to intervene early with closed-loop DBS.

242: Cross-frequency Interactions and Phase Coding in Piriform Cortex Support Human Working Memory: Intracranial EEG Study

Andrew I. Yang, MD, MS (Philadelphia, PA); Heidi Jiang, PhD; Gulce N Dikecligil; Stephan Schuele, MD, MPH; Joshua Rosenow, MD; Kathryn Davis; Timothy Lucas, MD, PhD; Jay Gottfried, MD, PhD

Introduction: Brain oscillations in anterior hippocampus (AH) as well as neocortex have been implicated in working memory (WM). How sensory regions may interact with downstream regions such as AH to enable precise sensory encoding and short-term storage of this information is poorly understood. We hypothesized that cross frequency interactions, in the form of phase amplitude coupling (PAC), and phase coding, would drive olfactory WM.

Methods: We obtained local field potentials (LFP) from 8 patients undergoing intracranial EEG for refractory epilepsy. Subjects completed an olfactory WM task (Sternberg), in which 3 odor items (selected randomly from a pool of 10 unique odors) were presented sequentially, followed by a maintenance period. Subjects were then delivered a probe odor, and asked to identify it as previously encountered or novel (object identity). If the former, they were also asked to report which item in the sequence of 3 cues matched the probe (object position).

Results: As in its visual counterpart, the olfactory task elicited theta-gamma PAC in AH. Specific to the olfactory task, we found elevated piriform cortex (PC)-AH theta coupling, as well as theta-gamma PAC in PC. Odor identity could be decoded from the latter. Network activity was reinstated in response to the probe in both structures, with the degree of reinstatement correlating with behavioral performance. As in its visual counterpart, successful encoding of odor position was accompanied by representations along distinct theta phases within AH. Odor position could additionally be discriminated from PAC dynamics in PC, only when subjects successfully recalled object position.

Conclusion: This is the first demonstration of how temporal processing in human olfactory system may enable encoding and maintenance of object identity and position. Theta-gamma PAC and theta phase coding may be central components of a neural substrate consistent with the sensory recruitment model of WM.

243: Potential therapeutic mechanism of centromedian-parafascicular complex deep brain stimulation in Tourette syndrome

Aaron Elliott Rusheen (Rochester, MN); Juan Rojas Cabrera; Abhijeet Barath; Hojin Shin; Michael Jensen; Kevin Bennet; Charles Blaha; Yoonbae Oh; Kendall Lee

Introduction: Tourette syndrome (TS) is a neurodevelopmental disorder characterized by chronic and disabling motor and vocal tics. For select severely affected subjects, deep brain stimulation (DBS) has emerged as an effective therapy. Despite the benefit of DBS, it is unknown if stimulation affects specific neural pathways that cause improvement in symptoms. Previous studies have demonstrated a major role of dopamine in TS and our own fMRI study of TS patients receiving DBS revealed hypoactivity in the striatum. Here, we directly investigate if centromedian-parafascicular complex (CMPf) DBS alters striatal extracellular dopamine concentrations in vivo.

Methods: In urethane anesthetized normal rats, the parafascicular nucleus (Pf; CMPf in humans) was electrically stimulated using concentric bipolar electrodes (90-130Hz; .4mA; .2-2ms pulse width; 2s-phasic, 30min-tonic). Voltammetry (FSCV-phasic, mCSWV-tonic) was used to measure stimulation-evoked phasic and tonic changes in extracellular dopamine concentrations using a carbon-fiber microelectrode. Pharmacological confirmation was performed with nomifensine and alpha-methyl-p-tyrosine (AMPT), and with escitalopram (inhibitors of dopamine reuptake and synthesis, and serotonin reuptake, respectively).

Results: Pf electrical stimulation (4 rats) elicited a time-locked phasic increase in striatal dopamine release (315 ± 136 nM). Nomifensine administration enhanced the phasic stimulation-evoked response by 50%, AMPT decreased the response by 40%, and escitalopram had no effect. Tonic striatal extracellular dopamine levels were recorded in response to 30 min continuous Pf stimulation, with time-locked, frequency-dependent fluctuations in dopamine concentrations (n=6 rats) that increased with dopamine reuptake blockade (nomifensine) and decreased with dopamine synthesis inhibition (AMPT).

Conclusion: Our results suggest CMPf DBS causes fast-phasic synaptic release of dopamine and stimulation parameter-dependent modulation of tonic extracellular dopamine concentrations in the dorsal striatum. These findings have important implications for the mechanism of motor tic reduction and for clinical stimulation parameterization. Precisely how DBS alters extracellular dopamine concentrations and if changes are correlated with motor tic amelioration are the subject of current study.

244: Radiofrequency Thermocoagulation (RF-TC) in Refractory Focal Epilepsy: The Montreal Neurological Institute (MNI) Experience

Farhan Arshad Mirza, MBBS (Lexington, KY); Jeffery Hall, MD, MSc

Introduction: Radiofrequency thermocoagulation (RF-TC) is a minimally invasive ablative option for refractory focal epilepsy. RF-TC can be delivered via Stereoelectroencephalography (SEEG) electrodes implanted for seizure localization. In this series, we describe our experience at the Montreal Neurological Institute (MNI).

Methods: Retrospective chart review was conducted of all patients who have undergone SEEG based RF-TC at our institution.

Results: Fourteen patients underwent robotic SEEG implantation and subsequent RF-TC (May 2016-Sept 2019). Mean age 34.43 +/- 10.12 years, and 13.77 +/- 6.39 years at seizure onset. On 3T MRI, eight patients had lesional findings: four Focal Cortical Dysplasia (FCD), three Peri-Ventricular Nodular Heterotopia (PVNH), and one cavernoma. After RF-TC, two PVNH patients were seizure free, and one required temporal neocortical/PVNH resection (Engle 1a); one of four patients with FCD was seizure free (Engle 1a), two attained seizure freedom after resection (Engle 1a and 1b), whilst one continues to have significant seizures (Engle 4b). One patient with cavernoma and low central area SOZ did not benefit from RF-TC and is planned for resection. In the six MRI negative patients, two achieved seizure-freedom for 3 months and 1 year, respectively, subsequently requiring resection (Engle 1a). One patient with non-lesional mesial temporal lobe epilepsy (MTLE) remains seizure free at six weeks. Three had seizure recurrence immediately (Engle 4b). Overall, seven patients (50%) achieved Engel 1a or 1b, one each 2b and 3a, and five Engle 4b. No significant peri-operative complications were noted with either SEEG implantation, RF-TC, or SEEG removal.

Conclusion: Radiofrequency thermocoagulation (RF-TC) is a safe ablative procedure for refractory focal epilepsy. For PVNH, FCD, and MTLE, it can be a frontline ablative method. In MRI negative cases, further study is needed. SEEG placement should take into consideration the ability to perform RF-TC in the SOZ if the hypothesis is confirmed by the study.

245: Real World Clinical Outcomes Using a Novel Directional Lead from a Multicenter Registry of Deep Brain Stimulation for Parkinson's Disease

Jan Vesper, MD, PhD (Dusseldorf, German); Roshini Jain, MS; Heleen Scholtes, MS; Alex Wang, MS; Steffen Paschen, MD; Michael Barbe, MD; Andrea Kühn, MD; Monica Pötter-Nerger, MD; Jens Volkmann, MD; Guenther Deuschl, MD

Introduction: Deep Brain Stimulation (DBS) systems have historically used ring-shaped electrodes that produce stimulation fields with limited control over field shape and volume of tissue activated. Directional current steering may permit a more personalized DBS approach with respect to individualized shape and pattern of electrical field and corresponding volume of tissue activated. In this report, initial real-world outcomes using a directional lead with a Deep Brain Stimulation (DBS) system capable of multiple independent current source control (MICC) for use in managing symptoms of levodopa-responsive Parkinson's disease (PD) are reported.

Methods: The Vercise DBS Registry (ClinicalTrials.gov Identifier: NCT02071134) is a prospective, on-label, multi-center, international registry sponsored by Boston Scientific. Subjects were implanted with a directional lead included as part of a multiple-source, constant-current directional DBS system (Vercise Cartesia, Boston Scientific). Subjects were followed up to 3-years post-implantation where their overall improvement in quality of life and PD motor symptoms was evaluated. Clinical endpoints evaluated at baseline and during study follow-up included Unified Parkinson's disease Rating Scale (UPDRS), MDS-UPDRS, Parkinson's disease Questionnaire (PDQ-39), and Global Impression of Change.

Results: As of March 2019, 283 enrolled patients have been implanted with the directional lead. Change in PDQ-39 Summary Index demonstrated improvement in Quality of Life following DBS implant with the directional lead out to 6- (n=120) and 12-months (n=129) post-implant, respectively (p<0.001). Several sub-domains such as Activities of Daily Living, Bodily discomfort showed sustained improvement at 1-year post-implant (p<0.0001). Improvements in motor function (change in MDS-UPDRS III scores-meds off condition) was observed at 6- and 12-months post-implant. Additional data is to be presented.

Conclusion: Enabling fractionalization of current using MICC can permit application of a well-defined, shaped, electrical field. This on-going registry represents the first comprehensive, large scale collection of real-world outcomes using a directional lead and an MICC-based DBS system.

246: Functional Activation Patterns Produced by Deep Brain Stimulation of the Anterior Nucleus of the Thalamus in Humans

Sanjeet Grewal, MD (Jacksonville, FL); Erik Middlebrooks; Lin Chen; Lela Okromelidze; William Tatum; Robert Wharen

Introduction: Deep brain stimulation (DBS) of the anterior nucleus of the thalamus (ANT) is a recently approved therapy for drug-refractory epilepsy for patients not amenable to resective surgical options. In this study, we propose a method for investigating the human in vivo effects of ANT DBS using blood-oxygen-level dependent (BOLD) MRI and present the first human data showing the whole brain activation pattern with DBS stimulation of the ANT.

Methods: Two patients undergoing ANT DBS for epilepsy were prospectively recruited. After DBS implantation, BOLD MRI was performed using a block design after the DBS was programmed to alternate ON/OFF in 30 second blocks. The scanner was triggered during the beginning of a DBS OFF block utilizing surface electrophysiological recording to detect the DBS cycle. Nine total runs were obtained. Each individual run then underwent general linear modeling (GLM) correlated to an "ideal" waveform followed by a fixed-effects model. The resultant group-level results were thresholded using a cluster threshold of $z > 3.1$ and cluster p threshold of 0.05.

Results: Active ANT stimulation produced activation within several areas, including the bilateral anterior cingulate (ACC) and posterior cingulate cortex (PCC), precuneus, medial prefrontal cortex, amygdala, ventral tegmental area, hippocampus, striatum, and right angular gyrus.

Conclusions: Utilizing block-design BOLD MRI, we were able to show widespread activation resulting from ANT DBS. Numerous studies have highlighted the potential role of the default mode and limbic networks in seizure propagation and seizure threshold. Importantly, our study shows overlap with multiple areas of both the default mode and limbic networks suggesting that these nodes may modulate the effect of seizure control with ANT DBS. Our findings may ultimately provide an imaging-based biomarker for successful DBS targeting and programming, but additional studies are needed.

247: Beta-Band Modulation in the Human Amygdala during a Conflict Response Task

Angad Gogia(Irvine, CA); Kuang-Hsuan Chen, PhD; Roberto Martin del Campo-Vera, PhD; Rinu Sebastian, MS; Morgan Lee, BS; Daniel Kramer, MD; Terrance Peng; Ali Tafreshi, BA; Michael Barbaro, BA; Charles Liu, MD, PhD; Spencer Kellis, PhD; Brian Lee, MD, PhD

Introduction: The human amygdala is a deep brain structure made of interconnected deep brain nuclei that play a role in emotional learning, fear response, reward-based behavior, and processing emotional conflict. However, it is unknown if it plays a role in processing non-emotional conflict as well. The Stroop Task is a well-studied color-word conflict scenario that has been used to study conflict response in humans. The limited intracranial electrophysiology work done in humans has shown that power changes in the beta-band (13-30 Hz) may be involved in processing non-emotional conflict. Here, we investigate beta-band power changes in the human amygdala during a modified Stroop Task in five patients with medically-refractory epilepsy.

Methods: Intracranial depth electrodes were implanted in five epileptic patients (3 female; age 20-61) for seizure localization and EEG monitoring. Local field potential (LFP) data from macro contacts sampled at 2000Hz was used for the analysis and was collected during a modified version of the classic Stroop Task with four distinct task conditions. A non-parametric cluster-permutation t-test was used to identify periods of significance during the cue processing period.

Results: Time-frequency analysis for the LFP data showed a statistically significant increase in amygdaloid beta-band (13-30 Hz) power during cue-processing (i.e. post-stimulus, pre-response) in the incongruent condition (650-875ms, cluster-based correction for multiple comparisons, $p < 0.05$) for three out of five patients. There was no significant beta-band power change observed during the cue processing period of the congruent condition in the amygdala of these three patients.

Conclusion: These findings suggest that human amygdaloid beta-band power changes play a role in successful conflict identification and automatic response inhibition. It builds upon work indicating the amygdala plays a role in processing emotional conflict and suggests that the amygdala plays a role processing non-emotional cognitive tasks as well.

248: Cyberknife Radiosurgery for Intractable Obsessive Compulsive Disorder: A Single-Center Experience

Sait Sirin, MD (Ankara, Turkey); Hasan Uysal, PhD; Mehmet Enkavi, MSc; Hulya Sirin; Kaan Oysul

Introduction: Severely impaired patients with obsessive and compulsive disorder may remain refractory to medical and behavioral treatments. These patients may benefit anterior capsulotomy using radiosurgery. We evaluated the safety and efficacy of Cyberknife radiosurgery in intractable patients with OCD.

Methods: At our center, we treated 15 consecutive patients with intractable OCD using Cyberknife Robotic Radiosurgery between February 2014 and August 2019. Yale-Brown Obsessive Compulsive Scale, Beck Anxiety Scale and Beck Depression Scale were used before the treatment and in the follow-up. Bilateral radiosurgical capsulotomies were performed using targets at the midputaminal point of the anterior limb of the internal capsule. Median prescription dose to the target margin was 80 Gy (range, 70-95 Gy) for each side.

Results: Median follow-up time was 28 months, ranging 2 to 68 months. In three patients, a second treatment was performed due to lack of bilateral lesions 7, 8 and 10 months after initial procedure. Patients tolerated the procedure well without significant acute adverse events. No patients developed transient edema or radionecrosis that required medical treatment. 50% of the patients showed marked clinical improvement.

Conclusion: Cyberknife radiosurgery may be a safe and effective treatment in patients with intractable OCD.

249: Thalamic Deep Brain Stimulation for Essential Tremor: Relation of the Dentato-Rubro-Thalamic Tract with Stimulation Parameters

Andrew I. Yang, MD, MS (Philadelphia, PA); Vivek Buch, MD; Sabrina Heman-Ackah, MD, PhD; Ashwin Ramayya, MD, PhD; Frederick Hitti, MD, PhD; Nathan Beatson, BS; Hanane Chaibainou; Melissa Yates, BA; Sumei Wang, MD; Ragini Verma, PhD; Ronald Wolf, MD, PhD; Gordon Baltuch, MD, PhD

Introduction: The primary target in deep brain stimulation (DBS) for essential tremor (ET), the ventro-intermedius (VIM) thalamic nucleus, cannot be visualized on conventional imaging. There has been much interest in the dentato-rubro-thalamic tract (DRTT) for target localization, but evidence for DRTT as a putative stimulation target in tremor suppression is lacking. We evaluated proximity of DRTT in relation to DBS stimulation parameters.

Methods: This is a retrospective analysis of 26 consecutive patients undergoing DBS with microelectrode recordings (46 leads). Deterministic fiber tracking was performed with neighboring corticospinal tract and medial lemniscus as landmarks for seed regions. Clinically-optimized stimulation parameters were obtained from the most recent follow-up (6.2 months). Volume of tissue activated (VTA) around contacts was calculated from a finite-element model.

Results: Tremor severity was reduced in all treated hemispheres, with 70% improvement in the treated-hand score of Clinical Rating Scale for Tremor. The DRTT in the commissural plane was anterior (1.5 ± 2.1 mm) and lateral (2.1 ± 1.9 mm) to the lead. At the level of the active contact (2.9 ± 2.0 mm superior to commissural plane), the tract was lateral to the contact (5.5 ± 2.4 mm). Distance from active contact to nearest fibers of DRTT were 2.4 ± 1.6 mm. The VTA overlapped with the nearest fibers in 77% of active contacts. Stimulation voltage requirements were positively correlated with distances from active contact to DRTT (Kendall's $\tau = 0.35$, $p = 0.003$). In contrast, there was a weaker correlation with distance to VIM (atlas-based stereotactic targeting formulas), which did not reach statistical significance ($\tau = 0.23$, $p = 0.06$).

Conclusion: Active contacts in proximity to DRTT had lower voltage requirements. Data from a large cohort provides support for DRTT as an effective stimulation target for tremor control.

250: Deep, Self-Supervised Learning For Patient-Specific Anomaly Detection in Stereoelectroencephalography*Michael Martini (New York, NY); Anthony Costa, PhD; Kanaka Rajan, PhD; Fedor Panov, MD; Eric Oermann, MD*

Introduction: Stereoelectroencephalography (SEEG) is a neurosurgical method for localizing seizures in patients with medically refractory epilepsy. Abnormal EEG waveforms can be rare and difficult to detect over days of continuous monitoring. Long Short-Term Memory (LSTM) networks can be exploited for self-supervised anomaly detection using novel dynamic thresholding methods to minimize false positives. This method has been adapted by our group for SEEG anomaly detection after original development by NASA for telemetry data from the Mars rover, Curiosity.

Methods: Recordings were acquired from 15 patients with medically refractory epilepsy who underwent continuous monitoring and SEEG lead implantation. Data were preprocessed with 50 Hz low-pass filtering, scaling to (-1,1), and a 50/50 train-test split. LSTM models were trained on recordings from each patient and tested on holdout sets. Errors were computed from differences in predicted and actual test sequences. Self-supervised dynamic thresholding was applied to the errors by identifying thresholds that maximize the decrease in the means and standard deviations (SD) of the errors if values above the thresholds were removed. Static error thresholding (mean $\pm$ 2 SD) was also used for comparison. Anomalous errors were scored by distance from the chosen threshold and compared to anomalies identified by a panel of fellowship-trained epileptologists.

Results: Self-supervised dynamic thresholding demonstrated versatility in detecting true anomalies and excellent metrics for precision (87%) and recall (82%) across all patients. By comparison, traditional static thresholding methods dramatically increased numbers of false positives. Crossover studies, in which train-test sample pairs were derived from different patients, also showed increased false positives and false negatives, underscoring that the models are patient-specific.

Conclusion: This study applies deep learning techniques adapted from NASA to construct predictive models for identifying anomalous events in SEEG recordings. The self-supervised and patient-specific nature suggest utility for improving the efficiency of seizure detection in clinical settings.

251: Advanced Age Does Not Increase Risk of Post-Operative Complications Following Deep Brain Stimulation Surgery*Andre Wakim (Phoenix, AZ); Margaret Lambert; Francisco Ponce, MD*

Introduction: Deep brain stimulation (DBS) is an elective procedure that can dramatically enhance an individual's quality of life. Since it is not considered life-saving, it is important that providers produce consistently good outcomes; one factor to consider is patient selection. While older age may sometimes be considered a relative contraindication to some elective surgeries, progression of disease may suggest that these patients stand to benefit significantly from surgery. To further the understanding of the risks of treating patient with advanced age with DBS, this study compares perioperative complication rates in patients aged 75+ to those younger than 75.

Methods: A total of 817 patients who had undergone DBS surgery at Barrow Neurological Institute for various indications between 2011 and 2019 were stratified into elderly (age $\geq$ 75, n=167, 22%) and young (age < 75, n=638, 78%). Risk of common perioperative complications and various outcome measures was compared between the two groups using risk ratio (RR) and a 95% confidence interval (CI).

Results: The elderly group was at no increased risk of an intracranial bleed (RR=1.37, CI:0.67-2.79), seizure (RR=0.40, CI:0.05-3.11), readmission within 90 days of discharge (RR=1.25, CI:0.83-1.90), surgical site infection (RR=1.34, CI:0.36-4.99), or nonsurgical site infection (RR=1.78, CI:0.33-9.65). However, the elderly group was at an increased risk of altered mental status (RR=2.32, CI:1.46-3.69), experiencing >1-night stay (RR=1.43, CI:1.17-1.75), transient neurological deficit (RR=1.84, CI:1.01-3.36), or transient urinary retention (RR=2.32, CI:1.24-4.36).

Conclusion: Although the elderly group had a higher risk of postoperative cognitive changes, this study found that the elderly group did not have an increased risk of intracranial hemorrhage, infection, or readmission. Advanced age alone should not be considered a contraindication for DBS.

252: Exploring the Latent State of Coma and Consciousness

Sima Mofakham (Port Jefferson, NY); Adam Fry; Joseph Adachi; Jordan Saadon; Theresa Gammel; Racheed Mani; Megan Cosgrove; Zhe Wang; Nathan Winans; John Servider; Susan Fiore; Charles Mikell

Introduction: Treatment of coma after traumatic brain injury(TBI) is primarily limited by a lack of understanding of the underlying mechanisms supporting consciousness. Several functional imaging studies have identified coordinated activity across frontal-parietal networks(FPN) as the seat of consciousness, however, direct recordings from FPN following TBI are sparse. To address this gap, we performed direct depth electrode recordings from FPN in comatose patients following TBI. We utilized dynamical system and machine learning methodology to characterize the latent state of FPN dynamics and its evolution as patients regain consciousness.

Methods: Experiments: One control (epilepsy) and five comatose TBI patients(GCS less than 8) were enrolled. Upon obtaining consent by a legally authorized representative, we implanted a seizure-monitoring stereotactic depth electrode spanning from the prefrontal cortex (DLPFC) to anterior cingulate gyrus(ACC). Single-pulses of stimulation were administered to these contacts to further interrogate FPN dynamics. Analysis: In addition to time-frequency analysis, we used principal component analysis (PCA), delay embedding, and Kalman filtering to extract the underlying dynamical system properties supporting coma and consciousness.

Results: We found that the complexity and dimensionality of the electrocorticography(EEG) recordings correlate with the level of consciousness after TBI and patient outcomes. We discovered that the phase-space of FPN in comatose patients who did not recover is confined within a 'limit-cycle attractor', which is highly repetitive and predictable. We characterized the extent to which single-pulse stimulation changed the trajectory of this attractor. Conversely, the phase-spaces in recovering comatose patients were high dimensional, chaotic and unpredictable.

Conclusion: The dynamical system supporting deep coma is a deterministic attractor that can be perturbed using single-pulses of stimulation. Understanding the characteristics of this attractor and its response to stimulation can guide future neuromodulatory therapies to facilitate the return of consciousness.

253: Spectral and phase-amplitude coupling signatures in human hippocampus oscillations during propofol-induced anesthesia

Kejia Hu (Shanghai, China); Bomin Sun

Introduction: General anesthesia (GA) is a drug-induced, reversible state comprised of several components: unconsciousness, amnesia (loss of memory), analgesia, akinesia, and hemodynamic stability with control of the stress response. The different components of general anesthesia may involve different brain structures and neural circuits. The involvement of the hippocampus in memory has been extensively established. However, the effect of general anesthesia on hippocampal neural activity in humans still remains unclear.

Methods: Bipolar local field potentials (LFPs) were directly recorded from the hippocampus using implanted deep brain stereo-electroencephalography (SEEG) electrodes in 6 patients with epilepsy, during induction of GA with propofol. Power-frequency spectra, and phase-amplitude coupling (PAC) were used to characterize the neural signatures in hippocampus when awake and during induction of GA.

Results: We found that GA is characterized by increased alpha power and decreased gamma power in the hippocampus. In addition, phase-amplitude coupling between hippocampal alpha and gamma oscillations strongly increased during unconscious state compared with awake state.

Conclusion: Our results suggest that this specific alpha phase-gamma amplitude coupling occurred in the hippocampus during propofol-induced unconscious state could be a possible electrophysiological mechanism for explaining propofol-induced amnesia. Key words: Hippocampus, epilepsy, local field potentials, unconscious, propofol, stereo-electroencephalography

254: Impulse Control Disorders Correlate with Relatively Preserved Mesolimbic Probabilistic Connectivity in Patients with Parkinson Disease

Hiro Dakota Sparks (Los Angeles, CA; Hannah Riskin-Jones, MS; Collin Price, MD; Nadia Hashoush, BS; Nader Pouratian, MD, PhD

Introduction: The relationship between Parkinson Disease (PD) pathology, dopamine replacement therapy (DRT), and impulse control disorder (ICD) development is still incompletely understood. Given the sensorimotor-lateral substantia nigra (SN) selective degeneration associated with PD, we posit that a relative sparing of the limbic-medial SN in the context of DRT drives impulsive, reward-seeking behavior in PD patients with ICDs.

Methods: Impulsive and control participants were selected from a consecutive list of PD patients receiving pre-operative deep brain stimulation (DBS) planning scans including 3T structural MRI and 64 direction diffusion tensor imaging (DTI). Using previously identified substantia nigra (SN) subsegment network connectivity profiles to develop classification targets, we first performed split-hemisphere target-based SN segmentation with probabilistic tractography. We then compared the relative subsegment volumes and strength of connectivity between the SN and the limbic, associative, and motor network targets.

Results: Our results show that there is greater probability of connectivity between the SN and limbic network targets relative to motor and associative network targets in PD patients with recent history of ICD as compared to PD patients without ICD ($P = 0.019$). We did not observe relative volumetric subsegment differences across groups.

Conclusion: Firstly, our results suggest that fine-grained, atlas-derived classification targets may be used in PD to parcellate and classify functionally distinct subsegments of the SN, with the apparent preservation of previously reported topographical limbic-medial SN, associative-ventral SN, and sensorimotor-lateral SN orientation. Furthermore, our results contribute to a growing body of evidence that suggest relative degeneration amongst SN-associated dopaminergic networks determines the impulsivity phenotype. Recognizing these neural correlates and potential predisposing factors of these severe behavioral symptoms is important for guiding future clinical practice and preventive strategies.

255: Repopulation of Microglia Using Bone Marrow Transplantation As A Novel Therapeutic Platform for Neurological Disorders

Kevin K. Kumar, MD, PhD (Stanford, CA); Yohei Shibuya, PhD; Yongin Yoo, PhD; Marius Mader, MD; Angel Ayala; Muna Rizal, PhD; Judith Shizuru, MD; Raag Airan, MD, PhD; Marius Wernig, MD, PhD

Introduction: Microglia are brain-resident myeloid cells that sense cellular damage and mediate inflammatory response, processes associated with several neurological disorders. Microglia exist in both resting and activated states. Microglia are activated with inflammation and have altered function during aging. We sought to assess microglial function in the aged brain and evaluate brain function can be rejuvenated by providing young regenerated microglia using bone marrow transplantation (BMT).

Methods: Bone marrow was isolated from young and aged UBC-GFP labeled C57BL/6 donor mice and injected into retro-orbital sinus of recipient mice after pre-treatment with busulfan, a myeloablative chemotherapeutic. On post-transplant day 28, recipient mice were treated with PLX5622, a selective CSF1R inhibitor, to deplete endogenous microglia. Brains were harvested from BMT-mice for flow cytometry, immunocytochemistry, and RNA-seq at 7-24 weeks. Additionally, a busulfan-free protocol composed of pretreatment with ACK2, a selective c-Kit antibody, followed by low-dose radiation was performed. These mice were treated with MR-guided focused ultrasound (MRgFUS) to permeabilize the blood brain barrier.

Results: PLX5622-treated BMT mice demonstrated repopulation of 90% of microglia niches by GFP+, IBA1+ circulation-derived microglia-like cells (CDMCs) compared to controls (10-20%) ($p < 0.001$). Efficient repopulation of CDMCs was also observed after transplantation of hematopoietic progenitors (Lin-, c-Kit+Sca-1+IL7R-CD34-FcR II/III-). BMT from young into aged recipients demonstrated that CDMCs acquired a cellular morphology and expression profile similar to aged microglia ($p < 0.01$). While the busulfan-free protocol had low efficiency (5-10%), preliminary studies suggest MRgFUS can enhance the amount of GFP+, IBA1+ CDMCs in the recipient brain.

Conclusion: Here we describe high efficiency repopulation of microglia with CDMCs after BMT. While transplanted CDMCs from young mice adopted aged-brain signature, this technique represents a novel cellular delivery platform to the brain. Our future work seeks to minimize toxicity of this protocol using ACK2 and MRgFUS. This work has potential application to the treatment of neurological disorders.

256: Pilot Study of Surgical Autonomy Program (SAP) For Resident In Pediatric Neurosurgery

Andrew Benjamin Cutler, MD (Durham, NC); Alexander Suarez; Charis Spears; Sarah Hodges; Lefko Charalambous; Rajeev Dharmapuri; Shivinand Lad; Michael Haglund

Introduction: Existing tools for evaluating resident operative competence are disruptive to operative workflow, are resource-intensive, and are completed long after the procedure in question making the feedback more summative than the preferred formative feedback. Duke Neurosurgery developed and implemented an innovative, smartphone-based tool, the Surgical Autonomy Program (SAP), in our pediatric neurosurgery workflow. We hypothesized that it would improve efficiency and efficacy of the resident and faculty feedback process. Here we present our experience in pediatric neurosurgery.

Methods: The SAP applies Vygotsky's Social Learning Theory to the process of acquisition of surgical skills and competence. We examined resident and faculty use for index pediatric neurosurgical cases in a 26-month pilot at Duke University Hospital. Between August 2017 and October 2019, Duke Neurosurgery implemented the IRB-approved SAP, which was made available to all Duke Neurosurgical faculty and residents. We present data from 171 pediatric neurosurgery cases performed at Duke University Hospitals and recorded within the SAP software, comprising 91 ventriculo-peritoneal shunts, 37 tethered cord repairs, 20 craniotomies for tumor, 10 craniotomies for epilepsy, 8 craniotomies for synostosis, and 5 Chiari decompressions.

Results: The SAP provides a scalable and efficient approach that divides each surgical procedure into four Zones of Proximal Development (ZPD). Furthermore, the TAGS scale provides insights into resident expectations and faculty perceptions. The SAP appeared to be both efficient and feasible for resident self-evaluation (median 16 sec, mean 26 sec) and faculty evaluation of residents (median 17 sec, mean 36 sec).

Conclusion: This pilot has demonstrated the ability of the SAP to easily and clearly measure resident learning and progress in performing pediatric neurosurgery and enhance the efficiency, frequency and timeliness of intraoperative assessment. This information can be used to advise individual residents, modify program curricula, and inform national training guidelines for pediatric neurosurgery.

257: Machine versus Human: Deep Learning to Automatically Detect and Diagnose Pediatric Brain Tumors in a Large Multi-Institutional Study

Jennifer Lauren Quon, MD (Stanford, CA); Wasif Bala, BS; Leo Chen, MD; Lily Kim, BA; Michelle Han, BS; Katie Shpanskaya, BS; Edward Lee, PhD; Gerald Grant, MD; Michael Edwards, MD; Samuel Cheshier, MD, PhD; Kristen Yeom, MD

Introduction: Pediatric brain tumors are the most common solid cancer in children. Tumor subtype often dictates prognosis and the optimal treatment regimen including the necessary degree of surgical resection. However, accurate and timely diagnosis based on imaging alone is limited outside of major academic centers. We sought to develop a deep learning model to automatically detect and classify the four most common pediatric posterior fossa brain tumors on MRI.

Methods: Pre-intervention T2-weighted brain MRIs were retrospectively collected from 185 normal and 617 patients with posterior fossa tumors from 5 academic institutions. Ground truth diagnoses were determined radiographically for 122 diffuse intrinsic pontine glioma (DIPG), and pathologically for 272 medulloblastoma, 135 pilocytic astrocytoma, and 88 ependymoma patients. A modified ResNeXt-50-32x4d deep learning architecture pre-trained on ImageNet was further trained with 493 tumor MRIs, with 135 tumor and 183 normal MRIs used as a held-out test set. Model performance was compared against four blinded, board-certified radiologists.

Results: On a held-out test set of 318 scans (135 tumor and 183 normal), the model correctly identified the presence of tumor with an AUROC curve of 0.99. The model's overall tumor subtype classification accuracy was 90% with an F1 score of 0.79 compared to an average radiologist accuracy of 87% and F1 score of 0.76. On principal component analysis, DIPG seem to occupy the most distinct feature space, followed by pilocytic astrocytoma, medulloblastoma, then ependymoma, consistent with model performance. Radiologists' performance varied by tumor subtype and subspecialty training.

Conclusion: We present the first deep learning model developed using a large multi-institutional dataset that accurately detects and classifies pediatric posterior fossa tumors using T2-weighted MRIs. This model can serve as a triaging tool for computer-aided diagnosis and the foundation for ongoing work to automatically characterize genetic subgroups within each tumor type based on imaging.

258: Early Obliteration of Pediatric Brain Arteriovenous Malformations after Stereotactic Radiosurgery: An International Multicenter Study

Rebecca Burke, MD (Charlottesville, VA); Ching-Jen Chen, MD; Dale Ding, MD; Thomas Buell, MD; Jennifer Sokolowski, MD, PhD; Cheng-Chia Lee, MD, PhD; Douglas Kondziolka, MD, PhD; Natasha Ironside; Robert Starke, MD; L. Dade Lunsford, MD; Jason Sheehan, MD, PhD

Introduction: Stereotactic radiosurgery (SRS) is a treatment option for pediatric brain arteriovenous malformations (AVMs), and early obliteration could encourage SRS utilization for a subset of particularly radiosensitive lesions.

Methods: We performed a retrospective review of the International Radiosurgery Research Foundation AVM database. Obliterated pediatric AVMs were sorted into early (obliteration ≤ 24 months after SRS) versus late (obliteration > 24 months after SRS) responders. Predictors of early obliteration were identified, and the outcomes of each group were compared.

Results: The overall study cohort comprised 345 pediatric patients with obliterated AVMs. The early and late obliteration cohorts comprised 95 (28%) and 250 (72%) patients, respectively. Independent predictors of early obliteration were female gender, single SRS treatment, higher margin dose, higher isodose line, deep AVM location, and smaller AVM volume. The crude rate of post-SRS hemorrhage was 50% lower in the early (3.2%) versus late (6.4%) obliteration cohorts but this difference was not statistically significant ($p=0.248$). The other outcomes of the early versus late obliteration cohorts were similar, with respect to symptomatic radiation-induced changes (RIC), cyst formation, and tumor formation.

Conclusion: Approximately one-quarter of pediatric AVMs that obliterate after SRS will achieve this radiological endpoint within 24 months of initial SRS. We identified multiple factors associated with early obliteration, which may aid in prognostication and management. The overall risk of delayed hemorrhage, RIC, cyst formation, and tumor formation, were not statistically different in patients with early versus late obliteration.

259: Surgical Outcomes of Revision Peri-Insular Hemispherotomy: A Single Institution Experience

Mohammed Omar Iqbal, MD (Newark, NJ); Martin Tisdall, MBBS; Zubair Tahir, MBBS

Introduction: Ongoing seizures after hemispherotomy for epilepsy present a diagnostic and therapeutic challenge in further patient management. Initial response to first hemispherotomy at 1 year may help predict prognosis for revision hemispherotomy. We report long term follow-up of a single institution experience with revision hemispherotomy.

Methods: Retrospective chart review of all medical records of patients who underwent revision peri-insular hemispherotomy. Data collected included diagnosis, age, Engel outcomes after first hemispherotomy and after final operation and time to recurrence of seizures.

Results: Between 1998 and 2018, 230 patients underwent peri-insular hemispherotomy (PIH). Of these patients, 24 (10.4%) underwent revision PIH for hemimegalencephaly (14), Rasmussens Encephalitis (3), Sturge-Weber Syndrome (2), cortical dysplasia (2), and Infantile Epileptic Encephalopathy (1). There were 15 males with a mean age of all children of 7.79 yrs at time of final revision. 18 patients underwent 1 revision, 4 with 2 revisions, 2 with 3 revisions. Mean time to seizure recurrence was 27 months. Engel outcome reported at 1 year or sooner when seizure frequency worsened after index hemispherotomy was 1 (38%), 2 (24%), 3 (24%), 4 (14%). Mean time to seizure recurrence for patients with initial Engel 1 outcome was 50.3 months. Engel outcome after final revision was 1 (52%), 3 (38%), and 4 (10%) with a mean follow up of 4.6 years. Of those with initial Engel 1 outcome, Engel outcome after final operation was 1 (50%), 3 (25%), 4 (25%). Of the patients with multiple revisions, 33% ended with Engel 1 outcomes after final operation.

Conclusion: Despite Engel 1 outcomes after PIH, seizures may return up to 4 years after operation. Revision PIH offers a 50% chance of Engel 1 outcome after final surgery. Long term surveillance for all patients with PIH is necessary to identify patients that may still benefit from further disconnection procedures.

260: Paroxysmal Discharges in Cortical Tissue Slices from Pediatric Epilepsy Surgery Patients: Critical Role of GABAB Receptors in the Generation of Ictal Activity

Simon Levinson (Los Angeles, CA); Conny Tran, MD; Michael Levine, PhD; Harry Vinters, MD; Gary Mathern, MD; Carlos Cepeda, PhD

Introduction: In pediatric epilepsy, a dysfunction in inhibitory neurotransmission is thought to contribute to epileptogenic activity. While much is understood about the inhibitory effects of the ionotropic GABAA receptor, the role of the metabotropic GABAB receptor remains to be elucidated.

Methods: We characterized the effects of bath application of 4-Aminopyridine (4-AP, 100 μ M) alone or in combination with GABAA and/or GABAB receptor antagonists in cortical dysplasia (CD type 1, n=18; CD type IIa/b, n=28), tuberous sclerosis complex (TSC, n=18) and non-CD (n=16) cortical tissue samples from tissue obtained from pediatric epilepsy surgery patients (average age 3 ± 0.3 yr). Whole-cell patch clamp recordings were obtained from cortical pyramidal neurons (CPNs, n=214), balloon/giant cells (n=10), and interneurons (n=21).

Results: In CPNs, bath application of 4-AP produced an increase in spontaneous synaptic activity as well as rhythmic membrane oscillations (2-29 oscillations/min) with or without action potentials. These oscillations were generally depolarizing or biphasic and were accompanied by increased membrane conductance. In interneurons, membrane oscillations were consistently depolarizing and accompanied by bursts of action potentials. Bicuculline (BIC, 20 μ M) reduced the amplitude of membrane oscillations induced by 4-AP, indicating they were mediated principally by GABAA receptors. In balloon/giant cells, 4-AP induced very low-amplitude, slow membrane oscillations (3.75 ± 0.3 /min) that echoed the rhythmic oscillations from CPNs. 4-AP alone or in combination with BIC increased cortical excitability but did not induce seizure-like discharges. Ictal activity was observed in CPNs and interneurons from CD and TSC cases only when phaclofen (25 μ M), a GABAB receptor antagonist, was added to the 4-AP and BIC solution. Ictal activity did not occur in tissue from non-CD patients.

Conclusion: These data emphasize the critical and permissive role of GABAB receptors in the transition to an ictal state in pediatric CD tissue indicating that it may be a useful future pharmacologic target.

261: Comparison of Two- and Three-Dimensional Visualization for Fetal Myelomeningocele Repair: A Pilot Study Using a Fetoscopic Surgical Simulator

Smruti K. Patel, MD (Cincinnati, OH); Smruti Patel, MD; Oleksandra Kashyrina, MD; Soner Duru, MD; Jose Peiro, MD, PhD; Charles Stevenson, MD

Objective: The objective of this study was to evaluate the utility of three-dimensional (3D) versus conventional two-dimensional (2D) endoscopy for fetal myelomeningocele (MMC) repair using a low-fidelity fetoscopic surgical simulator.

Methods: The box trainer consisted of a silicone fetal MMC model placed inside a ball resembling the uterus through a hand-assisted laparoscopic port. The ball was filled with water and insufflated air to simulate the uterine environment. Three trocars were introduced through the hand-assisted port as the working ports for the endoscope and instruments. Participants with varying surgical experience were recruited and completed three essential tasks (cutting skin, placing a dural patch, and suturing skin) using both 2D and 3D endoscopic visualization. Participants were randomized to begin all tasks in either 2D or 3D. Time to completion was measured for each task. Each participant completed the NASA Load Index Test and a questionnaire evaluating their experience.

Results: Sixteen participants completed the study tasks using both 2D and 3D endoscopic simulation. Surgical experience using endoscopy varied among all individuals. Seven participants were randomized to begin with the 2D tasks and 9 to begin with the 3D tasks. While the mean performance times across all tasks were shorter in the 3D versus 2D [cutting skin, 47 vs. 54 seconds ($p=0.67$); placing the dural patch, 38 vs. 52 seconds ($p=0.18$); and suturing the skin, 424 vs. 499 seconds ($p=0.12$)], the results did not reach statistical significance. However, subjective measures of performance favored 3D over 2D visualization (81.3% vs. 18.7%).

Conclusion: Three-dimensional endoscopy could potentially be used in the near future for relative improvement in visualization and performance in fetoscopic procedures such as prenatal MMC repair. Additional studies using this technology in animal models would further support clinical implementation of this technology.

262: Assessing the Incidence and Burden of Post-Neurosurgical Antidepressant Use in Children Undergoing Surgery for Refractory Seizures

Michael Chuwei Jin (Menlo Park, CA); Laura Prolo, MD, PhD; Jonathon Parker, MD, PhD; William Gallentine, DO; Gerald Grant, MD

Introduction: Post-operative depression following neurosurgical intervention is a source of morbidity and may be exacerbated in children with refractory seizures. The burden of pharmacotherapy and factors affecting its use for post-neurosurgical depression in pediatric epilepsy patients is not well understood.

Methods: The IBM MarketScan Administrative Database (2007-2016) was used to identify newly-diagnosed pediatric epilepsy admissions (age<18). ICD-9/10, CPT, and NDC codes were used to identify services/procedures. Antidepressant use was evaluated during the period of continuous enrollment spanning the index diagnosis and index surgery in children with at least 90 days of antidepressant-free follow-up prior to the index date. Follow-up was censored at interruption of continuous enrollment. Factors affecting antidepressant use in post-neurosurgical patients were assessed by multivariable regression analysis.

Results: A total of 26,908 patients were identified, with 1,054 receiving at least one surgery (median post-neurosurgical follow-up=21mo, IQR=8.6-40). Most surgical patients received lesionectomy (33.8%) or temporal lobectomy (25.9%). Median latency between diagnosis and surgery was 135.5 days (IQR=38-327). Risk of post-neurosurgical antidepressant use was 5.31%/patient-year post-surgery compared to 3.05%/patient-year in the non-surgical/pre-surgical settings. Of the 121 patients with post-neurosurgical antidepressant use with at least 365 days of continuous follow-up (n=99, 81.8%), 53.5% were prescribed at least 365 days of antidepressants. Risk of antidepressant use was increased in the post-neurosurgical setting compared to the non-surgical/pre-surgical settings (HR=1.75, 95%CI 1.37-2.22), particularly during the 180 days following surgery (HR=2.47, 95%CI 1.60-3.83). Antidepressant usage was not associated with type of surgery (p=0.829). On multivariable analysis, incidence of post-neurosurgical antidepressant use was independently associated with age (HR=1.07, 95%CI 1.03-1.12), past history of antidepressant use (HR=10.91, 95%CI 6.48-18.4), and length of neurosurgical inpatient stay (weeks, HR=1.21, 95%CI 1.01-1.44).

Conclusion: Prior antidepressant use and longer inpatient stay are associated with increased post-neurosurgical antidepressant use in pediatric epilepsy patients. Children receiving epilepsy surgery are at increased risk for antidepressant use compared to those with newly-diagnosed epilepsy not receiving or prior to surgery.

263: Endoscopic Transnasal/Transoral Odontoid Resection In Children: Results of A Protocolized Institutional Approach

Rajiv Iyer, MD (Salt Lake City, UT); Frederick Grimmer, MD; Douglas Brockmeyer, MD

Introduction: Odontogenic ventral brainstem compression can cause significant morbidity in patients with craniocervical pathology. The most common methods for odontoidectomy are the transoral and endoscopic endonasal routes. Here, we investigate the use of an institutional protocol for endoscopic transnasal/transoral odontoidectomy in the pediatric population.

Methods: From 2007 to 2017, an institutional protocol was developed and refined for the evaluation and treatment of patients requiring odontoidectomy. Preoperative assessment included airway evaluation, a sleep study if indicated, discussion of possible tonsillectomy/adenoidectomy, and thorough imaging review by the neurosurgery and otolaryngology teams. Preoperative anesthesia consultation was obtained for difficult airways. Intraoperatively, adenoidectomy was performed at the discretion of otolaryngology. The odontoidectomy was performed as a combined procedure. A post-odontoidectomy O-arm spin was performed to confirm extent of resection, the otolaryngologist primarily closed the posterior pharynx. Post-operative protocol called for immediate extubation, advancement to a soft diet at 24 hours, and no post-operative antibiotics. Outcome variables included time to extubation, operative time, estimated blood loss, hospital length of stay, and post-operative complications.

Results: A total of 13 patients underwent combined endoscopic transoral/transnasal odontoid resections with at least one year follow up. All patients had stable to improved neurological function in the post-operative setting. All patients were extubated immediately following the procedure. Average operative length was 201 (± 46) minutes and average estimated blood loss was (44.6 ± 40.0) mL. 9 of 13 patients underwent pre-operative tonsillectomy and adenoidectomy. Average hospital length of stay was 6.6 (± 5) days. The first patient in the series required revision surgery for removal of small residual odontoid. One patient experienced pharyngeal flap dehiscence requiring revision.

Conclusion: A protocolized, institutional approach for endoscopic transoral/transnasal odontoidectomies is described. The use of a combined, multidisciplinary approach leads to streamlined patient management and favorable outcomes in these complex patients.

264: Cost Effectiveness of Patient Selection Based On Advanced Imaging For Patient With Acute Ischemic Stroke

Dean Barone, PhD, PA-C (Jackson, NJ); Pinakin Jethwa, MD; James Parrott, PhD; Frederick Coffman, PhD

Introduction: Since 1996, the treatment of acute ischemic stroke has been based on time. Recent studies utilized advanced imaging to determine treatment instead of time alone. This research will evaluate if it is cost-effective and if there are improved outcomes with patient selection for stroke treatment using advanced imaging.

Methods: A decision tree model was built using TreeAge Pro (TreeAge Pro software (Version: 2017; Build-Id: 17.1.1.0-v20170211)) to evaluate the cost-effectiveness. The decision nodes for the tree were the standard of care per the AHA/ASA based on time (CT), and the comparison decision node (CT/CTA/CTP) an algorithm developed with the most recent studies using advanced imaging. The data were taken from the AHA/ASA (number of patients treated); previous studies associated with the treatment of acute ischemic stroke (outcomes and utilities); and from CMS (cost). After completing a base case, a Probability Sensitivity Analysis with Triangular and Beta distribution was performed. A second analysis was performed evaluating the mRs scores determining if there are improved outcomes with advanced imaging (CT/CTA/CTP) vs time (CT).

Results: The incremental cost per patient in the advanced imaging (CT/CTA/CTP) is \$17,049.00, more than the scenario of time (CT). Advanced imaging (CT/CTA/CTP) was more effective (0.58 Life Years); an (ICER) of \$29,149.00, an NMB of \$277,873.00, and C/E of \$5,946.00 favoring the advanced imaging (CT/CTA/CTP); making advance imaging (CT/CTA/CTP) more cost-effective. The PSA with Triangular and Beta Distributions were performed. Resulting in an (ICER) proportion of 73.48% and 78.44% favoring the base case, respectively. The second analysis performed evaluating the mRs scores showed patients in the advanced imaging (CT/CTA/CTP) group had a 5% higher rate of a mRs score of 0 and a 3% decrease in mortality.

Conclusion: It is cost effective and there are improved outcomes in selecting patients for stroke treatment with advanced imaging.

265: The Association Between Residential Greenspace and Stroke

Richard A. Rovin, MD, FAANS, FACS (Milwaukee, WI); Heloise Cheruvalath; Jennifer Homa; Maharaj Singh; Paul Vilar; Amin Kassam

Introduction: Greenspace, both residential and public, is associated with improved outcomes for a variety of medical conditions. Its effect on stroke incidence is not as well established. In this study, we sought answers to these questions: Does an increase in residential greenspace, as measured by the Normalized Difference in Vegetation Index (NDVI), lessen the odds of stroke? Is socioeconomic status (SES), as measured by the Area Deprivation Index (ADI), correlated with NDVI?

Methods: This is a matched (1:4) case-controlled study. The cohort was adult patients admitted to Aurora St Luke's Medical Center in Milwaukee, WI between 2016 and 2018. Non-stroke controls (N=328,868) were matched to stroke cases (N=2336) on known cardiovascular risk factors after excluding patients with prior stroke, addresses outside of Milwaukee County, and residences within 250 meters of a water feature. The matched study sample included 5870 patients (stroke cases=1174 and non-stroke controls = 4696). The mean NDVI within a 250 meter radius around the patients' residence were calculated using satellite imagery and geographical information systems (GIS) software. State decile and national percentile ADI were obtained from the Neighborhood Atlas. A Spearman's rank-order correlation determined the relationship between the NDVI, state and national ADI. Conditional logistic regression was used to examine the relationship between a stroke event and NDVI and ADI.

Results: We found a protective association between higher NDVI values and stroke (OR = 0.33, 95% CI = 0.111-0.975, p = 0.045). There was a negative correlation between NDVI and national (rs(5870) = -.548, p < .001) and state (rs(5870) = -.550, p < .001) ADI, both statistically significant.

Conclusion: An increase in residential NDVI significantly decreases the odds of stroke. As NDVI increases, area deprivation decreases. These findings have implications for mitigation of social disparities in health and urban planning.

266: Increased Risk of Vasospasm Following Subarachnoid Hemorrhage in Patients with Premorbid Opioid Use Disorders: A Nationwide Analysis of Outcomes

Michael Martin (New York, NY); Sean Neifert, BS; Kurt Yaeger, MD; Trevor Hardigan, MD, PhD; Travis Ladner, MD; Christopher Kellner, MD; R. Loch Macdonald, MD, PhD; J Mocco, MD, MS; Eric Oermann, MD; Dominic Nistal, BA

Introduction: Subarachnoid hemorrhage (SAH) is the most morbid sequelae of intracranial aneurysms. While SAH mortality has been declining due to treatment advances, opioid use in the United States population has surged, and neurosurgeons are increasingly tasked with operating on patients with opioid use disorders (OUDs). However, little information exists for how OUDs impact SAH outcomes, particularly post-operative symptomatic vasospasm. This study sought to characterize the perioperative risks faced by OUD patients following acute SAH hospitalization to improve care during the critical time surrounding SAH treatment.

Methods: Data was acquired from the 2012-2014 National Inpatient Sample (NIS). Patients were included if they had a coded diagnosis of subarachnoid hemorrhage and underwent either microsurgical clipping or endovascular coiling. Patients were included in the OUD cohort if they also carried a diagnosis of opioid dependence or non-dependent opioid abuse along with SAH. The NIS-SAH Severity Scale (NIS-SSS), an externally validated metric with strong correlation to Hunt and Hess grade was used to control for case severity. The primary outcome was rate of vasospasm following SAH treatment.

Results: A total of 25,330 patients undergoing either microsurgical clipping or endovascular coiling procedures for SAH were included, of which 310 patients (1.22%) also carried a diagnosis of OUD. Multivariate regression revealed OUD patients faced significantly increased odds of post-procedural vasospasm (OR 2.17; 95%CI 1.19-3.97; p=0.0115). OUD status was not associated with increased odds of other adverse outcomes, including complication, in-hospital mortality, poor outcome by a validated NIS-SAH Outcome Measure, non-home discharge, or extended hospitalization.

Conclusion: Evidence from this study suggests that OUD patients face significantly higher odds of vasospasm events during hospitalization for acute SAH. These findings suggest utility in screening patients for OUD to identify individuals who may benefit from a higher level of clinical scrutiny for post-SAH vasospasm.

267: Patterns of Aneurysm Healing and Neointima Formation after Stent or Coil Treatment in a Rat Aneurysm Model

Cerebrovascular Section Best Basic Scientific Paper

Basil Erwin Gruter, MD (Zurich, Switzerland); Stefan Wanderer, MD; Fabio Strange; Dominik Täschler; Jeanine Rey; Edin Nevzati; Denis Grandgirard; Hans Rudolf Widmer; Michael von Gunten; Daniel Coluccia; Javier Fandino; Serge Marbacher

Introduction: Whereas clipping provides an immediate post-procedural mechanical barrier for aneurysm perfusion, endovascular therapy (EVT) rely on a biological response. Cells need to migrate into the EVT induced thrombus and promote growth of a neointima. Of yet, it remains unclear if these cells are mainly recruited from the aneurysm wall, if they origin from circulating progenitor cells or whether they migrate from the parent artery.

Methods: In this experimental study, saccular aneurysms were transplanted on the abdominal aorta of male Lewis rats and endovascularly treated with coil (n=20) or stent embolization (n=19). Of them, in n=20 cases decellularized wild-type aneurysms were sutured on green-fluorescent protein expressing (GFP+) rats and in n=19 cases GFP+ aneurysms were sutured on wild-type rats. On follow-up examinations at 3, 7, 14, 21, and 28 days post-intervention aneurysms were evaluated for recurrence and the underwent macroscopical and histological examination.

Results: Aneurysms demonstrated progressive healing with increasing neointima thickness and gradually advancing thrombus organization over time (or: during follow-up). Qualitative histological assessments revealed migration of aneurysm wall cells into the thrombus. Cell counts for specific regions of interest showed a similar distribution of GFP+ cells for either coil or stent treatment in the aneurysm wall (54.4% vs 48.7%), and inside the thrombus (20.5% vs 20.2%) but significantly more GFP+ cells in the neointima of coiled (27.2%) versus stented aneurysms (10.4%), p=0.008.

Conclusion: Neointima formation and thrombus organization are concurrent (parallel?) processes in aneurysm healing after EVT and depend on cell migration from parent artery and aneurysm wall. In stent treated aneurysms cells forming the neointima origin mainly from the parent artery whereas in coiled aneurysms neointima formations relays more on cell migration from the aneurysm wall. We hypothesize this to be a substantial reason for better healing in stent assisted coiling versus coiling alone.

268: Functional Connectivity Deficits after Experimental Subarachnoid Hemorrhage

Julian Clarke (St. Louis, MO); Lindsey Brier, BS; Deepti Diwan, PhD; Gregory Zipfel, MD; Jane Yuan, BA; Ananth Vellimana, MD; Joseph Culver, PhD

Introduction: Delayed cerebral ischemia (DCI) is the largest modifiable risk factor for poor patient outcome after subarachnoid hemorrhage (SAH). Previously, we showed that hypoxic conditioning is protective against two components of DCI (large artery vasospasm and microvascular thrombi) and improves neurological outcome after SAH. This conditioning-induced neurovascular protection is mediated via Sirtuin 1 (SIRT1). Functional connectivity (FC) refers to the zero-lag Pearson correlation analysis performed across cortical regions and is used as a readout of coordinate neural activity, due to the close coupling of neurovascular activity. FC can be measured via Optical Intrinsic Signal (OIS) imaging — an imaging modality that measures correlations in vascular reactivity via quantitation of fluctuations in oxy- and deoxy-hemoglobin in cortical brain regions. To date, the impact of experimental SAH and conditioning-based therapy on FC as a measure of microcirculatory function has not been examined. This study examined three questions: 1) Does experimental SAH induce FC deficits; 2) Does hypoxic conditioning provide protection against these FC deficits and is this protection SIRT1-mediated; and 3) does treatment with the SIRT1 activator, resveratrol, mimic the protective effect of hypoxic conditioning against these FC deficits?

Methods: Cranial windows were adhered on C57BL/6 mice. Mice underwent sham or SAH surgery. Mice were then treated with hypoxic conditioning (with or without EX527, a SIRT1-inhibitor) or resveratrol beginning 3hr after surgery. Mice were serially imaged post-surgery.

Results: Experimental SAH induces deficits in FC by day 3, corresponding with the time frame of DCI in mice. Hypoxic conditioning provides SIRT1-mediated protection against FC deficits post-SAH, as does resveratrol.

Conclusion: OIS imaging is a useful technique for identifying FC deficits following experimental SAH. SIRT1 targeted therapies attenuate FC deficits observed post-SAH and may be an important step in treatment of DCI after SAH.

269: The SAFIRE grading scale as a predictor of long-term outcome in the Barrow Ruptured Aneurysm Trial

Joshua Catapano, MD (Phoenix, AZ); Mohamed Labib, MD; Fabio Frisoli; Megan Cadigan; Candice Nguyen; Alexander Whiting; Tyler Cole; Jacob Baranoski; Michael Lawton

Introduction: The SAFIRE grading Scale is a novel scale that predicts the outcome of aneurysmal subarachnoid hemorrhage (aSAH) patients in acute follow-up. However, this scale may have prognostic significance in long-term follow-up.

Methods: Patients enrolled in the Barrow Ruptured Aneurysm Trial (BRAT) had SAFIRE grades calculated. Outcomes at 1-year and 6-year post-aSAH were analyzed for each SAFIRE grade with a poor outcome defined as a mRS >2. Univariate analysis was performed for patients with a high SAFIRE grade (IV/V) for odds of poor outcome at 1 and 6-year follow-up.

Results: 405 patients with confirmed aSAH enrolled in the BRAT were analyzed. 357 patients had 1-year follow-up and 333 patients had 6-year follow-up available. At 1-year follow-up 17 Grade I (n=93, 17%), 20 Grade II (n=92, 22%), 26 Grade III (n=80, 33%), 38 Grade IV (n=88, 43%), and 3 Grade V (n=4, 75%) were found to have poor outcomes. At 6-year follow-up 23 Grade I (n=79, 29%), 21 Grade II (n=89, 24%), 29 Grade III (n=77, 38%), 50 Grade IV (n=84, 60%), and 4 Grade V (n=4, 100%) were found to have a mRS >2. On univariate analysis at both 1-year (OR 2.5, 95% CI 1.5-4.2, p<0.001) and 6-year (OR 3.7, 95% CI 2.2-6.2, p<0.001) follow-up, a SAFIRE grade of IV or V was associated with an increase risk of a poor outcome.

Conclusion: The SAFIRE grading scale predicts long-term outcome in aSAH patients. In particular, high SAFIRE grades are at an increased risk of a poor recovery at late follow-up.

270: Brainstem Cavernous Malformations: A Novel Grading System To Predict Clinical Outcome

Julia Velz (Zürich, Switzerland); Marian Neidert; Yang Yang; Flavio Vasella; Luca Regli; Oliver Bozinov

Introduction: To develop a novel grading system which predicts long-term clinical outcome in patients with non-surgically and surgically treated brainstem cavernous malformations (BSCM).

Methods: We included all consecutive patients with BSCM treated and followed at our Department between 2006-2018. Patient data were collected and analyzed retrospectively. Clinical outcome was dichotomized in favorable (mRS score, 0-1) and unfavorable (mRS score, 2-6) outcome, candidate risk factors were identified, and a new grading system based on the area under the receiver-operating characteristic curve (AUROC) was established.

Results: A total of 117 patients (mean age, 41.3 years; 54.7% female) were analyzed including 58 patients with favorable and 59 with unfavorable outcome. Age ($p < 0.001$), gender ($p < 0.042$), lesion size ($p < 0.001$), Zabramski type ($p < 0.002$), number of BSCM-hemorrhages ($p < 0.001$), neurological deficits ($p < 0.001$), as well as the number of affected cranial nerves ($p < 0.001$) were the most significant predictors for clinical outcome in patients with BSCM. Based on these results, we created a new score, which we named the BSCM Zurich Outcome Score. BSCM grades ranged from 0 to 18 points and predicted outcomes with high accuracy (receiver operating characteristic = 0.85, 95% confidence interval: 0.78-0.91, $p < 0.001$).

Conclusion: The BSCM Zurich Outcome Score predicts outcome in non-surgically and surgically treated patients with BSCM with high accuracy.

271: Pearls and pitfalls of the transradial approach for neurointerventions: lessons learned after 520 cases

Ahmad Sweid (Philadelphia, PA); Omaditya Khanna, MD; Ahmad Sweid, MD; Somnath Das, BS; Julie Kim, BS; Darcy Curtis, BS; Joshua Weinberg, BS; Tara Cahanap; Stavropoula Tjoumakaris, MD; Reid Gooch, MD; Pascal Jabbour, MD; Lohit Velagapudi, BS

Introduction: Trans-radial catheterization is an alternate route of access that has started to gain more widespread use for neuroendovascular procedures. There are several randomized controlled trials from cardiac field that had established its safety and efficacy. We present our institution's experience in performing neuroendovascular interventions via a transradial approach.

Methods: We conducted a retrospective analysis and identified 520 patients who underwent consecutive neuroendovascular interventions via radial artery access. Data collection was performed on indication for procedure, sheath size, catheter type, number of vessels selectively catheterized, fluoroscopy time, procedure duration, radiation exposure, conversion to femoral approach, access site complication, and procedure success.

Results: Of 520 patients with an average age of 59.4-years, 406(71.2%) underwent diagnostic angiograms and 164(28.7%) underwent therapeutic procedures. The overall mean number of vessels catheterized was 2.9 ± 1.7 per procedure. The RCCA was the most frequent selectively catheterized artery; 340 (22.9%), followed by LCCA; 306(20.6%), RICA; 250(16.8%), LICA; 238(16.0%), RVA; 159(10.71%), LVA; 76(5.1%), RECA; 61(4.1%), and lastly the LECA selectively catheterized in 54 (3.6%). The average amount of contrast given was $83.4 \text{ cc} \pm 51$. Successfully completed therapeutic procedures included aneurysm simple coiling (34 patients), stent assisted coiling (30 patients), flow diversion (34) patients), ICA balloon angioplasty and stenting (20 patients), Web device(8), AVM embolization (14), IAC for retinoblastoma (1 patient), and stroke thrombectomy (23 patients). The average duration was 72 mins, and average fluoroscopy time was 13.20 mins. Seventeen patients (3.2%) required conversion to transfemoral access. Twelve minor complications (2.3%) were reported including mild oozing after deflation of the balloon, ecchymosis, mild swelling. No major complications were encountered.

Conclusion: Radial artery catheterization is a safe and effective access site to perform a wide range of diagnostic and therapeutic procedures. Complication and conversion rate are low making it a safe alternative.

272: How reliable are the Los Angeles Motor Scale (LAMS), its S-LAMS variant, and S-LAMS-based prehospital stroke transportation protocols in predicting a large vessel occlusion? Real-world data from The Bronx, NY

Ralph Rahme, MD (Bronx, NY); Brittany Owusu-Adjei Thomson; Rose Fluss, BA; Christy Chon; Nkemdirim Ukoha; Barbara Badio; Chidinma Nwaogbe; Kaitlyn Zugibe; Stephanie Moawad; Scott Segan, MD; Ridwan Shabsigh, MD

Introduction: In 2019, NY state and New York city issued new prehospital stroke transportation guidelines directing emergency medical services (EMS) to screen stroke victims using S-LAMS, a modified version of the Los Angeles Motor Scale (LAMS) that incorporates speech. Absent certain thrombectomy exclusion criteria, all patients with S-LAMS score 4 or more are suspected to have LVO and are thus directly transferred to the nearest thrombectomy-capable stroke center (TSC). To the best of our knowledge, the validity and accuracy of these new triage protocols have not been previously assessed.

Methods: All stroke cases brought by EMS in 2018, prior to implementation of the new guidelines, were retrieved from a prospectively maintained database. Demographic, clinical, radiologic, and outcome data were extracted. LAMS and S-LAMS scores were calculated retrospectively and 2019 prehospital transportation criteria were applied to the 2018 stroke cohort.

Results: 181 patients (98 women, 83 men, mean age: 68 years) were identified. A LVO was confirmed in 16 patients. Patients with LVO had higher mean LAMS (3.7 vs. 1.6, $p < 0.00001$), S-LAMS (4.5 vs. 2.1, $p < 0.00001$), and NIHSS (15.1 vs. 6.0, $p < 0.00001$) scores than those without. The specificity and negative predictive value (NPV) of either LAMS or S-LAMS score 4 or more were high (LAMS:84.5% and 95.1%, respectively; S-LAMS:75.8% and 96.0%, respectively). In contrast, sensitivity and positive predictive value (PPV) were poor (LAMS:53.3% and 24.2%, respectively; S-LAMS:66.7% and 20.4%, respectively). The addition of thrombectomy exclusion criteria slightly increased sensitivity and PPV to 66.7% and 31.2%, respectively. Overall, NY prehospital transportation criteria correctly identified two-thirds of LVO strokes (10/15), while missing a third (5/15). Moreover, 22 non-LVO strokes were misdiagnosed as LVOs, potentially triggering direct transfer to the nearest TSC.

Conclusion: The sensitivity and PPV of LAMS, S-LAMS, and NY transportation protocols for LVO strokes remains poor. More than twice as many non-LVO strokes are flagged using these guidelines than are LVO strokes, and up to a third of LVOs are missed. A more reliable alternative is needed.

273: Endovascular Thrombectomy for Pediatric Acute Ischemic Stroke: A Multi-Institutional Experience of Technical and Clinical Outcomes

Vijay Mysore Ravindra, MD (San Diego, CA); Matthew Alexander, MD; Ameer Hassan, DO; Mouhammad Jumaa, MD; Muhammad Hafeez, MD; Fabio Nascimento, MD; Philipp Taussky, MD; Robert Bollo, MD; Sandi Lam, MD; William Couldwell, MD, PhD; Peter Kan, MD; Ramesh Grandhi, MD

Introduction: Acute ischemic stroke is a growing event in the pediatric population. We chose to examine the role of endovascular thrombectomy for pediatric large vessel occlusion.

Methods: We conducted a multi-center retrospective study from April 2017 to April 2019 with immediate, 30, and 90 day follow up from five tertiary, level-one pediatric trauma centers in the United States with direct affiliation with accredited stroke centers. Primary outcomes included Thrombolysis in Cerebral Infarction (TICI) grade of $\geq 2b$ and mRS score of 0–2 at 90 days.

Results: Twenty-one pediatric patients (<20 years of age) who experienced acute ischemic stroke underwent 23 thrombectomy procedures, with a mean age at thrombectomy of 11.6 ± 4.9 years of age (median 11.5, range 2.1–19 years); 52% of the patients were female. The median National Institutes of Health Stroke Scale score (NIHSS) was 13 on presentation (range 4–33). A cardiogenic cause was identified in 14 cases (61%), dissection in 6 cases (26%), and cryptogenic in 3 (13%). The median time from puncture to recanalization was 56 minutes (mean 73.3 ± 48 ; range 18–158). Nineteen of 23 (83%) procedures resulted in TICI grade 2b or 3 recanalization. The median NIHSS score at discharge was 2 (range 0–26) with a mean reduction of 11.3 ± 6.1 . Fourteen (66%) patients had a mRS score of 0–2 at 30-day follow-up; 18/21 (86%) achieved that by 90 days. The median mRS was 1 (range 0–4) at 30 days and 1 (range 0–5) at 90 days. There was one adverse event in which a patient required a blood transfusion after thrombectomy.

Conclusions: This is the largest study of pediatric endovascular thrombectomy to date. Successful recanalization was accomplished via a variety of approaches with excellent clinical outcomes. Further prospective longitudinal study is needed determine thresholds specific for children.

274: Validation of the TAG Score as a Predictive Model for Symptomatic ICH following Mechanical Thrombectomy

David Lee Dornbos III, MD (Memphis, TN); Nitin Goyal, MD; Georgios Tsivgoulis; Abhi Pandhi; Rashi Krishnan; Andrei Alexandrov; Adam Arthur, MD

Introduction: The indication for mechanical thrombectomy for acute ischemic stroke (AIS) secondary to large vessel occlusion has substantially increased in the past few years, but predictors of symptomatic intracranial hemorrhage (sICH) remain largely unstudied. A recent study assessing these predictors, led to the development of the TICI-ASPECTS-glucose (TAG) score, an internally validated model to predict sICH following thrombectomy.

Methods: To externally validate this scoring system and identify other potential risk factors for hemorrhagic conversion following endovascular therapy for AIS, 420 consecutive patients treated with mechanical thrombectomy from 2014-2017 were retrospectively reviewed. Data were collected pertaining to admission factors, procedural metrics, and functional outcomes. The components comprising the TAG score consist of thrombolysis in cerebral infarction (TICI) score (TICI 0-2a=2 points; 2b-3=0 points), Alberta stroke program early CT (ASPECTS) score (<6=4 points, 6-7=2 points, ≥8=0 points), and glucose (≥150 mg/dL=1 point, <150 mg/dL=0 points). Statistical analyses including univariate analysis, logistic regression analysis, and area under the receiver-operating curve (AUROC) were performed to validate the predictive capability of the model.

Results: There were no significant differences in baseline demographics between groups. Regarding the TAG score, patients with sICH presented with lower ASPECTS (8.13 ± 1.55 v 9.16 ± 1.24 , $p < 0.001$), but no significant correlation between TICI scores and admission glucose was observed. Decreasing ASPECTS correlated with increased risk of sICH (OR 1.57, 95% CI 1.25-1.96, $p < 0.001$), and TAG score was associated with increased sICH (OR 1.46, 95% CI 1.11-1.94, $p < 0.01$). AUROC of the model was 0.633. Stratifying patients into low (TAG 0-2), intermediate (3-4), and high (5-7) risk groups identified similar results to the original study with sICH risks of 5.2%, 10.5%, and 33.3%, respectively.

Conclusion: The TICI-ASPECTS-glucose (TAG) score adequately predicts sICH following mechanical thrombectomy, and appropriately stratifies individual patient risk. Further inclusion of additional predictors of sICH would likely yield a more robust model.

275: Experimental Chronic Cerebral Hypoperfusion Results in Increased Blood-Brain Barrier Permeability and White Matter Injury

Krista Lamorie-Foote (Los Angeles, CA); Michelle Connor; Qinghai Liu; Kristina Shkirkova; Hans Baertsch; Arati Patel; Mikko Huuskonen; Axel Montagne; Berislav Zlokovic; William Mack

Introduction: Chronic cerebral hypoperfusion (CCH) can result in small vessel white matter ischemic injury and neurocognitive decline. Our lab demonstrated blood-brain barrier (BBB) dysfunction with decreased pericyte coverage in the corpus callosum (CC) of mice following CCH using histological analysis. The present study aims to characterize the temporal pattern of BBB integrity and white matter injury with MRI following murine CCH secondary to bilateral carotid artery stenosis (BCAS).

Methods: Mice underwent BCAS (n=5) or Sham (n=5) surgeries. MRIs were performed on days 1, 3, 7, and 30 postoperatively. T2w-MRI, dynamic contrast-enhanced (DCE)-MRI, and dynamic susceptibility contrast (DSC)-MRI protocols were used to characterize anatomical changes, BBB permeability, and cerebral blood flow, respectively. DCE and DSC-MRI data were analyzed with Rocketship software to calculate regional BBB permeability and CBF values.

Results: BBB permeability in the CC was increased on postoperative days 1, 3, and 7 in BCAS mice compared to sham, with a peak on day 3 ($p < 0.01$) and recovery by day 30. BBB permeability in the hippocampus increased in BCAS mice compared to sham, with a peak on day 3 ($p < 0.01$) and recovery by day 30. White matter hyper intensities were noted in BCAS mice but not in sham mice at day 30. In BCAS mice, blood flow in the middle cerebral artery (MCA) decreased compared to sham mice. Blood flow in the posterior cerebral artery (PCA) increased in BCAS mice on day 30 compared to sham mice.

Conclusion: CCH secondary to BCAS temporally increases BBB permeability in the CC and hippocampus, with the greatest increase on postoperative day 3 and recovery by day 30. Increased blood flow in the PCA may compensate for decreased MCA blood flow in the BCAS model of CCH. BBB breakdown precedes white matter injury and may contribute to its pathogenesis following CCH.

276: Establishing a Clinically Relevant Animal Model of Intracerebral Hemorrhage: Investigating the Effect of Hypertension, Metabolic Syndrome, And Sex on the Histologic and Neurobehavioral Response in the Ren-2 Transgenic Rat (mREN-2)27

Anthony Anzalone (Winston Salem, NC); Christine Tschoe, MD; Keyan Peterson; Zhidan Xiang, PhD; Stacey Wolfe, MD

Introduction: Spontaneous intracerebral hemorrhage (ICH) is a catastrophic illness without the identification of a successful therapeutic target to date. Neuroinflammation is emerging as a key factor in the overall outcome of ICH. However, our current understanding is based upon data from healthy, young, male murine models with normal immune responses. We propose the use of transgenic (mREN-2)27 rats as a better model of the chronic pro-inflammatory state seen in ICH patients to identify feasible therapeutic targets for ICH. These animals overexpress the murine Ren2 gene, developing hypertension, and metabolic syndrome (hyperlipidemia, insulin resistance, obesity) by 12-14 weeks.

Methods: Validation of this model is performed in male and female (mREN-2)27 and Sprague-Dawley (SD) rats 16-20 weeks old (N=5/group). Neurobehavioral testing was performed weekly for four weeks, followed by sacrifice, histology, and immunohistochemistry to evaluate for hypertensive cerebrovascular changes and neuroinflammatory characteristics.

Results: The (mREN-2)27 transgenic rats are chronically hypertensive by age 14 weeks, with baseline systolic blood pressures 176 ± 3 mmHg. They display an increased fat mass index and glucose-insulin index (a marker of reduced insulin sensitivity), three times greater than controls. The (mREN-2)27 animals demonstrate end-organ damage (renal, cardiac, and cerebrovascular) consistent with that seen in humans with chronic hypertension. There is delayed disease severity in the female sex.

Conclusion: The (mREN-2)27 transgenic rat model better mimics the pathophysiologic state of the ICH population to allow for (1) a better understanding of how chronic comorbidities affect the neurobehavioral and neuroinflammatory process after ICH; and (2) an improved understanding of how sex may affect the neurobehavioral and neuroinflammatory responses. We hypothesize that this transgenic rat line will be a more clinically relevant model for the translation of future therapeutic targets.

277: Microglia Activation State as a Novel Biomarker for Outcomes after Spontaneous Intracerebral Hemorrhage: A Proof of Concept Study

Christine Tschoe (Winston-Salem, NC); Laura Cox, PhD; Timothy Howard, PhD; Yong Ahn, MD, MS; Carl Langefeld, PhD; Reto Asmis, PhD; Stacey Wolfe, MD

Introduction: Spontaneous intracerebral hemorrhage (ICH) is a catastrophic illness, resulting in 40-50% 30-day mortality with only 20% of patients reaching functional independence at 6months. The inflammatory process following ICH is incompletely understood, but transition to an inflammation-resolving phenotype appears necessary for neuronal regeneration and tissue repair. We hypothesize that earlier conversion of microglia away from a pro-inflammatory activation state correlates with decreased perihematoma edema and improved clinical outcome. We aim to determine the activation states of microglia purified from post-surgical drain fluid from the hematoma bed following ICH evacuation, and follow these changes over time.

Methods: This is a proof of concept study on 5 patients with ICH requiring surgical intervention. Patients underwent minimally invasive ICH evacuation and a drain was placed into the hematoma bed post-operatively. Drain fluid was collected over a 3-day period; longer if it began functioning as an EVD due to communication between the hematoma bed and ventricles. Blood was collected at enrollment, 24hours, 72hours, 5days, 10days, and 30days post ictus. Post-ictus imaging was obtained at 24hours, 72hours, and at 30days.

Results: Preliminary data suggest that the vast majority of cells in the hematoma bed drain fluid are leukocytes (82-99%; $1.5 - 2.5 \times 10^6$ cells per ml of CSF), with microglia making up over 75% of this leukocyte population. Western blot analysis is performed to determine the phosphorylation status of the pro-inflammatory transcription factors STAT1 and STAT3, vs. inflammation-resolving STAT6.

Conclusion: To date, ICH treatments have failed to significantly impact outcomes. This study is the first to describe the presence of microglia in the post-operative fluid of ICH patients, and their activation state over time. These cells will also undergo RNA-seq to identify signaling pathways involved in any phenotype shift from pro- to anti-inflammatory. This study will inform potential outcome biomarkers and therapeutic targets to treat neuroinflammation after ICH.

278: Traumatic Brain Injury is associated with Higher Rates of Dementia: A Two-Institution Experience

Brittany Stopa (Boston, MA); Elisabetta Mezzalana, RN; Alessandro Boaro, MD; Ayaz Khawaja, MD; Saef Izzy, MD; William Gormley

Introduction: There are approximately 2.87 million cases of traumatic brain injury (TBI) in the United States each year. Some research studies suggest a connection between TBI and increased risk of dementia, but there remains a need to evaluate this connection from an institutional perspective.

Methods: In this retrospective cohort study of two academic medical centers (2000-2018), patients with TBI aged 45-100 years were identified by ICD9/10 code, and then age-matched controls were identified. Variables included age, TBI severity (AIS score: 0-2 mild, 3-6 severe), pre-existing dementia, dementia after TBI, and dementia-mimicking comorbidities, like depression, anxiety, psychiatric disorder, endocrine disorder, and stroke.

Results: Overall, there were 19,498 patients with TBI, and 19,488 controls. There were 1,728(9%) cases of pre-existing dementia in the TBI cohort, and 397(2%) in the control cohort ($p<0.001$). There were 1,607(16%) cases of dementia diagnosed after TBI, and 85(<1%) after control diagnosis date ($p<0.001$). There were significantly more cases of depression (996(5%)vs57(<1%), $p<0.001$), anxiety (761(4%)vs53(<1%), $p<0.001$), psychiatric disorder (298(2%)vs18(<1%), $p<0.001$), endocrine disorder (346(2%)vs51(<1%), $p<0.001$), and stroke (779(4%)vs50(<1%), $p<0.001$) in the year after TBI diagnosis than in the control group. The incidence of dementia after TBI was significantly higher in every age group than in the age-matched controls (45-54years:107(3%)vs0(0%), $p<0.001$; 55-64years:161(5%)vs3(<1%), $p<0.001$; 65-74years:389(10%)vs10(<1%), $p<0.001$; 75-84years:604(12%)vs43(1%), $p<0.001$; 85-100years:346(11%)vs29(1%), $p<0.001$). This significance was also seen when TBI patients were analyzed by severity.

Conclusion: We report here a higher incidence of dementia after TBI than in age-matched controls (16%vs<1%). This is noted in all age groups and TBI severity levels, which indicates a need for dementia monitoring after TBI in all adults, regardless of TBI severity. This further intimates the need for TBI-prevention efforts, as the neurodegenerative impact of TBI is seen in patients as young as 45. The connection between TBI and dementia observed here adds to the evidence that TBI is a silent epidemic that warrants greater monitoring and resources.

279: A role of the NLRP3 inflammasome in traumatic brain injury

Seung-Ho Yang, MD (Suwon, Republic of Korea); Ho Jun Yi

Objective: Perilesional edema is a predominant mechanism of secondary brain injury after traumatic brain injury (TBI). Perilesional edema coincides with inflammation, production of pro-inflammatory cytokines, and migration of peripheral immune cells into the brain. The nucleotide binding domain, leucine-rich repeat-containing, pyrin domain-containing-3 (NLRP3) is a key component of the secondary injury. Pioglitazone regulates NLRP3 and other inflammatory cytokines. The present study investigated a role of NLRP3 and pharmacological effects of pioglitazone in animal models with traumatic brain injury.

Methods: Brain contusion induced by a weight-drop model in three group of mice, C57 BL/6 (sham group), NLRP3 knock-out (K/O group) and pioglitazone-treated (treatment group). Brain water contents were compared among three mice groups by date. Western blot, immunohistochemistry, and immunofluorescence examination were performed to investigate NLRP3-related inflammasome and the effect of pioglitazone on TBI models.

Results: Brain edema was highest at day 3 after TBI in the sham group. Brain edema in both K/O group and treatment group was lower than that in the sham group. In western blot, the expression of inflammasome was increased after TBI in the sham group, but the expression of IL-1, caspase-1 and NLRP3 was decreased significantly in treatment group with pioglitazone. GFAP and Iba1 expression decreased in both K/O group and treatment group. In addition, reduction of activated microglial cell and astrocyte by pioglitazone was revealed in confocal microscopy.

Conclusions: The NLRP3 inflammasome plays a pivotal role in regulation of cerebral edema and secondary inflammation. Interestingly, pioglitazone reduce cerebral edema and immune response after TBI by down regulation effects of NLRP3. These results suggest that clinical application of pioglitazone could be possible for neuroprotective strategy in TBI.

280: Elucidating Incidence and Outcomes of Perioperative Status Epilepticus after Neurosurgical Procedures

Michael Chuwei Jin (Menlo Park, CA); Michael Zhang, MD; Jonathon Parker, MD, PhD; John Ratliff, MD; Stephen Skirboll, MD

Introduction: Status epilepticus (SE) is neurosurgical emergency requiring rapid identification and management to limit secondary neurological injury. Incidence of post-neurosurgical SE in patients without prior seizure syndromes is not well understood.

Methods: Patients without a past history of localizable seizures receiving neurosurgical procedures between 2007 and 2015 were identified from the IBM MarketScan Administrative Database. The post-operative period was defined as the duration between neurosurgery and discharge. Procedures were categorized as either supratentorial, infratentorial, burr hole, deep brain stimulation (DBS), endoscopic, CSF-diversion, or endovascular. The index procedure was defined as the final eligible neurosurgical procedure during the index admission. Multivariable logistic regression was used to evaluate factors associated with post-neurosurgical SE.

Results: A total of 286,089 eligible neurosurgical admissions and 731 post-operative cases of SE were identified. Prevalence of post-neurosurgical SE increased between 2007 (0.12%) to 2015 (0.31%, $p < 0.001$) with no corresponding decrease in inpatient mortality after post-neurosurgical SE ($p = 0.263$). Onset of post-neurosurgical SE was variable, averaging 3.5 days ($SD = 7.7$). Of those developing post-neurosurgical SE, 18.5% ($n = 135$) either died inpatient or were discharged to hospice care, compared to 3.6% of neurosurgical patients not developing SE. On multivariable analysis, supratentorial craniotomy ($OR = 6.09, 95\% \text{ CI } 4.85-7.62$), burr hole ($OR = 2.32, 95\% \text{ CI } 1.65-3.19$), and CSF-diversion ($OR = 3.22, 95\% \text{ CI } 2.55-4.03$) were associated with increased risk of SE. After discharge, incidence of readmission for recurrent seizures was 18.2%/year. Readmission risk for recurrent seizures was highest in patients receiving endoscopic procedures (44.1%/year), DBS (27.6%/year), and CSF-diversion (27.2%/year) and lowest in patients receiving burr hole (4.6%/year).

Conclusion: Post-neurosurgical SE most frequently occurs after supratentorial craniotomy, burr hole procedures, and CSF-diversion. Occurrence of post-operative SE is associated with increased mortality, which has not decreased over the past decade. Readmissions for recurrent seizures in patients with post-operative SE is common. Ongoing analyses to define specific risk factors for post-neurosurgical SE are being conducted.

281: Factors Associated with Post Traumatic Hydrocephalus in Pediatric Traumatic Brain Injury Patients in the Emergency Setting

Aladine Abdalla Elsamadicy, BE, MD (New Haven, CT); Aladine Elsamadicy, MD; Victor Lee, BS; Cheryl Zogg; Andrew Koo, BS; Wyatt David, MS; Adam Kundishora, MD; Tyrone Despenza, BS; Benjamin Reeves; Charles Matouk, MD; Michael DiLuna, MD; Kristopher Kahle, MD, PhD

Introduction: There is a paucity of data identifying factors predisposing patients to post-traumatic hydrocephalus (PTH) following traumatic brain injury (TBI). The aim of this study is to identify patient- and hospital-level risk factors associated with the development of PTH following TBI in a pediatric emergency cohort.

Methods: The Nationwide Emergency Department Sample years 2010–2014 was queried. Pediatric patients with a diagnosis of primary TBI were identified using the International Classification of Diseases, Ninth Revision, Clinical Modification coding system. Patients were split into two cohorts based on the presence or absence of PTH following injury. Weighted multivariate analysis assessed the impact of various patient- and hospital-level characteristics associated with the development of PTH.

Results: A total of 1,244,087 pediatric TBI patients were identified, of which 930 (0.07%) developed PTH following injury. Age 0–5 years, Medicaid insurance status, and low-income status were significantly more prevalent in the PTH cohort while gender was similar between cohorts. Urban hospital location, teaching-hospital status, and presence of a trauma center were significantly more prevalent in the PTH cohort. Clinical presentation, type of TBI, nature of injury, and etiology of injury were all significantly associated with the development of PTH following TBI. Furthermore, rate of complications, disposition from ED, and disposition from inpatient were similarly associated with presence of PTH. On multivariate logistic regression, age 0–5 years, prolonged loss of consciousness, in-hospital complications, and open injury were found to have statistically significant increases in the Odds Ratio of developing PTH.

Conclusion: Our study demonstrates that various patient- and hospital-level risk factors predispose pediatric patients in the emergency setting to develop PTH following TBI. Further study is warranted to elucidate the teleological impact of these various characteristics.

282: Serum GFAP, UCH-L1, and S100B Concentrations Predict Traumatic and Hypoxic Brain Death in the Acute Setting

Brett Eric Sterk (Columbia Heights, MN); Daniel Rafter, MD; Zhuliu Li; Rui Kuang, PhD; Uzma Samadani, MD, PhD

Introduction: Accurate classification and prognostication of brain injury is critical for targeting therapeutics, optimizing resources and managing expectations. The ability to predict which traumatic (TBI) and hypoxic brain injuries will progress to brain death is limited. We investigated how accurately neurologic serum markers can predict brain death and differentiate its etiology.

Methods: This prospective observational study enrolled brain injury subjects presenting to a trauma center within 32 hours of injury. Levels of glial fibrillary acidic protein (GFAP), ubiquitin carboxy-terminal hydrolase L1 (UCH-L1), and S100 Calcium-Binding Protein B (S100B) were compared between clinically brain dead (BD), CT positive TBI survivors (CTp), CT negative TBI survivors (CTn), non-traumatic brain injury survivors (NT) and healthy control subjects (CTL). BD subjects were subdivided into high velocity trauma with presumed diffuse axonal injury (DAI), cardiopulmonary/respiratory arrest (CA/RA), and found down (FD). The prognostic value of various biomarker combinations in identifying subjects progressing to brain death was assessed using support vector machine (SVM) supervised learning. Prediction accuracy was determined by area under the curve (AUC) of the receiver operating characteristic (ROC) curve and average precision (AP) for both gaussian and polynomial kernel functions.

Results: The AUC for GFAP, UCH-L1, S100B in combination to predict brain death was 0.98 among all other cohorts (CTL, NT, CTn, CTp) and 0.96 versus all other brain injury subjects (NT, CTn, CTp) with AP of 0.92 for both comparisons. This model was also able to distinguish CA/RA BD from combined NT and DAI BD with an AUC of 0.99 (AP = 0.98).

Conclusion: Serum concentrations of GFAP, UCH-L1, and S100B measured within 32 hours of traumatic and hypoxic brain injury have utility in prognosticating brain death. Moreover, these biomarkers can categorize brain death by mechanism of injury as either hypoxic (CA/RA) or traumatic/unknown (DAI and FD).

283: Chronic subdural Hematomas: The Crucial Role of Eosinophils in the Lifecycle, Radiographic Architecture, And Risk Of Recurrence

2019 Codman Award

Benjamin Andrew Davidson, MD (Toronto, Canada); Karl Narvacan, MD; Shudong Zhang, BSc; David Munoz; Michael Cusimano, MD, PhD

Introduction: Chronic subdural hematoma (cSDH's) are a common neurosurgical disorder, with symptomatic recurrence rates as high as 30%. Recurrence is thought to be caused by inflammatory/angiogenic processes, although predictors are sorely lacking. Eosinophils, present in only a subset of hematomas, are believed to cause hyperfibrinolysis and hematoma liquidity, and yet, their association with clinical/radiographic outcomes has never been studied. Here, we quantified eosinophilic infiltration in cSDH's, hypothesizing that eosinophils would be present primarily in radiographically homogeneous or laminar cSDH's, and associated with recurrence.

Methods: The histological specimens from 51 primary cSDH's and 11 recurrent cSDH's were graded for eosinophilic infiltration as 0(absent), 1(sparse), 2(moderate), 3(dense). Eosinophils were graded by two blinded physicians. Clinical data was recorded and preoperative computed tomography (CT) scans were classified as homogeneous, laminar, separated, or loculated.

Results: Of the 51 primary specimens, 43 had an eosinophil grade of 0-1 and 8 had grade 2-3. 6 of the 43 had a symptomatic recurrence, none of the grade 2 or 3 patients had recurrence. In the 11 recurrent cSDH's, 1 had moderate-to-dense eosinophil infiltration. 2/11 went on to require another surgical evacuation - both were graded as 0 for eosinophil infiltration. There was no association between eosinophil infiltration and CT classification, but specimens graded 2-3 were associated with a subacute component on CT.

Conclusion: Dense eosinophil infiltration occurs in only a subset of cSDH's. Eosinophilic infiltration occurs early on in the cycle of cSDH's, as they are seen primarily in hematomas with a subacute radiographic component. The rate of recurrence in cases with a dense eosinophil infiltration was much lower than expected, suggesting the presence of dense eosinophilic infiltrate may signify a favourable timepoint in the course of evolution in cSDH's. cSDH's without dense eosinophil infiltration may be at an elevated risk for recurrence.

284: The Economic Value of an On-Call Neurosurgical Resident Physician**Byron Cone Pevehouse Young Neurosurgeon Resident Award**

William Edward Gordon, MD (Memphis, TN); Paul Klimo, MD; Lattimore Michael, MD

Introduction: The cost of training neurosurgical residents is especially high considering the duration of training and the technical nature of the specialty. Despite these costs, on-call residents are a source of significant economic value, both through indirect and directly supervised activities. We sought to identify the economic value of "on-call" services provided by neurosurgical residents.

Methods: A personal call log kept by a single junior neurosurgical resident over a 2-year period was used to obtain total number of consultations, admission, and procedures. Current Procedural Terminology (CPT) codes were used to estimate the resident's on-call economic value.

Results: A single on-call neurosurgical resident at our institution produced 8,220 work relative value units (wRVUs) over the study period from indirectly supervised activities. Directly supervised activities (emergency operations performed with an attending physician present) yielded an additional 7,002 wRVUs. Using the billing rate assigned to non-physician providers and the Medical Group Management Association (MGMA) nationwide median neurosurgery reimbursement rate, the on-call activities of a single resident generated \$773,876 over the 2-year period, or \$386,938 annually. As a program, our on-call residents collectively produced nearly 74,000 wRVUs over the study period, or 37,000 wRVUs annually. This results in potential reimbursements of \$1,873,724 annually from activities performed while on-call.

Conclusion: Neurosurgery residents at our institution produce enough theoretical economic value exclusively from on-call activities to far exceed the cost of their education. This information could be used to more precisely estimate the true overall cost of neurosurgical training and determining future GME funding.

285: Safety and Costs Analysis of Early Hospital Discharge after Brain Tumor Surgery: A Pilot Study

Alexandra Santos (Sao Paulo, Brazil); Iuri Neville, MD, PhD; Francisco Ureña, MD; Danilo Quadros, MD; Davi Solla, MD; Mariana Lima, MD; Vitor Cavalheiro; Robson Amorim, MD, PhD; Wellingson Paiva, MD, PhD; Manoel Teixeira, MD, PhD

Introduction: To evaluate whether there was a difference in length of stay (LOS), rate of complications, and hospital costs after the introduction of the daily algorithm for hospital discharge (DAHD) compared to the traditional postoperative management of patients who underwent brain tumor resection.

Methods: This is a retrospective cohort study. All consecutive patients who underwent brain tumor resection in 2017 were analyzed. Demographic and procedure-related variables, clinical outcomes, and healthcare costs within 30 days after surgery were collected and compared in patients before (pre-implementation) and after (post-implementation) the daily algorithm for hospital discharge (DAHD).

Results: 61 patients who had been submitted to brain tumor resection were studied (pre-implementation 32, post-implementation 29). The baseline demographic characteristics were similar between the groups. After the DAHD implementation, LOS after surgery in days decreased significantly (median 5 versus 3 days; $p=0.001$). The proportion of patients who were discharged within day 1 or 2 after surgery was significantly higher after DAHD protocol (44.8% vs 3.1%; $p<0.001$). Major and minor complications rates, readmission rate, and unplanned return to hospital in 30-day follow-up were comparable between the groups. There was a significant reduction in the median costs of hospitalization in DAHD group (US\$2,135 vs US\$2,765, $p=0.043$), mainly due to a reduction in median ward costs (US\$922 vs US\$1,623, $p=0.009$).

Conclusion: Early discharge after brain tumor surgery was safe, inexpensive, reduced the LOS, and hospitalization costs without increase in readmission rate or postoperative complications.

286: Medicare Reimbursement for Services Billed By Neurosurgeons From 2010–2018

Jordan R Pollock (Scottsdale, AZ); Kent Richter, BS; Jack Haglin, BS; Jakub Godzik, MD; Naresh Patel, MD

Introduction: The complexity and lack of transparency in Medicare billing and reimbursement is well known to medical providers; updates occur on an annual basis and are difficult to track and implement in clinical practice. This paper examines Medicare reimbursement for services billed by neurosurgeons from 2010-2018.

Methods: The 2010 and 2018 physician/supplier files from the Centers for Medicare and Medicaid website were accessed. Payments were sorted by Provider ID, and all payments being submitted by neurosurgeons (provider ID 14) were included and analyzed in this study.

Results: In 2010 and 2018, neurosurgeons billed Medicare for \$3,441,742,892 (4,003,438 services) and \$4,513,528,985 (3,919,454 services) respectively. Although number of services billed by neurosurgeons has decreased from 2010 to 2018, Medicare has increasingly denied payment for services, which totaled 732,678 denied payments (\$446,956,533, 18% of submitted charges) in 2010 and 833,872 denied payments (\$580,742,056, 21% of submitted charges) in 2018. In 2010, the average submitted charge by neurosurgeons was \$859.70, the Medicare allowed charge was \$166.73 (19% of billed amount), and the Medicare payment amount was \$130.65 (15% of billed amount). In 2018, these same values were \$1,151.57, \$206.79 (18% of billed amount), and \$158.78 (14% of billed amount).

Conclusion: From 2010 to 2018, the number of services billed to Medicare by neurosurgeons has decreased. Additionally, Medicare has denied an increasing amount of billed services and is paying a smaller portion of the billed amount. Complex billing practices might be resulting in more denied payments and rising charges by neurosurgeons for services. As Medicare is one of the largest healthcare insurers in the United States, relevant trends in billing practices are important to understand given the direct financial impact on providers and patients.

287: Resource Utilization and Radiation Exposure in Shunted Idiopathic Intracranial Hypertension: An Institutional Experience

Tyler Cho (Columbus, OH); Daniel Kreatsoulas, MD; Luciano Prevedello, MD; Douglas Hardesty, MD

Introduction: Patients with idiopathic intracranial hypertension (IIH) frequently utilize healthcare services and undergo numerous radiological studies to assess refractory symptoms despite CSF diversion. We reviewed our shunted IIH experience to delineate the clinical utility of acute imaging, and to estimate cumulative patient radiation exposure.

Methods: An IRB-approved retrospective review of 100 patients with IIH and a prior CSF diversion procedure treated at our institution between July 2008 and August 2018.

Results: A majority of patients were female, Caucasian, obese, and of childbearing age. Patients had an average of 16.3 office visits (SD $\pm$ 13.8), 12.4 emergency department (ED) visits ($\pm$ 21.0), and 4.6 inpatient admissions ($\pm$ 5.1) over an average 4.8 years of clinical follow up. Patients underwent an average of 9.0 head CTs ($\pm$ 8.1), 10.3 shunt series x-rays ($\pm$ 11.2), and 4.3 MRIs ($\pm$ 3.7). Approximated radiation exposure per patient over the study period was 21.4 mSv ($\pm$ 18.7). Radiological studies performed for acute evaluation of symptoms in the hospital ED consisted of 263 CT, 436 shunt series, and 62 MRI scans. Of these imaging studies, 91% showed no actionable findings (82.5% of CTs, 97.5% of shunt series x-rays, 79.6% of MRIs). The most common actionable findings on acute imaging (9% total) were overshunting/decreased ventricles (2.4%), effects of increased ICP (1.7%), and sinus disease/infection (1.5%).

Conclusion: Shunted patients with IIH undergo numerous radiological studies and are subject to considerable radiation exposure. In our cohort, acute imaging in the ED led to actionable findings in less than 10% percent of all radiographic studies, with MRI the most useful (20.4% yield). Considering the potential health risks of radiation exposure and the overall low clinical utility of radiological studies, patients with IIH may benefit from radiation-reducing ED protocols and the use of imaging modalities such as fast MRI protocols.

288: The Clinical Efficacy and Direct Healthcare Cost of Repeat Head CT in Mild Traumatic Brain Injury*Alex Patrick Michael, MD (Springfield, IL); Matthew Weber, MD; Jeffrey Nie, BS; Jose Espinosa, MD*

Introduction: Intracranial hemorrhage (ICH) is frequently found on head CT imaging after mild traumatic brain injury (mTBI), prompting transfer to a trauma center with repeat imaging to confirm hemorrhage stability.^{1,2} Several studies suggest that repeat imaging has little clinical utility in patients with minimal ICH, who do not use anticoagulant/antiplatelets and who have no change in neurologic status.³⁻⁷ We sought to assess the clinical utility and cost effectiveness of repeat head CT's in low-risk mTBI patients.

Methods: A retrospective evaluation of patients receiving a neurosurgical consultation for mTBI during a 5-year period was performed at a level 1 trauma center. Exclusion criteria included GCS $\leq$ 13, current anticoagulant/antiplatelet use, displaced skull fracture, $\geq$ 8 mm ICH, scattered subarachnoid hemorrhage or intraventricular hemorrhage. Clinical efficacy and associated healthcare costs of repeat head CT and transfer from outlying hospitals were assessed.

Results: Of 531 eligible patients, 121 met inclusion criteria. Thirty-one patients (25.6%) had one head CT, 90 patients (74.4%) received two or more. Direct cost of all repeat imaging was \$281,111. Thirty-seven patients (30.6%) were transferred from tertiary medical centers. Direct cost of ground transfer via emergency medical services was \$55,944. Four patients developed evolution of ICH on repeat CT. No patient had neurosurgical intervention (i.e. craniotomy, placement of intracranial pressure monitor) or in-hospital mortality. Two patients had a mTBI related 30-day readmission for seizure.

Conclusion: Repeat head CT did not change management of low risk mTBI patients in this study. Serial neurological examinations without repeat imaging appears to be safe and effective for select mTBI patients. Additionally, telemedicine may eliminate the need to transfer low-risk mTBI patients from small outlying hospitals and could provide future cost savings. A large prospective analysis is warranted for further evaluation.

289: Hospital Competitive Intensity is Associated with Perioperative Outcomes for Cranial Neurosurgery*Oliver Tang (Providence, RI); Krissia Rivera Perla, BS; Rachel Lim; Steven Toms, MD, MPH*

Introduction: Earlier research has demonstrated that interhospital competition may influence surgical outcomes, such as mortality, complications, and resource utilization. However, the potential impact of these competitive dynamics on cranial neurosurgery remains poorly characterized.

Methods: Using Diagnosis-Related Group codes, we extracted all admissions for cranial neurosurgery from the National Inpatient Sample in 2006 and 2009. These two chosen years contain data on the Herfindahl-Hirschman Index (HHI), a validated economic measure of hospital market competition ranging continuously from 0 (significant competition) to 1 (monopolization). We assessed how HHI was associated with inpatient mortality, complication during admission, favorable discharge disposition, length of stay (LOS), and hospital costs. Multivariate regression adjusted for twelve confounding variables: patient demographics (age, sex, race, insurance, income), severity measures (severity of illness and risk of mortality scores, comorbidities), and hospital characteristics (bed size, location/teaching status, ownership, region).

Results: We analyzed 513,271 total cranial neurosurgery admissions. The median HHI for hospitals in the study population was 0.275 (range=0.099—0.724). While higher interhospital competition was associated with increased LOS (+4.9% or +0.30 days per -0.10 HHI, $P<0.001$), it was not significantly correlated with mortality, complications, or favorable discharge. From subspecialty analysis, patients in more competitive hospital markets had greater LOS following cerebrovascular, shunting, tumor, and neurotrauma operations (all $P<0.05$), but not functional neurosurgery. However, patients undergoing brain tumor surgery in more competitive geographies exhibited lower mortality (odds ratio=0.74 per -0.10 HHI, $P=0.02$). Finally, although interhospital competition was not associated with overall neurosurgical costs, shunting patients exhibited higher costs (+2.8% or \$900 per -0.10 HHI, $P=0.031$) in more competitive markets.

Conclusion: Increased interhospital competition was associated with greater LOS for neurosurgical admissions, reduced inpatient mortality for brain tumor patients, and higher shunting costs. Amidst ongoing practice consolidation, further research should characterize the mechanisms by which hospital competitive intensity may impact patient outcomes.

290: Conflict Of Interest Disclosures In Neurostimulation Device Studies

Ilya Frid (Scranton, PA); Daniel Kaufman, MS; Gabi Waite, PhD; Brian Piper

Introduction: Conflict of Interest (Col) statements are standard practice in scientific literature. The Center for Medicare and Medicaid Services (CMS) has published physician compensation data for medical devices. Using the Mayo Clinic's guidelines on neurostimulation devices, the likelihood of non-disclosure in publications of the highest earning authors for each respective device were explored.

Methods: Highest earning authors were identified by using ProPublica's Dollars for Docs database. The search was performed for Deep Brain Stimulation (DBS), Sacral Nerve Stimulation (SCS), Responsive Neurostimulation (RNS), and Vagus Nerve Stimulation (VNS). Publications for each author were collected between the years 2014-2016 and each publication was explored for a disclosure statement. The accuracy of each statement was checked by referencing the CMS database. Author demographics and journal impact factors were collected. Analysis of data was performed via one-way ANOVA and Tukey's Multiple Comparison Test using GraphPad Prism 8.

Results: From a cohort of 47 authors (10.6% female), a total of 313 publications were identified between 2015-2016. One-seventh (14.7%) of publications had no disclosure statement. Nearly one-quarter (23.9%) publications had a statement but did not list a disclosure. Analysis of each author's compensation depending on the type of disclosure present in each publication revealed that authors are more likely to disclose a Col who had higher compensation amounts compared to the authors that did not have disclosure statements ($P < 0.0001$). The mean compensation of the non-disclosed publications was \$320,394.

Conclusion: Payments from device manufacturing companies can create biases in reported findings and physician practice. This study found that an appreciable portion of publications from authors who receive payments for medical devices do not contain disclosure statements. Col studies are an increasing area of research due to the need of improved author guidelines. Self-reports of disclosures may too often be an inadequate reporting strategy.

291: Obesity Negatively Effects Cost Efficiency and Outcomes in Adult Spinal Deformity Surgery

Peter Gust Passias (Brooklyn Heights, NY); Avery Brown, BS; Katherine Pierce, BS; Cole Bortz, BA; Haddy Alas, BS; Sara Naessig, BS; Waleed Ahmad, MS; Shaleen Vira, MD; Burhan Janjua, MD; Michael Gerling, MD; Peter Passias, MD

Introduction: Obesity has risen to epidemic proportions within the U.S. As the rates of obesity have increased, it is unknown what effect there has been on cost efficiency in ASD, which often involves complex, invasive procedures.

Methods: Included: ASD patients ≥ 18 years, undergoing ≥ 4 level fusions. Descriptive analysis assessed mean demographic, radiographic, and surgical data. Patients were stratified into NIH defined obesity groups based on their preoperative BMI: underweight 18.5<(U), normal 18.5—24.9(N), overweight 25.0—29.9(O), obese I 30.0—34.9(OI), obese II 35.0—39.9(OII), and extreme obesity 40.0+(EO). Total surgery costs for each group were calculated using the PearlDiver database, reflecting both private insurance and Medicare reimbursement claims. Complications and comorbidities(CC) and major complications and comorbidities(MCC) were assessed according to CMS.gov manual definitions. QALYs and cost per QALY for obesity groups were calculated using a 3% discount rate to account for residual decline to life expectancy(78.7yrs).

Results: 505 patients included. Baseline demographics and surgical details: 60.8 $\pm$ 14.8yrs, 67.6%F, 28.8 $\pm$ 7.30kg/m², 81.0%posterior approach, 18%combined approach, 10.1 $\pm$ 4.2 levels fused, op time 441.2 $\pm$ 146.1minutes, 1903.8 $\pm$ 1594.7cc, LOS 8.7 $\pm$ 10.7days. There were 17U, 154N patients, 151 O patients, 100 OI, 51 OII, and 32 EO patients. Revision rates by obesity group were: 0%U, 3%N patients, 3%O patients, 5%OI, 4%OII, and 6% for EO patients. The total surgery costs by obesity group were: \$48,757.86U, \$49,688.52N, \$47,219.93O, \$50,467.66OI, \$51,189.47OII, and \$53,855.79EO. In a sub analysis of 158 patients with BL and 1Y EQ5Df/u, the cost per QALY was: \$153,737.78U, \$229,222.37N, \$290,361.68 O, \$493,588.47 OI, \$327,876.21 OII, and \$171,680.00 EO. If that benefit was sustained to life expectancy, the cost per QALY was \$8,588.70U, \$12,805.72N, \$16,221.32 O, \$27,574.77 OI, \$18,317.11 OII, and \$9,591.06 for EO.

Conclusion: Among ASD patients, those with BMIs in the OI, OII, or EO range had higher total surgery costs. When assessing 1Ycost per QALY, obese patients had costs 32%higher than non-obese(\$224,440.61 vs. \$331,048.23). Further research is warranted on the utility of optimizing modifiable health factors preoperatively in ASD surgery.

292: Cost Analysis and Clinical Utility of Routine Postoperative CT Imaging In Glioblastoma Resection

Danielle D. Dang, MD (Bethesda, MD); Luke Mugge, MD; John Dang, MD; Alexandra Laskey, PA-C; Weeda Nejrab, PA-C; Mateo Ziu, MD, MBA

Introduction: The clinical use of routine postoperative CT imaging following glioblastoma resection is a controversial topic with variable expert recommendations at our institution. Socioeconomic studies investigating the clinical utility and cost-effectiveness of this valuable resource in neurosurgical oncology are lacking.

Methods: An institutional retrospective chart review was conducted on all patients who underwent a craniotomy for glioblastoma (GBM) resection from 2012-2018 performed by 9 individual surgeons. Records were analyzed for use of post-operative CT imaging prior to routine MR imaging, indications for CT, and changes in clinical management after CT imaging was obtained. Further, a cost analysis was estimated based upon the average regional cost of noncontrast CT head imaging assuming insured patient status.

Results: 236 total patients met inclusion criteria. 22.03% of patients obtained CT imaging postoperatively prior to routine MR imaging in which only 3 scans (5.77%) effected change in medical management. No statistical significance was found on the rate of obtaining CT imaging based on immediate post-operative examination. The average cost of obtaining a noncontrast CT Head is estimated \$286. Our patient population thus required 18 CT scans at an estimated total minimum cost of \$5,076 in order to change clinical management in one patient. Finally, of the patients who did not receive a routine CT scan, none experienced postoperative neurologic deficits whose detection was therefore delayed.

Conclusion: While MR imaging offers clear postoperative value in the assessment of extent of resection, residual tumor, and parenchymal edema, it is not clear what clinical knowledge is gleaned from routine CT imaging. No clear guidelines exist, however, close neurologic monitoring in the intensive care unit may be more clinically useful and represent a more efficacious and effective use of hospital resources than routine postoperative CT imaging following glioblastoma resection.

293: Audio-Video Recording Of Patient-Physician Encounter Does Not Increase the Risk of Malpractice Claims

Komal Naeem (Phoenix, AZ); Randall Porter, MD; Malika Bhargava, MD

Introduction: Recording patient-physician communication improves recall of medical information by patients and strengthens trust between the patient and physician. Despite being an efficient and cost-effective tool for better healthcare provision, its use has been limited due to the presumed concerns regarding unfavorable medico-legal consequences. In this paper we present the medico-legal implications of the video recording system used in out-patient setting at our high-volume center.

Method: A detailed analysis of institution's loss run from 2000-2017 was performed. We calculated claims per physician-year for all the physicians and analyzed if the rates have been changed after initiating the use of audio-video recording. We formally started audio-video recording of clinic visits in 2014. The password protected video is uploaded on a HIPAA compliant secure computer server and can only be accessed by the patient and relevant healthcare personnel. They can be shared by the patients.

Results: Institution's loss run analysis showed 146 occurrences, 94(64%) precautionary claims, 14(14.6%) claimactions and 38(26%) lawsuits. Out of 52 claims only 7(13.5%) were paid/settled. In three years of video recording of clinic visits, only one precautionary claim and 2 claimactions (dismissed) have been identified. Around 40,000 videos have been recorded and 7 physicians are regularly using this but there has been no report of lawsuits (paid or unpaid) or paid claims. Plotting risk probability curves depicted that the use of this technology does not increase the risk of paid claims when compared with the risk among the physicians who are not using this.

Conclusion: We report that the video recording of patient-physician encounter does not increase the risk of malpractice lawsuits, as it was feared earlier. It can actually help in developing a trustworthy relationship between the patient and the doctor.

294: Stereotactic Radiosurgery vs. Whole Brain Radiation Therapy For Patients With Brain Metastases: Determining Cost-effectiveness at a Regional Medical Center

Vikash Deendyal (Yardley, PA); Soraya Sanchez-Molero, MD; Smit Shah; Shirnett Williamson, MD; Timothy Chen; Navid Redjal, MD

Introduction: We wanted to assess whether stereotactic radiosurgery (SRS) was more cost effective than whole brain radiation therapy (WBRT) in patients with brain metastases at our regional medical center.

Methods: The model we created designated three health states for each treatment arm: 1) stable after treatment, 2) progression of disease, and 3) death. Each state was given a utility as proposed by Lester-Coll et al (0.85 for stable after SRS, 0.70 for stable after WBRT, 0.55 for progression of disease, and 0.0 for death). We calculated progression free survival (PFS) and overall survival (OS) and used these metrics in the calculation of quality adjusted life years (QAL). The cost of radiation therapy was based on Medicare facility fees (\$15,234 for 5 fractions of SRS and \$2,340 for 10 fractions of WBRT) and the costs accrued during disease progression were based on the findings by Kaye et al (\$13,565/yr). Total costs and QAL were then used in the calculation of incremental cost-effective ratio (ICER). Willingness to pay (WTP) was set a threshold of \$100,000 per QAL. We initiated a retrospective search and identified patients who either received SRS or WBRT as an initial therapy for brain metastases between 2010-2015.

Results: Twenty-nine patients who received SRS and thirteen patients who received WBRT met inclusion criteria. SRS patients had a mean QAL of 1.13 years and WBRT patients had a mean QAL of 0.82 years (p-value: 0.05). Mean total costs were \$32,783 and \$16,571 (p-value: 0.0009) for SRS and WBRT patients respectively. SRS (vs. WBRT) had an ICER of \$50,473 per QAL added.

Conclusion: Our analysis indicates that SRS, compared to WBRT, may be a cost-effective initial treatment modality for brain metastases when performed at our regional medical center when WTP is set to \$100k.

295: Night Float Call for Neurosurgical Resident Training

Evan Paul McNeil (Hanover, NH); Tobi Cooney; Jennifer Hong, MD

Introduction: One solution to strict ACGME duty hour restrictions is to reformat the night call schedule to a "night float" system in which one resident adapts to a 12-hour "nocturnist" schedule for several weeks. Though night float seems to be a ready solution to ACGME's more stringent duty hour restrictions, there may be concern that reduced weekly duty hours could negatively impact total operative experience over the course of neurosurgery residency.

Methods: The Dartmouth-Hitchcock Medical Center's neurosurgery residency switched from traditional call to night float in 2016, creating a natural experiment of the effect of night float on resident operative experience. The notes for all neurosurgical cases between 2014 and 2019 (N=12,259) were opened. The number of minutes of operative participation by each resident was recorded. Additionally, it was noted whether the surgery took place as scheduled/elective or nonscheduled/emergent. ACGME violations were collected from the ACGME for all years 2014 through 2019. To get a sense for the overall adoption of night float among US programs, program coordinators (N=112) were contacted via telephone or e-mail and asked to take a brief survey regarding their call system.

Results: After switching to night float, there was no reduction in total operative minutes in any PGY year. The fraction of cases which were nonscheduled/emergent relative to scheduled/elective increased for the PGY-2 through PGY-5. All categories of ACGME violations were significantly reduced after the adoption of a night float call schedule. Most neurosurgery programs (65%) retain some version of a traditional 24-hour call system. Larger programs are more likely to use traditional call.

Conclusion: Night float is a viable and nationally popular call format for smaller programs, because it minimizes ACGME violations while not negatively impacting operative experience.

296: Women in Neurosurgery: Positive Recruitment Trends Since the 2000s, but Gender Disparities in Resident Attrition Rates Remain

Varun Shah (Broadview Heights, OH); Tala Nashawati, BS; Sarah Burns, BS; Kristin Huntoon; Douglas Hardesty, MD

Introduction: Women comprise a minority of incoming neurosurgical residents, and studies show women have a higher neurosurgery residency attrition risk than men. The number of women in neurosurgery is increasing, albeit disproportionately slower compared to women in medicine overall. This study aims to determine if the attrition rates in female neurosurgical residents remains elevated in the last decade, with a particular focus on 2011 onwards

Methods: The American Association of Neurological Surgeons database was queried for all residency matches between 2000–2017. Primary outcomes were attrition rates in male and female residents, and changes in gender composition of residency cohorts.

Results: Women comprised 14.7% of matching neurosurgery residents from 2000–2017. Over that era, women had a significantly elevated risk of attrition from residency compared to men (RR = 2.1697, 95% CI = 1.4195–3.3163, $p = 0.0003$). However, neither the 2003 nor the 2011 duty hour restrictions significantly impacted attrition for either gender ($p > 0.05$ for each). The percentage of women matched increased significantly after 2011, from 14% overall from 2000–2011, to 22% overall from 2012–2017 ($p = 0.018$). In 2000, women made up 11% of the incoming residency class, compared to 2017 where they made up 21% of the class. Only 4 former residents left medicine altogether, going into business. The majority of attrition occurred during the first 3 years of residency, with most leaving during PGY 2, regardless of gender.

Conclusion: In the last decade, women have increasingly matched into neurosurgery compared to prior decades. Unfortunately, attrition among those women residents remains elevated compared to men. Continued attention directed towards the retention of female neurosurgery residents is warranted, which may in turn continue the positive increase in women matching into neurosurgery.

297: A Survey of Applicant Views Regarding the Neurosurgical Fellowship Process

Michael Karsy, MD, PhD (Salt Lake City, UT); Rimal Dossani, MD; Michael Karsy; Bharat Guthikonda, MD

Introduction: Training of fellowships in neurosurgery remains important in facilitating the transmission and expansion of specialized knowledge to residents. The process of fellowship selection remains unclear and heterogeneous among different subspecialties in neurosurgery. This survey aimed to evaluate the experience of senior neurosurgical residents applying for neurosurgical subspecialty fellowships and find areas of improvement.

Methods: In collaboration with the Council of State Neurological Surgeons, a survey was disseminated among senior U.S. neurosurgical residents identified via the American Association of Neurological Surgeons resident database.

Results: A total of 69 residents responded to the survey representing a wide variety of subspecialties. Most residents applied for 2–5 programs (44.9%) and completed 2–5 interviews (44.9%). The primary method of finding fellowships was via faculty mentors (66.7%), followed by websites and reaching out to fellowship directors (53.6%) and online database searching (46.4%). Most residents applied for fellowships in their post-graduate year 5 of training (49.1%). Significant variability in times for interviews and offer letters was seen. Most residents accepted their first offer (63.8%). Most residents (86.4%) reported that national neurosurgical societies should aid in the improvement of the fellowship process with reasons including: a common application and due dates (29.2%), fellowship database with program details (29.2%), and improved coordination of interviews (22.9%). In regards to a nationalized match system, most residents were opposed (38.6%) rather than neutral (26.3%) or supportive (35.1%).

Conclusion: This survey suggested that the neurosurgical fellowship process could be improved by a common application, public listing of programs, standardized dates for application, and improved coordination of interviews. Most residents opposed the implementation of a national match system at this time.

298: Specialized Social Media Team to Increase Online Impact and Presence: The *Journal of Neurosurgery* Experience

Joseph R. Linzey, MD (Ann Arbor, MI); Joseph Linzey, MD, MS; Faith Robertson; Ali Haider; Christopher Graffeo; Justin Wang; Gillian Shasby; Aaron Cohen-Gadol; James Rutka; Naif Alotaibi

Introduction: Social media use continues to gain momentum in academic neurosurgery. To increase journal impact and engage more broadly, many journals have turned to social media to disseminate research. The *Journal of Neurosurgery* established a dedicated, specialized social media team (SMT) in November 2016 to provide targeted improvement in digital outreach. The goal of this study was to examine the impact of establishing a SMT.

Methods: This study analyzes metrics including impressions, engagements, retweets, likes, profile clicks, and URL clicks from consecutive social media posts from the JNS's Twitter and Facebook platforms between 2/1/2015-2/28/2019. Standard descriptive statistics were utilized.

Results: Between 2/2015-10/2016, when a specialized SMT was created, 170 tweets (8.1 tweets/month) were posted compared to 3,220 tweets (115.0 tweets/month) between 11/2016-2/2019. All metrics significantly increased including: the impressions per tweet ($1,646.3 \pm 934.9$ vs. $4,605.6 \pm 65,546.5$, $p=0.01$), engagements per tweet (35.2 ± 40.6 vs. $198.2 \pm 1,037.2$, $p<0.0001$), retweets (2.5 ± 2.8 vs. 10.5 ± 15.3 , $p<0.0001$), likes (2.5 ± 4.0 vs. 18.0 ± 37.9 , $p<0.0001$), profile clicks (1.5 ± 2.0 vs. 5.2 ± 43.3 , $p<0.0001$), and URL clicks (13.1 ± 14.9 vs. 38.3 ± 67.9 , $p<0.0001$). Tweets that were posted on the weekend compared to weekdays had significantly more retweets (9.2 ± 9.8 vs. 13.4 ± 25.6 , $p<0.0001$), likes (15.3 ± 17.9 vs. 23.7 ± 70.4 , $p=0.001$), and URL clicks per tweet (33.4 ± 40.5 vs. 49.5 ± 117.3 , $p=0.0002$). Between 11/2015-10/2016, 49 Facebook posts (2.3 posts/month) were sent compared to 2,282 posts (81.5 posts/month) between 11/2016-2/2019. All Facebook metrics significantly increased including: impressions ($5,475.9 \pm 5,483.0$ vs. $8,506.1 \pm 13,113.9$, $p=0.0005$), engagements (119.3 ± 194.8 vs. 283.8 ± 733.8 , $p<0.0001$), and reach ($2,266.6 \pm 2,388.3$ vs. $5,344.1 \pm 8,399.2$, $p<0.0001$). Weekend Facebook posts had significantly more impressions per post ($7,967.9 \pm 9,901.0$ vs. $9,737.8 \pm 19,013.4$, $p=0.03$) and a higher total reach ($4,975.8 \pm 6,309.8$ vs. $6,108.2 \pm 12,219.7$, $p=0.03$) than weekday posts.

Conclusion: Social media has been established as a crucial tool for the propagation of neurosurgical research and education. The implementation of a specialized SMT has a demonstrable impact on increasing the online visibility of social media content.

299: Gender and Fellowship Completion among Academic Neurosurgeons in the United States

Rosemary Behmer Hansen (Jersey City, NJ); Rosemary Behmer Hansen, MA, MPH; Nicole Silva, BS; Rebecca Cuevas; Angela Richardson, MD, PhD; Antonios Mammis, MD; Anil Nanda, MD, MPH

Introduction: On average, more women in the United States graduate from medical school compared to men. Yet, women comprise 17% of neurosurgery residents and are less likely to pursue fellowship subspecialty training. Those who pursue surgical fellowships tend to be disproportionately concentrated within pediatrics, a phenomenon that occurs not only in neurosurgery, but also in urology, orthopedics, general surgery, and otolaryngology. The objective of this study is to determine gender differences regarding selection of fellowship training in neurosurgery.

Methods: A quantitative analysis of fellowship training information of practicing, United States academic neurosurgeons was conducted. Information was extracted from publicly-available websites and analyzed with SPSS statistical software.

Results: Of the 1641 total academic neurosurgeons on publicly available websites, 1403 (85.50%) contained information on fellowship training and were therefore included in the analysis. There were disproportionately more men 1261 (89.9%) compared to women 142 (10.1%). A significant association was found between gender and fellowship completion (73.90% men versus 85.00% women, $p=0.037$). Significant associations between gender and fellowship completion were found for some subspecialties: pediatrics (25.35% women, 8.09% men, $p=0.000$), spine (9.15% women, 17.37% men, $p=0.006$), vascular (6.34% women, 11.26% men, $p=0.043$), neuro-oncology (13.38% women, 7.06% men, $p=0.009$), and critical care/trauma (6.34% women, 1.59% men, $p=0.001$). We present a survey for future distribution to practicing neurosurgeons for utilization in a mixed methods research project.

Conclusion: Women were found to have higher rates of fellowship completion compared to their male counterparts. Among subspecialties, greater proportions of women completed fellowships in pediatrics, neuro-oncology and critical care/trauma compared to men. Spine and vascular, alternatively, had significantly greater proportions of men. While the presence of gender disparities in neurosurgical fellowship completion is apparent, reasons contributing to said choice remain unknown.

300: Quality Of Life of Patients with Unruptured Intracranial Aneurysms Before and After Endovascular Coiling: A HEAT Trial Secondary Study

Bernard R. Bendok, MD, FAANS (Phoenix, AZ); Karl Abi-Aad, MD; Rudy Rahme, MD; Arjun Syal, MD; Devi Patra, MBBS; Jodee Winter; Chandan Krishna, MD; Bernard Bendok, MD

Introduction: The change in quality of life (QOL) of patients with unruptured intracranial aneurysms (UIAs) following endovascular treatment is a reflection of the physical and psychosocial outcomes following the procedure. In this study, using the Hydrogel Endovascular Aneurysm Treatment (HEAT) trial database, we evaluated the QOL of patients with UIAs pre/post-coiling.

Methods: Subjects from the HEAT database with 3-14mm UIAs who completed both preoperative and 18-24-month QOL surveys were included. QOL was recorded using the Short Form 36, which consists of 36 questions and 8 components: physical functioning, role physical, role emotional, vitality, emotional well-being, social functioning, body pain, and general health. Subject scores were recorded at the preoperative visit and at 18-24-month follow-up visits and the change of QOL was evaluated. Multivariate analyses were performed to find predictors of change in QOL

Results: 270 patients were included with an average age of 59.7 years, and a F:M ratio of 4.5:1. At presentation, 192 (71%) of subjects were asymptomatic. There was an increase in the role physical ($p=0.043$), vitality ($p=0.022$), and emotional well-being ($p<0.001$) components of QOL when comparing the preoperative visit to the 18-24-month follow-up. All other parameters were unchanged. Younger age (<60 years) predicted improvement in role emotional ($p=0.012$), vitality ($p=0.024$), and social functioning ($p=0.035$). The absence of serious adverse events predicted improvement in vitality ($p=0.031$) and social functioning ($p=0.035$). Employed subjects had better improvement in general health than unemployed subjects ($p=0.039$).

Conclusion: Patients with 3-14 mm UIAs had improvements in the role physical, vitality, and emotional well-being components of the SF-36 at 18-24 months following endovascular coiling treatment.

301: Thirty- and 90- Day Readmissions after Treatment of Traumatic Subdural Hematoma: A National Trend Analysis

Aladine Abdalla Elsamadicy, BE, MD (New Haven, CT); Aladine Elsamadicy, MD; Andrew Koo, BS; Wyatt David, MS; Adam Kundishora, MD; Nanthiya Sujjantararat, MD; Stephanie Robert, MD, PhD; Branden Cord, MD, PhD; Ryan Hebert, MD; Farhad Bahrassa, MD; Ajay Malhotra, MD; Charles Matouk, MD

Introduction: Subdural hematoma (SDH) is one common form of traumatic brain injury which requires extensive patient management and use of resources. However, there is a paucity of national studies examining the likelihood of readmission after surgical intervention for SDH. The aim of this study was to investigate differences in 30- and 90-day readmissions for treatment of traumatic SDH in a nationwide readmission database.

Methods: The Nationwide Readmission Database years 2013 — 2015 was queried. Patients with a diagnosis of traumatic SDH and a primary procedure code for incision of cerebral meninges for drainage were identified using the International Classification of Diseases, Ninth Revision, Clinical Modification coding system. Patients were grouped by no readmission (Non-R), readmission within 30 days (30-R), and readmission within 31 to 90 days (90-R). Weighted multivariate analysis assessed impact of clinical factors associated with 30- and 90-day readmissions.

Results: A total of 14,355 patients were identified, with 3,106 (21.6%) patients encountering a readmission (30-R: $n = 2,193$ [15.3%]; 90-R: $n = 913$ [6.3%]; Non-R: $n = 11,249$). There were similar proportions of median household income percentile and primary insurance between all 3 cohorts. The most common complications during index admission were postoperative infection, seizures, and genitourinary complication. The most prevalent 30- and 90- day diagnoses seen among the readmitted cohorts were postoperative infection, sepsis, and epilepsy. On multivariate logistic regression analysis, Medicare, Medicaid, hypertension, diabetes, renal failure, congestive heart failure and coagulopathy were independently associated with 30-day readmission; Medicare and rheumatoid arthritis/collagen vascular disease were independently associated with 90-day readmission.

Conclusion: In this study, we identify the readmission rates and complications associated with treatment intervention for traumatic subdural hematoma. We find that the most common reasons for readmission are postoperative infection, sepsis and epilepsy-related complications. Furthermore, multiple patient-specific variables were independently associated with hospital readmission.

302: The impact of resident work-related factors on risk of burnout: a global neurosurgery pilot study

Natasha T. L. Ironside, MD (Charlottesville, VA); Daniel Felbaum, MD; Hasan Syed, MD; Walter Jean, MD

Introduction: There may be geographical differences in work-related factors affecting burnout among neurosurgical residents worldwide. This study aimed to examine the risk of burnout among neurosurgery trainees, and to evaluate for international differences in work-related factors affecting burnout.

Methods: A 16-question survey was broadcasted throughout the social media networks of neurosurgery trainees worldwide. The survey examined training program-related factors and emotions towards training, patients and work environment. Responses were collected on a 5-point scale and anonymized. The relationship between work-related factors and risk of burnout, defined as a total survey score of >18, was assessed using univariable and multivariable logistic regression analyses.

Results: A total of 797 trainees responded to the survey, 246 (30.9%) of which were from low-to-middle income (LMIC) countries. 192/797 (20.7%) of respondents were found to be at risk for burnout. Higher number of work hours (OR=2.471 [1.471, 4.152]; p=0.001) and European training location (OR=1.634 [1.074, 2.485]; p=0.022) were associated with increased risk of burnout, whereas higher number of operative cases (OR=0.561 [0.345, 0.910]; p=0.019) and USA/Canada training location (OR=0.474 [0.244, 0.918]; p=0.027) were associated with reduced risk of burnout in the multivariable model. Although LMIC trainees had higher work hours and more frequent on-call shifts without work-hour limits, their average total burnout score and proportion at risk for burnout were identical to the global cohort.

Conclusion: Risk of burnout in neurosurgery trainees was driven by multiple factors. Globally, higher work hours was associated with increased risk, and higher operative volume was associated with reduced risk of burnout. Despite restrictions on work hours, European trainees were at highest risk for burnout, which may be related to the eroding case load perpetrated by these restrictions. LMIC trainees were comparatively immune to burnout, in spite of long hours and frequent overnight shifts, pointing to a resilience, the origins of which this study was not equipped to examine.

303: Surgical Efficiency: Identifying Causes and Reducing Delays in Operating Room Workflow

Mark Zaki (Chestnut Hill, MA); Chris Collier, BS; Blake Hauser; Scott Farren, RN; Maya Babu, MD, MBA; Oluwaseun Akeju, MD; Wilton Levine, MD; Brian Nahed, MD, MSc

Introduction: Operating room (OR) workflow efficiency optimizes healthcare delivery and reduces healthcare costs. Our multidisciplinary team analyzed the electronic medical record (EMR) to identify variables that could help identify patterns of inefficiencies. We hypothesize educational interventions based upon objective data will result in significant and lasting improvement in OR efficiency.

Methods: We extracted EMR data specifying time-stamp and procedure characteristics for all first start neurosurgery cases at the Massachusetts General Hospital from 7/1/18-7/1/19. A delay was defined as an actual start (time patient wheeled into OR) occurring after a scheduled start by ≥ 15 minutes. To minimize confounding factors, we focused on first start operative cases of patients arriving from home (n=1064 procedures). In addition, we corroborated EMR data with in-person shadowing of OR workflow from patient arrival through the OR.

Results: Of 1064 first cases, 283 were delayed (27%). Average delay was 33 ± 28 minutes (Median: 25; Q1-Q3: 19-33). The pre-op complete to in room interval was longer for delayed cases compared to all first starts (86 ± 41 min vs 69 ± 33.4 min, p<.01). Documented arrival time for delayed patients tended to occur after the instructed time of 2 hours prior to case start. Total delay time was 9432 minutes (157 hours). We validated findings by observing the OR workflow process and identified variations which we will direct an educational intervention towards and reevaluate. To mitigate the Hawthorne effect, an independent party observed neurosurgery first case workflows for one month prior to educational intervention implementation in Nov 2019.

Conclusion: Improvements in OR workflow efficiency result in significant improvement when based upon objective educational interventions. We propose a workflow efficiency algorithm to identify variables to target with strategic intervention aimed to improve OR efficiency and healthcare delivery.

400: Intra-arterial Transplantation of Mitochondria after Ischemic Stroke Reduces Cerebral Infarction*Pedro Norat Magno (Charlottesville, VA); Yashar Kalani; Petr Tvrdek*

Introduction: Stroke is a leading cause of death and severe disability in the United States. Current treatment options for stroke patients are limited to restoring blood flow via intravenous administration of thrombolytics (tPA) or endovascular thrombectomy. However, reperfusion intervention itself has been shown to trigger secondary injury. Mitochondrial function is fundamental for metabolic homeostasis and within minutes after arterial occlusion, brain mitochondria begin to lose electrochemical proton gradients, causing cessation of ATP synthesis and overproduction of reactive oxygen species (ROS), leading to cell death. Here, we show that infused mitochondria integrate into the cells of the central nervous system and reduce stroke burden.

Methods: Using murine stroke models of middle cerebral artery occlusion, we demonstrate that it is feasible to deliver viable mitochondria to ischemic brain parenchyma via an intra-arterial route of administration. We also show the beneficial supplemental effects of concurrent focused ultrasound (FUS) activation of microbubbles, which serves to open the blood-brain barrier without hemorrhagic complications.

Results: We provide evidence that mitochondrial transplantation may be beneficial as therapeutic intervention for ischemic stroke. First, we show that healthy muscle-derived mitochondria can be isolated in a clinically relevant timescale. Second, we demonstrate that intra-arterial injections of mitochondria result in perfusion of extravascular spaces in a minimally invasive manner, and that this outflow can be further enhanced by FUS. Third, mitochondria from the interstitial spaces become integrated by multiple cell types in the ischemic region. Fourth, mitochondrial transplantations elevate ATP concentrations in the brain parenchyma which might provide a basis for a partial metabolic rescue of ischemic tissue. Finally, cerebral infarction volume is reduced and cell survival is increased after mitochondrial infusions.

Conclusion: Our results have implications for the development of interventional strategies after ischemic stroke and suggest a novel potential modality of therapy after mechanical thrombectomy.

401: The Heart-Brain Axis in Subarachnoid Hemorrhage*Ran Xu (Berlin, Germany); Christian Oeing; Ulf Schneider; Peter Vajkoczy*

Introduction: Cardiac pathologies occur in up to 30% after subarachnoid hemorrhage (SAH), ultimately contributing to systemic complications. The underlying pathology of the interplay between cardiac dysfunction and cerebral perfusion is poorly understood. We sought to describe an in-vivo mouse model to investigate cardiac function after experimental SAH.

Methods: Experimental SAH was induced in male C57Bl/6 mice via a filament perforation model and confirmed via MRI, while Sham operation was conducted for the control group. Transthoracic echocardiography (TTE) was performed to elicit diastolic and systolic function on three timepoints (d1, d7, d14; ntotal=72). Diastolic function was assessed by determining mitral inflow patterns (E/E' ratio) and mitral annulus velocities (E/A ratio), while left ventricular ejection fraction (LVED) was measured for systolic function. Cardiomyocyte size was quantified using Hematoxylin/Eosin stainings. Masson Trichrome staining was performed to determine percentage of fibrotic tissue.

Results: In SAH mice, impaired diastolic function was observed as demonstrated by reduced E/A ratio (Sham vs. SAH: 2,3 vs. 1,5; $p=0,04$), while left ventricular ejection fraction was not affected in the setting of SAH (Sham vs. SAH: 68% vs. 64%). To elicit whether diastolic dysfunction may stem from cardiac hypertrophy, heart weight was measured. Indeed, the heart weight increased in SAH mice by 11,7% (Sham vs. SAH: 136 mg vs. 152 mg; $p<0,05$). Concomitantly, cardiomyocyte size was also significantly increased in SAH mice (Sham vs. SAH: 114 μm^2 vs. 141 μm^2 ; $p<0,01$). This was also accompanied by an increase in interstitial fibrosis.

Conclusion: In experimental SAH mice, a significant impact on diastolic dysfunction is observed after inducing SAH injury, paralleled by an increase in heart weight and cardiomyocyte size. The above-mentioned model can be utilized to examine the brain-heart axis in the setting of SAH.

402: Impact of Blood Pressure Changes in Cerebral Blood Perfusion of Patients with Ischemic Moyamoya Disease Evaluated by SPECT

Hugo A. Andrade Barazarte, MD (Barquisimeto, Venezuela); Zhao Liming, MD; Sun Weiliang, MD; Jia Jia, MD; Hao Liang, MD; Liu Yang, MD; Felix Goehre, MD, PhD; Ajmal Zemar, MD, PhD; Christopher Ludtka, MD; Tianxiao Li, MD; Juha Hernesniemi; Chaoyue Li, MD

Introduction: Up to now, quantitative cerebral hemodynamic imaging studies failed to provide information regarding cerebral blood flow (CBF) and its variations through blood pressure (BP) modifications in patients with certain cerebrovascular pathologies. Our aim was to determine the impact of targeted BP modifications on CBF in moyamoya disease (MMD) patients assessed by single-photon emission computed tomography (SPECT).

Methods: From March to September 2018, we prospectively collected data of 154 MMD patients and selected 40 patients with ischemic MMD. Initially, all patients underwent in-hospital blood pressure (BP) monitoring to determine mean arterial pressure (MAP) baseline values. The study cohort was subdivided into two subgroups: 1) Group A or relative high BP (RHBP) with an induced MAP 10-20% higher than baseline, and 2) Group B or relative low BP (RLBP) including patients with MAP 10-20% lower than baseline. All patients underwent an initial SPECT study at admission-day, and on the following day every subgroup underwent a second SPECT study under their respective targeted BP values.

Results: RHBP patients showed a reduction in perfusion deficit areas of $10.55 \pm 4.11\%$ and of $10.74 \pm 5.08\%$, when the left hemisphere and right hemisphere were respectively affected. RLBP patients showed an increment of perfusion deficit areas of $11.36 \pm 2.29\%$ on the left-side hemispheres and of $7.84 \pm 2.53\%$ on the right-side hemispheres.

Conclusion: Cerebral blood flow of MMD patients is susceptible to small ($\pm 10\text{-}20\%$ of MAP) BP changes. SPECT imaging is useful to demonstrate CBF variations under targeted BP values. Cerebral autoregulation in MMD patients might be affected due to short dynamic variations in BP. In these patients is important to maintain a strict BP monitoring during the perioperative management to prevent further complications.

403: Evaluation of the Inter-rater Reliability of Aneurysm Occlusion Classifications: A HEAT Trial Secondary Study

Bernard R. Bendok, MD, FAANS (Phoenix, AZ); Karl Abi-Aad, MD; Rudy Rahme, MD; Arjun Syal, BS; Devi Patra; Philius Turcotte, PA; Chandan Krishna, MD; Bernard Bendok, MD

Introduction: Aneurysm occlusion scales are commonly used to assess the success of aneurysm treatment and monitor for aneurysm recurrence. However, there is the potential for disagreement in imaging interpretation between multiple reviewers. In this study, using the Hydrogel Endovascular Aneurysm Treatment (HEAT) trial database, we assessed the inter-rater reliability of aneurysm occlusion scales between treating physicians and a third-party blinded core lab.

Methods: This study is based on the HEAT trial patient database, which included 600 aneurysms treated with endovascular coiling in 46 sites across the US and Canada. The treating site and the core lab independently reviewed the immediate post-operative and the follow-up (3-12 and 18-24 months) catheter angiography and/or magnetic resonance angiography images. The treating physicians and core lab independently evaluated the Raymond-Roy scale (3-point scale), recanalization status of aneurysms (Yes/No; 2-point scale), and the Meyer volumetric scale (6-point scale).

Results: There was minimal agreement in overall Raymond-Roy scores of 1501 imaging (kappa: 0.386, 95% CI [0.372, 0.405]) and Meyer scale scores of 91 imaging (kappa: 0.228, 95% CI [0.102, 0.364]). There was weak agreement in the recanalization (Yes/No) assessment of 931 imaging (kappa: 0.448, 95% CI [0.375, 0.521]). For the Raymond-Roy scale, the agreement was higher at final follow-up than at immediate post-operative imaging (screening visit imaging kappa: 0.240, 95% CI [0.227, 0.290]; 18-24 month imaging kappa: 0.422, 95% CI [0.387, 0.435]).

Conclusion: The minimal inter-rater agreement in the Raymond-Roy and Meyer scale values and weak inter-rater agreement in the recanalization survey reinforces the need for a core lab in imaging-based studies. The use of a blinded core lab would mitigate physician assessment variability when using these scales in clinical trials.

404: Mechanical Thrombectomy-Related Subarachnoid Hemorrhage: Characteristics And Outcomes

Patrick Brown (Winston-Salem, NC); Stacey Wolfe, MD; Kyle Fargen, MD

Introduction: Endovascular management of stroke has become the mainstay treatment for intracranial emergent large vessel occlusion (ELVO). As techniques have advanced and practitioners have become more aggressive with more distal occlusions, hemorrhagic transformation and associated symptomatic intracranial hemorrhage (sICH) have been well studied and rates have remained relatively stable. However, discussions of procedural-related subarachnoid hemorrhage (SAH) have been sparse. The mechanisms and associated effects are less well understood. We present our single-center experience with procedure-related SAH and associated procedural factors and outcomes.

Methods: We conducted a retrospective review of our single-center experience of procedure-related SAH after mechanical thrombectomy (MT) for ELVO from January 2015 to July 2019 with regards to technique, device(s) used, number of passes, procedure time, short- and long-term outcomes. We report salient findings in the twenty-six such patients at our institution during this period.

Results: We report twenty-seven cases of MT-related SAH during the evaluation period. One of these patients was lost to follow up. Procedural-related SAH was more highly correlated with stent retriever utilization (92.8% vs. 61.7%), longer procedures (65.1 min vs. 47.8 min), more passes (3.12 vs. 2.37), and worsened long-term outcomes (mRS 3 or greater, 76.9% vs. 66.9%).

Conclusion: Previous discussions of mechanical thrombectomy-related SAH have suggested a benign course for this entity. However, our data suggest correlative procedural characteristics and overall less favorable outcomes for thrombectomy-related SAH. These findings warrant further multicenter study with larger groups of patients.

405: Multicenter Study on Pipeline embolization Of Posterior Circulation Aneurysms: Experience with 118 Aneurysms

Christoph Johannes Griessenauer, MD, FAANS (Danville, PA) ; Alejandro Enriquez-Marulanda; Philipp Taussky; Arundhati Biswas; Ramesh Grandhi; Lorenzo Rinaldo; Guiseppe Lanzino; Waleed Brinjikji; Jan-Karl Burkhardt; Mandeep Ghuman; Victor Yang; Adam Dmytriw

Introduction: The Pipeline Embolization Device (PED) is a flow diverting stent that has been used off label for the treatment of challenging posterior circulation aneurysms. Data on this treatment modality is primarily limited to small retrospective single center series. For the present study, an international, multicenter collaboration was established to assess safety and efficacy of this treatment.

Methods: Consecutive posterior circulation aneurysms treated with the PED between 2012 and 2019 across 11 international neurovascular centers were retrospectively reviewed. Baseline demographics, aneurysm and treatment characteristics, complications, occlusion status, and functional outcome were assessed.

Results: There were 118 posterior circulation aneurysms treated with the PED in 115 patients. Twenty-four (20.9%) patients presented with aneurysmal subarachnoid hemorrhage (aSAH). Most aneurysms were fusiform (36.4%) in morphology, followed by saccular (35.6%) and dissecting/blister (28%). The median diameter was 9.8 mm and 18.6% were larger than 20 mm. The most common locations were the vertebral (44.1%) and basilar arteries (27.1%). Complete or near complete occlusion (>90%) was achieved in 89.5% of aneurysms at a median follow-up of 14 months. Dissecting/blister aneurysms were most likely to have occluded ($p = 0.03$). Symptomatic neurologic complications occurred in 10.2% and were associated with larger aneurysm size, ruptured presentation, or presentations with brain stem compression, cranial nerve palsy, or stroke. Favorable functional outcome (mRS 0-2) was achieved in 83.3% of patients. There were 7 mortalities of which 4 occurred in aSAH patients.

Conclusion: This multicenter study shows flow diversion with the PED for the treatment of posterior circulation is preferentially used for the treatment of fusiform and dissecting/blister aneurysm morphologies. Despite the challenges presented by these less common morphologies, flow diversion may be performed with a neurologic complication rate of 10% and favorable long term aneurysm occlusion rates.

406: Arachnoid Granulations Poised For a Role in Immune Surveillance after Intracerebral Hemorrhage

Jennifer D. Sokolowski, MD (Charlottesville, VA); Kaan Yagmurlu, MD; Petr Tvrdik, PhD; James Mandell, PhD; Beatriz Lopes; Min Park; M. Yashar Kalani; Kevin Lee, PhD

Introduction: Long-standing dogma holds that, in humans, CSF produced by the choroid plexus flows convectively along with interstitial fluid through parenchymal paravascular spaces, via the glymphatic system, and drains through arachnoid granulations (AGs) into venous sinuses. More recent evidence suggests that meningeal lymphatics have a role in CSF drainage and immune surveillance takes place via drainage of antigens to cervical lymph nodes. However, the preponderance of such evidence was obtained studying the meninges of rodents, which lack AGs resembling those seen in humans. Therefore, we sought to help clarify relations among the glymphatic system, AGs, and meningeal lymphatics in humans, in order to further define CSF drainage and immune surveillance in the CNS.

Methods: We collected meninges during autopsy from five patients without intracranial pathology and from three patients with a history of intracerebral hemorrhage. Immunostaining utilized markers of lymphatic endothelial cells, including podoplanin, Lyve1, CD31, as well as multiple immune markers, including CD45, CD209, CD3, CD4, CD8, CD20 and MHCII. Imaging was performed using confocal microscopy.

Results: We found lymphatic networks in arachnoid projecting to AGs; these are distinct from previously-described dural lymphatic vessels that reside within dura and have no distinct connection to subarachnoid CSF-filled space. We show lymphatic endothelial cells and CD45+ cells within AGs express MHCII, suggesting they function in antigen presentation. We also demonstrate that AGs contain monocytes/macrophages, dendritic cells, T cells, and B cells. After hemorrhagic injury, CD45+ immune cells in AGs increase in density (from 5.21%±0.96% to 10.22%±2.75%, p=0.04) and exhibit morphological changes suggestive of activation.

Conclusion: Our data are consistent with a novel model for immune surveillance of the CNS in humans, and suggest AGs could serve as a hub where immune activation or tolerance to CNS antigens occurs.

407: Peripheral Nerve Tumors of Uncertain Behavior: Risk of Percutaneous Biopsy

Courtney Pendleton, MD (Philadelphia, PA); Robert Spinner, MD

Introduction: The decision to biopsy peripheral nerve tumors is largely based on presumed behavior determined via patient history, clinical exam, and radiologic characteristics. Management is often to avoid biopsy in tumors that are likely benign, and to routinely biopsy tumors that are likely malignant, as tissue diagnosis will significantly change patient management. The role of biopsy in peripheral nerve tumors of uncertain character remains controversial, and the risk of biopsy of these tumors is unknown.

Methods: Records of a single surgeon were reviewed from 2000-2018, and patients who underwent percutaneous biopsy for a peripheral nerve tumor were selected. Inclusion criteria were documented uncertain nature of the tumor, percutaneous biopsy performed at the request of the neurosurgeon, biopsy obtained at our institution, pathology report available, and follow-up documentation.

Results: 76 patients met inclusion criteria. 25 patients had NF1, 1 had NF2, 2 had other non-specified tumor syndromes, 1 had a prior MPNST at a distant site, and 8 patients had prior unrelated malignancies. 57 patients had concerning clinical findings including 32 with moderate-to-severe pain and 29 with weakness. 65 had radiologic findings including growth, necrosis, irregular shape/borders, or hypermetabolic findings on PET. Biopsy was performed under image guidance by the radiology team. Three patients had new onset of pain following biopsy (3.95%). As a comparison, we evaluated the complications in our population of likely malignant tumors undergoing percutaneous biopsy, where the rate of new onset pain, weakness, or numbness was 8.0%.

Conclusion: Published complication rates for percutaneous biopsy of peripheral nerve tumors vary widely (0-12%). We had a complication rate of 3.95% in percutaneous biopsy of tumors of uncertain behavior, demonstrating that biopsy of these lesions is a reasonably safe procedure which may alter patient management.

408: The Risk of Peripheral Nerve Tumor Biopsy in Suspected Benign Etiologies

Roberto J. Perez Roman, MD (Miami, FL); Stephen Burks, MD; Luca Debs, MD; Iahn Cajigas, MD, PhD; Allan Levi, MD, PhD

Introduction: Peripheral nerve sheath tumors (PNST) are tumors with unique clinical and imaging features that present to a variety of physicians. These lesions are often referred for biopsy which can put nerve fascicles at risk. Pre-operative biopsy may cause distortion of normal anatomical planes, making definitive resection difficult. We aim to evaluate the neurological risks of pre-operative biopsy in benign PNST.

Methods: Surgical cases collected retrospectively using a prospectively established database of PNST treated by a single surgeon between 1997 and 2019. Patients were dichotomized depending on pre-operative biopsy. Effects of biopsy were assessed via history and physical examination both pre- and post-definitive resection.

Results: Total of 151 cases were included. Only 23.2% (35) of patients underwent pre-operative biopsy, but 42.9% of these experienced new or worsening neurologic exam immediately following biopsy. After definitive resection the rate of neurologic deficit was significantly different between the two groups with 60% of biopsy patients and 19% of those patients not biopsied experiencing decline in exam ($F=25.72$ $p<0.001$). Odds ratio for any post-operative deficit for biopsy was 6.40 (CI [2.8, 14.55], $p<0.001$). Univariate logistic regression of neurologic deficit with patient age, sex, tumor type, and biopsy status showed that only biopsy was associated with occurrence of any post-operative deficit.

Conclusion: Biopsy of benign PNST is associated with a high rate of neurologic deficit both immediately following the procedure and definitive resection. Careful selection it's imperative prior to proceeding with biopsy of nerve sheath tumors exhibiting benign features given the unacceptably high rate of neurologic decline.

409: Endoscopic Decompression of Peripheral Nerve Entrapment Syndromes

Baher Medhat Labib Hanna (Egypt, Arab Rep.); Baher Hanna; Mohamed Farhoud; Mostafa El Henawy

Introduction: Carpal tunnel syndrome is a very common condition in hand surgery. The gold standard in therapy is the surgical release of the flexor retinaculum. Endoscopic carpal tunnel release, cubital tunnel release, tarsal tunnel release and meralgia paresthetica provides superior convalescence and patient safety.

Methods: 45 patients underwent endoscopic decompression using Krishnan retractor endoscope system (40 CTS, 2 cubital tunnel, 2 TTS, 1 meralgia paresthetica).

Results: significant improvement in the patient were noticed post operatively, small incision.

Conclusion: endoscopic decompression of peripheral nerve entrapments is effective method and alternative method to open surgery, with rapid return to work, small incision and less pain the scar.

410: Neurosurgery Resident Exposure to Peripheral Nerve Surgical Procedures and Assessment Of Their Technical Abilities to Perform Nerve Repairs

Andrew Jack, MD (San Francisco, CA); Line Jacques, MD, MSc, FRCSC; Beata Durcanova, BSc

Introduction: Peripheral nerve surgery (PNS) exposure during neurosurgical residency training is variable. There is currently no systematic evaluation of the technical aspect of PNS in the US, and only recently with implementation of a Competency-by-Design (CBD) curriculum for in Canada. Identifying and defining PNS competencies is crucial to ensuring adequate resident training. Here, we examine PNS training at neurosurgical centers in Canada and the US to gauge trainee self-reported competency with current PNS competencies. Furthermore, self-reported competency results were compared to technical abilities in 3 peripheral nerve anastomosis (PNA) repairs.

Methods: Residents across Canada and at a large, academic, US neurosurgical center completed a questionnaire evaluating exposure and self-reported competency of PNS procedures. Resident exposure and competency scores were correlated with procedure-based skills from 3 PNA-repairs using in-cadaveric specimens: direct-nerve (DS), connector-assisted (CA), and connector-only (CO). Variables collected included: time-to-completion, nerve-handling (video-analysis), sutures required, visual grading by 3 judges (blinded), and level-of-training. ANOVA/2-way ANOVA (parametric) and Kruskal-Wallis/Mann-Whitney (non-parametric) analyses with post-hoc testing were completed. Statistical significance was set at $p<0.05$.

Results: Level of training was significantly related to PNS exposure ($p<0.01$): senior residents report more exposure to cubital tunnel release ($p<0.01$), brachial-plexus surgery ($p=0.01$), direct-nerve-repair ($p=0.03$), and nerve-transfer ($p=0.02$). No difference was observed between level of training and PNA grading ($p=0.41$), although a difference was seen between types of PNA with DS ($p=0.02$) and CA-repairs ($p<0.01$) scoring better than CO. A discrepancy was observed

between trainee self-reported PNS procedure competency and PNS case exposure that increased upon stratifying trainees based on level of training.

Conclusion: This study was performed in order to gain a better appreciation of the exposure and training that residents in neurosurgery receive for PNS. This information will provide insight into the direction of PNS training, and its role in the implementation of a CBD curriculum.

411: Iatrogenic Post Intramuscular Injection Related Peripheral Nerve Palsy-A Retrospective Study of 292 Surgically Treated Patients

Abhijit G Warade (Mumbai, India); Ketan Desai

Introduction: Iatrogenic intramuscular injection related peripheral nerve injury is a common problem in rural parts of developing countries like India. The major cause being untrained medical staff and misconception that injections have better outcome than oral medications. A retrospective analysis of outcomes in patients surgically treated for iatrogenic peripheral nerves palsies following intramuscular injections was done.

Methods: 292 patients from 2000-2018 were operated by senior author, M:F ratio was 4:1, mean age was 18.7 years and average duration of presentation was 6.7 mths. Commonest nerve involved was sciatic nerve in gluteal region presenting as foot drop in 151 patients. Radial nerve in arm presenting as wrist drop in 132 & axillary nerve in shoulder presenting as restricted abduction in 9 patients. The mean follow-up was 9.7 months (6 months to 3-years)

Results: Neurogenic pain and paresthesias in nerve distribution area was noted in 28% patients and muscle wasting in 38% patients. Electrophysiological study was performed in all patients prior to surgical intervention. Pre-operative Magnetic resonance imaging (MRI) and neurography was performed in 11% patients. 210 (71.9%) patients underwent external neurolysis and 82(28.1%) underwent excision of neuroma and sural nerve cables grafting was performed with Intraoperative electrophysiological monitoring. Functional recovery was excellent in radial (90%) and axillary nerves (88.9%). Patients with sciatic nerve palsy, it was 56.5% in tibial and 23.7% in common peroneal nerves. Good outcomes were seen when surgery was performed earlier (<6 months) with external neurolysis having better outcome than nerve grafting.

Conclusion: The outcome of iatrogenic post intramuscular injection peripheral nerve injury largely depends on timing of surgery in patients who failed conservative management.

414: Prospective Randomized Trial of Temporary Inferior Vena Cava Filter in Thrombophilic Patients That Had Cranial or Spinal Surgery

Scott A. Shapiro, MD, FAANS (Indianapolis, IN); Brandon Lane, MD; Nicolas Villeli, MD

Introduction: The outcomes for thrombophilic patients with known DVT/PE who are anticoagulated and need elective neurosurgery are poorly documented.

Methods: We conducted from 2003-2018 a randomized trial comparing the placement of a temporary inferior vena cava filter in 93 thrombophilic patients before surgery versus no IVC filter placed in 94 thrombophilic patients. Chi square and logistic regression multivariate statistics were performed.

Results: For the 93 that had a temporary IVC filter placed before surgery(17craniotomies and 76 spine surgeries), there were 0 pulmonary embolisms, 0 hemorrhagic complications and 0 deaths. Of the 93 temporary IVC filters removed 20(22%) had clot on the filter that would have lead to a PE. For the 94 without a temporary IVC filter(16 craniotomies and 78 spine surgeries) there were 14(15%) pulmonary embolisms, 9 hemorrhagic complications requiring reoperation and 8 sudden deaths due to PE. The temporary IVC filter significantly lessened PE($p<0.001$), sudden death due to PE($p<0.01$) and hemorrhages requiring reoperation($p<0.01$). Logistic regression multivariate analysis found that only the placement of a temporary IVC filter significantly lessened complications($p<0.01$) Sex, length of surgery, type of surgery or type of thrombophilia were statistically insignificant.

Conclusion: Our results significantly support the placement of a temporary IVC filter in thrombophilic patients with known DVT/PE before elective neurosurgery.

415: Early Results from the Multi-Center Prospective, Randomized CSM-S Study: Overall Quality Of Life Improvement, Complications, And Health Resource Utilization

Sanford Larson Award for Best Research Award

Zoher Ghogawala, MD, FAANS (Burlington, MA); Adam Kanter, MD; Praveen Mummaneni, MD; Erica Bisson, MD; James Harrop, MD; Subu Magge, MD; Robert Heary, MD; Michael Fehlings, MD; Paul Arnold, MD; Fred Barker II, MD; Edward Benzel, MD

Introduction: The Cervical Spondylotic Myelopathy-Surgical study is a randomized prospective study conducted to compare the effectiveness of ventral versus dorsal (fusion or laminoplasty) surgery for patients with multi-level CSM.

Methods: A multi-center prospective, RCT was conducted on patients aged 45-80 years with multi-level CSM. Patients were enrolled between 2014-2018. Patients were randomized (2:3 randomization) to ventral or dorsal (fusion or laminoplasty — discretion of surgeon) surgery. Outcome assessments were obtained pre-operatively, 3 months, 6 months, and 1 year post-operatively.

Results: 15 sites randomized 163 patients - 63 (38.7%) ventral and 100 (61.3%) dorsal. Average age 62.2 years (49% male). Baseline characteristics were comparable. Crossover rate was 3%. Follow-up was 95% at 1 year. Analysis as randomized demonstrated no difference in improvement in SF-36 PCS at 1 year between ventral (5.7) and dorsal (6.3) surgery ($P=0.69$). We conducted a planned analysis of patients as treated. 66 patients ultimately underwent ventral fusion (VF) and 97 (69 dorsal fusion (DF) and 28 dorsal laminoplasty (DL)) underwent dorsal surgery. Patients, regardless of strategy, demonstrated improvements in NDI, mJOA, and EQ-5D. DL had superior outcomes in primary outcome SF-36 PCS when compared with VF ($P=0.04$) and DF ($P=0.04$). DL patients had fewer complications (42.4% VF vs. 27.5% DF vs. 10.7% DL; $P=0.007$) and DL hospital charges were lower (VF \$90,687 vs. DF \$ 111,705 vs. DL \$ 55,332; $P<0.05$). Ongoing utilization of physical therapy and opioids were lower with DL ($P<0.05$).

Conclusion: Patients undergoing ventral or dorsal surgery for CSM demonstrate improved overall quality of life at 1 year. Dorsal laminoplasty surgery for CSM is associated with greater improvements in health-related quality of life, fewer complications, and lower hospital charges.

416: A Transcriptomic Map of Pediatric Brain Tumors

Akshithkumar Maheshbhai Mistry, MD (Nashville, TN); Chi Le; Robert Naftel

Introduction: We aimed to develop a clinically-annotated transcriptomic map of pediatric brain tumors (PBTs) utilizing publicly-available PBT samples. It is needed to complement the recently generated mutational landscape of PBTs to develop better therapies of PBTs, the near-second most common form of childhood cancer.

Methods: We retrieved all the raw transcriptomic data generated on the most common platform from public genomic repositories (e.g., NCBI GEO, EGA/ArrayExpress, ICGC). We developed and tested a semi-automatic computational pipeline for harmonization and integration of raw transcriptomic data. Clinical data corresponding to the samples were obtained from associated metadata and publications.

Results: Raw transcriptomic data of >4400 PBTs were identified. Majority of the data (>1300 samples) were generated using Affymetrix Human Genome U133 Plus 2.0 microarray. A harmonized integration of these raw data was performed using our developed computational pipeline, which consisted of quality control (removing samples with higher RNA degradation or abnormal distributions of RNA probe intensities), transcript-level data retrieval, reduction of non-biological variation by adjusting for surrogate parameters, and gene-level annotation and summarization. 1130 samples passed the quality control that consisted of 306 medulloblastomas, 294 ependymomas, 194 high-grade gliomas, 134 pilocytic astrocytomas, 104 atypical teratoid rhabdoid tumors, 76 conventionally-defined primitive neuroectodermal tumors, and 22 neuro-glial tumors. We further annotated samples with age, sex, tumor subtype, grade, location, and overall survival. On unsupervised hierarchical clustering and dimensionality reduction, which generated a transcriptomic map, samples clustered based on their known molecular tumor subtype rather than the source of the samples or overall histology.

Conclusion: We generated a first-of-a-kind resource in the form of a PBT transcriptomic map for the scientific community. Using this resource, for the first-time, the scientific community can discover and robustly compare clinically-relevant genes, gene expression networks or signatures among the different types of PBTs independent of their source.

417: B-cell Lymphoma 2 (BCL2) Single Nucleotide Polymorphism (rs17759659) Is Associated with Intracranial Hypertension in a Prospective Cohort of Severe Traumatic Brain Injury

ThinkFirst Injury Prevention Award

Hansen Deng, MD (Pittsburgh, PA); Hansen Deng, MD; Benjamin Zusman, BA; Ruchira Jha, MD; Enyinna Nwachuku, MD; John Yue, MD; Sue Beers, PhD; Yue-Fang Chang, PhD; Lori Shutter, MD; Yvette Conley, PhD; David Okonkwo, MD, PhD; Ava Puccio

Introduction: Traumatic brain injury (TBI) initiates a cascade of apoptotic-related events. B-cell lymphoma 2 (BCL2) encodes a pro-survival protein that inhibits apoptosis, and the variant allele affects BCL2 expression. We evaluated the relationship between BCL2 and intracranial pressure (ICP).

Methods: A single-center, prospective database of severe TBI patients from 2000-2014 were studied. Inclusion criteria were: age 16-80, Glasgow Coma Scale (GCS) score 4-8 and at least 24 hours of ICP monitoring. The BCL2 single nucleotide polymorphism (SNP) rs17759659 was grouped by major allele (A) and minor allele (G). Outcomes were mean ICP, proportion of ICP spikes >20 mmHg and >25 mmHg, radiographic findings of edema, and operative management.

Results: In 264 patients, mean age was 39.2±17.4 years old and 78.0% were male. Mechanism of injury consisted primarily of motor vehicle accidents (44.7%) and falls (22.7%). One-hundred and five (39.8%) subjects were homozygous wild-type (AA), 127 (48.1%) were heterozygous (AG), and 32 (12.1%) possessed homozygous variant genotype (GG); mean ICPs were 11.4±4.3 mmHg, 12.8±6.3 mmHg, and 14.3±6.6 mmHg, respectively ($p=0.023$). The variant allele of rs17759659 was associated with more episodes of ICP>20 mmHg ($p=0.017$) and >25 mmHg ($p=0.048$). Multivariate analysis demonstrated that presence of the variant allele was associated with increased ICP (B=1.4 mmHg increase, 95%CI 0.4-2.4, $p=0.005$). AG (OR 1.9, 95%CI 1.1-3.3, $p=0.033$) and GG (OR 2.4, 95%CI 1.01-5.9, $p=0.048$) genotypes were at increased risk for cerebral edema. GG was associated with increased risk of surgical decompression (OR 3.9, 95%CI 1.6-9.5, $p=0.003$) compared to AA.

Conclusion: BCL2 SNP rs17759659 alleles were associated with intracranial hypertension, cerebral edema, and the need for surgical intervention. These data support a potential physiological role for BCL2 in the pathophysiology of severe TBI including mRNA stability or processing. Targeted screening and genotype-based therapies may further improve risk stratification and outcomes following severe TBI.

418: Thalamus Gates Progression of Mesial Temporal Seizures by Modulating Thalamocortical Synchrony

Adeel Ilyas, MD (Birmingham, AL); Adeel Ilyas, MD; Ganne Chaitanya; Emilia Toth, PhD; Kristen Riley, MD; Sandipan Pati

Introduction: The anterior nucleus of the thalamus (ANT) regulates hippocampal seizures in experimental models of temporal lobe epilepsy (TLE) by altering synchronization, but a clinical study demonstrating this is lacking. Therefore, the objective of this study is to investigate thalamocortical coupling during seizures.

Methods: Following IRB approval, adults (N=10) with suspected TLE undergoing stereotactic electroencephalography (SEEG) implantation were recruited prospectively. Seizures in which ANT recruitment was robust were selected for functional thalamocortical analyses using measures of synchrony and direct electrical stimulation of the ANT.

Results: Seizure onset was characterized by a decrease in alpha-band thalamocortical synchrony ($p=0.024$) whereas termination was characterized by an increase in theta-band synchrony ($p<0.001$). In addition, seizure termination in the thalamus displayed a stereotypical electrographic pattern of transition between a spike-and-wave signal to slow wave delta activity in the post-termination period. Furthermore, ictal thalamocortical synchronization patterns varied by seizure type ($p=0.001$). Electrical stimulation of the ANT with low and high frequencies produced distinct, opposite effects in the cortex: Low frequency stimulation resulted in cortical activation whereas high-frequency stimulation resulted in deactivation.

Conclusion: HANT facilitates seizure onset by decreasing inhibitory influences on the hippocampus. As the seizure evolves, inhibition within thalamotemporal networks is restored by theta synchrony that contributes to seizures termination. The ANT gates information flow to the temporal lobe, and this endogenous mechanism can be targeted for identifying stimulation parameters for thalamic deep brain stimulation in TLE.

419: Ultra High-Density Microgrid Recordings during Awake Craniotomy Reveal Submillimeter Structure of Human Language Processing

Daniel Cleary, MD, PhD (San Diego, CA); Eric Halgren, PhD; Sang Heon Lee, MS; Andrew Bourhis, BS; Youngbin Tchoe, PhD; Dominic Siler, MD, PhD; Ilker Yaylali, MD, PhD; Sydney Cash, MD, PhD; Seunggu Han, MD; Ahmed Raslan, MD; Sharona Ben-Haim, MD; Shadi Dayeh, PhD

Introduction: Brain-computer interfaces (BCI) offer hope to treat otherwise intractable neurological disease, but fundamental biological and engineering problems still remain. A multi-institute collaborative group has developed ultra high-density arrays of electrodes for cortical recordings that surmounts many of the major hurdles facing neural interface devices. These devices are thin, light-weight, and conform to the surface of the brain. Here, we demonstrate the utility of these devices by studying cortical processing during receptive speech.

Methods: Ultra high-density, conformal electrode arrays with either 128 channels at 50-micron pitch or 1024 channels at 200-micron pitch were used to record neural activity from the exposed brain surface during awake craniotomies. Cortical sites involved in speech processing were identified using clinical testing with either electrocorticography or bipolar stimulation, and then surface cortical activity was recorded using our grids. During recordings, patients were presented with sounds and instructed to distinguish between consonant-vowel combinations of real words, nonsense words, or noise-vocoded (inarticulate) words. Results were processed off-line.

Results: Seven patients' recordings showed modulation of neural activity during listening tasks. Recordings from superior temporal gyrus (STG) showed modulation of neural activity in both the beta- and gamma-bands, starting shortly after stimulus onset. One patient had a recording from the inferior frontal gyrus, wherein gamma-band modulation of neural activity started later, as compared with STG activity. In both cases, spatial patterns of highly related gamma-band activity were seen in clusters less than 1mm in diameter, and transition zones between processing clusters could be observed. Compared to the tightly localized gamma-band activity, beta-band activity was more spatially dispersed.

Conclusion: Here we show the fine spatial structure of cortical activity during speech processing, as recorded through conformal surface electrodes. These results demonstrate the utility of ultra high-density microgrids for recording neural activity and have important implications for further clinical and research applications.

420: Investigating Prefrontal Cognitive Networks in Parkinson's Disease: Subcortical Intermittent Theta-burst Stimulation Increases Theta Power in Dorsolateral Prefrontal Cortex (DLPFC)

Nicole Bentley, MD (Birmingham, AL); Zachary Irwin, PhD; Sarah Black, BS; Megan Roach, BS; Ryan Vaden, PhD; Christopher Gonzalez, MS; Anas Khan, BS; Galal El-Sayed, MD; Robert Knight, MD; Barton Guthrie, MD; Harrison Walker, MD

Introduction: Cognitive symptoms of Parkinson's disease (PD) cause severe disability and significantly limit quality of life. Little is known about the mechanisms, although aberrant oscillatory activity in basal ganglia-thalamo-prefrontal circuits likely plays an important role. While conventional deep brain stimulation (DBS) improves motor symptoms, it is generally ineffective for cognitive symptoms. Recent studies with transcranial magnetic stimulation (TMS), applying intermittent theta-burst stimulation (iTBS) to dorsolateral prefrontal cortex (DLPFC), suggest beneficial effects for certain aspects of cognition, possibly through a mechanism of long-term potentiation. However, TMS effects are transient, requiring repeated application. Subcortical DBS targets have strong reciprocal connections with prefrontal cortex, such that iTBS through the DBS lead might be more durable. Here we demonstrate safety and feasibility for delivering iTBS from the DBS electrode and explore changes in DLPFC electrophysiology.

Methods: We enrolled seven participants with medically refractory PD for DBS surgery, targeting either the subthalamic nucleus (STN) or globus pallidus interna (GPI). We temporarily placed an electrocorticography strip over DLPFC through the DBS burr hole. After placement of the DBS electrode into either GPI (n=3) or STN (n=4), awake subjects rested quietly during iTBS. We contrasted power spectra in DLPFC during iTBS versus rest, as well as between iTBS and high-frequency stimulation (HFS).

Results: Dominant frequencies in DLPFC at rest varied among subjects and along the subdural strip electrode, though were generally localized in theta (3-8 Hz) and/or beta (10-30 Hz) ranges. iTBS was imperceptible, and increased theta-frequency activity more than HFS. GPI stimulation resulted in significantly greater theta-power versus STN stimulation in our sample.

Conclusion: Acute subcortical iTBS from the DBS electrode is safe and well-tolerated. This novel stimulation pattern increases theta-power in ipsilateral DLPFC. Future studies will evaluate whether changes in DLPFC activity during iTBS are associated with improvements in cognitive or behavioral symptoms from PD.

421: A Systematic Exploration of Parameters Affecting Evoked Intracranial Potentials in Patients with Epilepsy

Bornali Kundu, MD (Salt Lake City, UT); Tyler Davis, MD, PhD; Brian Philip; Elliot Smith, PhD; Amir Arain, MD; Angela Peters, MD; Blake Newman, MD; Christopher Butson, PhD; John Rolston, MD, PhD

Introduction: Corticocortical evoked potentials (CCEPs) have been used to quantify brain connectivity and to discern brain areas involved in both brain function and disease. Importantly they have been used to try to discern the seizure onset zone in epilepsy patients. However, how varying stimulation parameters influences the measured CCEP across brain areas has not been well characterized. To better understand the factors that influence the amplitude of the CCEPs as well as evoked gamma-band power (70 — 150 Hz) resulting from single-pulse stimulation via cortical surface and depth electrodes.

Methods: CCEPs from 4370 stimulation-response channel pairs were recorded across a range of stimulation parameters and brain regions in 11 patients undergoing long-term monitoring for epilepsy. A generalized mixed-effects model was used to model cortical response amplitudes from 5 to 100 ms post-stimulation

Results: Stimulation levels <5.5 mA generated variable CCEPs with low amplitude and reduced spatial spread. Stimulation at ≥ 5.5 mA yielded a reliable and maximal CCEP across stimulation-response pairs over all regions. These findings were similar when examining the evoked gamma-band power. The amplitude of both measures was inversely correlated with distance. For the first time we show that CCEPs and evoked gamma power were largest when measured in the hippocampus compared with other areas. Importantly, evoked gamma power was 120% larger within the seizure onset zone compared with outside this zone.

Conclusion: These results will help guide future stimulation protocols directed at quantifying network connectivity across cognitive and disease states. Evoked gamma power may be a helpful marker of the seizure onset zone in epilepsy patients.

422: Cortical Oscillatory Dynamics in Patients with Parkinson's Disease and Essential Tremor

Hristos Courellis, MS (Los Angeles, CA); Alon Kashanian, BS; Shakthi Visagan, BS; Guy McKhann, BS; Mahsa Malekmohammadi, PhD; Nader Pouratian, MD, PhD

Introduction: The treatment of movement disorders such as Parkinson's disease (PD) and Essential Tremor (ET) is facilitated by the characterization of electrophysiological markers. One marker, the cortical β -oscillation (13-35Hz), exhibits many movement-related dynamics of interest. Previous work comparing these conditions has led to inconsistencies that could be clarified with larger patient populations. To this end, a framework is employed wherein ECoG data recorded from patients undergoing Deep Brain Stimulation (DBS) surgery are co-localized to a common cortical surface, thus allowing for β -band and associated γ -band (70-200Hz) power distributions to be characterized in the sensorimotor cortices of ET and PD patients.

Methods: ECoG signals were recorded from sensorimotor cortex in 48 patients (34 PD) intraoperatively during a unilateral alternating rest/movement finger tapping task. Digitized ECoG electrode positions were co-localized onto an MNI cortical surface for group-level analysis. Spectral power and phase-amplitude coupling analyses were initially conducted in channel space, followed by projection down onto the cortical surface for further spatial profiling.

Results: Resting β -activity was maximally desynchronized over the hand-knob region of precentral gyrus during movement in both PD and ET. Increased γ activity (both low and high) was co-localized with this β -desynchronization. Analysis of the low- β and high- β revealed an ET-PD dissociation, with low- β being significantly greater in ET, and high- β being significantly greater in PD. Also, highly significant phase-amplitude coupling between β and high γ was shown to persist during periods of movement in both ET and PD.

Conclusion: These findings recapitulate some key electrophysiological characteristics known to be present in the cortex of patients with PD, help clarify the relationship between ET and PD cortical neurophysiology, and better characterize distinct electrophysiological information channels that are known to be implicated in disease phenotype.

423: Creation of a Diffusion Tractographic Atlas of the Anterior Limb of the Internal Capsule for Psychiatric DBS Planning

Garrett P. Banks, MD, PhD (New York, NY); Megan Frankowski, PhD; Sarah Heilbronner, PhD; Kelly Bijanki, PhD; Eric Storch, PhD; Ashwin Viswanathan, MD, PhD; Evangelia Tsolaki, PhD; Nader Pouratian, MD, PhD; Wayne Goodman, MD; Sameer Sheth, MD, PhD

Introduction: Understanding white matter connectivity of DBS targets may improve efficacy of DBS for psychiatric disorders. Whereas subgenual cingulate and median forebrain bundle (MFB) targets are defined tractographically, the anterior limb of the internal capsule (ALIC) is not. We analyzed diffusion MRI data from healthy controls and patients receiving DBS for OCD to create a tractographic atlas of the ALIC.

Methods: We built a normative distribution connectivity atlas of the posteroventral (pv) ALIC using diffusion data from 100 human connectome project subjects using FSL. We then used the atlas to analyze the connectivity profile of 47 DBS contacts stimulated intraoperatively in 5 OCD patients. We calculated volume of tissue activated (VTA), transformed those VTAs onto the atlas to determine the fiber bundles engaged by each stimulation, and compared these to the behavioral effects elicited by each stimulation.

Results: We previously showed that anterior ALIC fibers follow corticotopic organization. However, posteroventrally, near the anterior commissure and the DBS target region, fibers coalesce into a two-dimensional profile, with thalamic fibers medially and subthalamic fibers laterally. Of the 47 regions tested with intraoperative stimulation, 26 elicited positive affect responses. The VTA-behavior analysis showed that of all the fiber bundles between cortex (dlPFC, ACC, lateral OFC, vmPFC) and deep structures (thalamus, midbrain/subthalamic area), stimulation of the vmPFC to subthalamic area bundle most frequently elicited positive affect responses (25/26).

Conclusion: This analysis of the pvALIC helps settle discrepancies in the literature regarding the connectomic profile of DBS targets, particularly regarding the relative contribution of anterior thalamic radiations and the MFB. We found the strongest mood-elevating effects with stimulation of the vmPFC to the subthalamic/midbrain fibers, which may represent the vmPFC-STN hyperdirect pathway. We are currently using this atlas to prospectively plan DBS for OCD and depression cases to test this working hypothesis.

424: Restoration of volitional hand grasp in cervical quadriplegia with a brain computer interface that decodes continuously

Benyamin Meschede-Krasa (Newton, MA); John Abel; John Tauber; Indie Garwood; Noeline Prins; Michael Ivan; Abhishek Prasad; Jonathan Jagid; Emery Brown; Iahn Cajigas

Introduction: Brain computer interfaces (BCI) could pave the way the 5.3 million paralysis patients to regain at-home autonomy. We developed a BCI for a patient with cervical spinal cord injury to regain hand grasping via the use of an external hand orthosis (ClinicalTrials.gov NCT02564419). In a clinical setting, the patient could initiate movement using motor imagery with a high degree of accuracy, but this paradigm was not implemented for real-time use. Here we adapt the BCI to allow for continuous decoding of movement intent as would be required for at home use.

Methods: Electrocorticographic (ECoG) activity was recorded during motor imagery of hand movement or rest. The desired motor imagery state was randomly prompted to mimic the subject volitionally initiating movement. Spectral features were extracted by multitaper spectral analysis and a hidden Markov model (HMM) was used for decoding motor intent. We used two model fitting approaches. First, a static HMM was trained for implementation without future updating. Second, an updating HMM was built to retrain the decoder periodically. We used cross validation to perform model selection and identify optimal multitaper parameters. The resulting classifier was then tested on new data.

Results: The decoder correctly classified grasping intention with an area under the receiver operating characteristic curve (AUROC) of 0.71 over the training data, but performance decreased to an AUROC of 0.60 in the test data. Model performance decreased between early trials (mean AUCROC= 0.75) and later trials (mean AUCROC=0.55), indicating time-dependent degradation of performance rather than over-fitting. The inclusion of a parameter updating procedure improved performance.

Conclusion: These results demonstrate that fully implanted BCI can be effectively implemented to restore continuous control of volitional hand grasp such as would be required for use outside of the lab environment. Further work will assess the efficacy of at-home use.

425: Dynamic Changes in Rhythmic and Arrhythmic Neural Signatures in the Subthalamic Nucleus Induced by Anaesthesia and Intubation

Kejia Hu (Shanghai, China); Bomin Sun; Ziv Williams

Introduction: Communication between cortical and subcortical structures including the basal ganglia has been proposed to be crucial for arousal, consciousness, and behavioural responsiveness. However, how basal ganglia contributes to the loss and recovery of consciousness during anaesthesia has not been well characterized.

Methods: Bipolar local field potentials (LFPs) from subthalamic nucleus (STN) and EEG from frontal cortex were recorded in 12 patients with Parkinson's disease (24 hemispheres) during anaesthesia induced by propofol for bilateral deep brain stimulation surgery. Moreover, the response of neural activity to intubation in anaesthesia was also evaluated to investigate whether an arousal intervention in anaesthesia induces changes of neural signatures in the STN.

Results: Propofol induced anaesthesia resulted in more apparent power changes in oscillatory activities in the STN than cortical EEG, with significantly increased low frequency activities (slow-wave oscillation, delta, theta, and alpha bands) and decreased higher frequency activity (beta, gamma and broadband high-gamma bands) in the subthalamic nucleus. This was also accompanied by increased STN-frontal cortical coherence in alpha frequency band. The power in beta and high-gamma frequency bands in the STN temporally increased during intubation comparative to loss of consciousness. Apart from the oscillatory activities, non-oscillatory (scale-free) activities also contribute actively to brain functioning, however, scale-free activities in the STN has seldom been investigated. Here we show that propofol induced steeper slope, or the power-law exponent, in the power spectra in STN LFPs, and intubation resulted in rebalance of the slope. Moreover, we found the fluctuation of the power-law exponent was correlated with the high-gamma power.

Conclusion: Our findings suggest that anaesthesia and intubation modulate the excitation/inhibition balance in the STN, which is reflected in the power-law exponent, and further modulate the high frequency activity in the STN LFPs.

426: Ethical Issues in Intraoperative Neuroscience Studies: Assessing Subjects' Understanding of Study Purpose and Motivations for Participation

Anna Wexler (Philadelphia, PA); Rebekah Choi, MPH; Ashwin Ramayya, MD, PhD; Nikhil Sharma, MS; Brendan McShane, BA; Love Buch, BS; Melanie Donley-Fletcher, PhD; Joshua Gold, PhD; Gordon Baltuch, MD, PhD; Eran Klein, MD, PhD; Sara Goering, PhD

Introduction: Intraoperative neuroscience studies on neurosurgical patients are a novel method of research with unique ethical considerations (Chiong et al. 2018). However, little is known about subjects' motivation for participating in such studies, nor the extent to which subjects understand study purpose and concomitant risks. The present study aimed to assess these questions in Parkinson's disease patients undergoing neurosurgery for deep brain stimulation, who had consented to participate in an intraoperative study of decision-making.

Methods: Semi-structured interviews of approximately 30 minutes in length were conducted via telephone by an embedded ethicist at a mean of 7.8 days following informed consent (and a mean of 4.4 days prior to surgery).

Results: Eighteen subjects participated in the study (mean age=61.5, mean time since Parkinson's diagnosis = 8.6 years). Half of all participants had a bachelor's degree or higher. Nearly all subjects (n=16; 88.9%) reported participating in the intraoperative study for altruistic reasons. Most (n=14; 77.8%) reported that there was either no risks or did not recall being informed about risks, despite documentation of informed consent discussions both about added infection risk from additional time in the operating room and about potential loss of confidentiality. Only six participants (33.3%) recalled that the purpose of the study was related to neuroscience; others did not recall or recalled incorrectly (n=10; 55.6%) or thought the aim of the study was directly related to Parkinson's disease (n=2; 11.1%).

Conclusion: Even though standard informed consent procedures were followed, subjects' recall of risk information was poor. However, nearly all subjects correctly understood that the study would not confer a direct benefit for Parkinson's disease research. Given that the National Institute of Health has prioritized funding of intraoperative neurosurgical studies, future work should focus on ensuring subject understanding and retention of information presented during the informed consent process.

427: Early Versus Late Surgical Intervention for Central Cord Syndrome: A Nationwide All-Payer Inpatient Cost-Benefit Analysis

Ryan Chiu (Grayslake, IL); Neha Siddiqui, MS; Angelica Fuentes, BS; Amy Zhu, BS; Saavan Patel, BS; Mandana Behbahani, MD; Ankit Mehta

Introduction: Central cord syndrome (CCS) is the most common incomplete spinal cord injury (SCI), resulting in various degrees of neurologic compromise below the level of the affected cervical cord. The management of CCS is controversial regarding not only whether to surgically intervene, but also when surgery should occur. This study analyzes inpatient outcomes associated with early versus late surgical intervention for CCS in the context of length of stay and hospitalization costs.

Methods: The National Inpatient Sample (NIS) was queried for years 2012-2015 for patients who underwent surgery with a primary diagnosis of CCS. The median interval between admission and intervention was noted. Patients operated upon prior to this timepoint were placed in the early surgery group, and others into the later surgery group. The groups were then compared, while using 1:1 propensity score matching to control for baseline presentation, with respect to mortality, discharge disposition, length of stay, and total charges.

Results: A total of 422 patients met inclusion and exclusion criteria. The median time from admission to intervention was 2 days. Patients with higher initial severity of injury were more likely to undergo early surgery. Upon controlling for severity of initial presentation, earlier intervention did not appear to affect mortality or post-operative length of stay. However, patients operated upon earlier had more favorable discharge dispositions ($p=0.025$) and a lower associated cost of care (\$198,050.70 vs. \$243,048.10, $p=0.009$).

Conclusion: Earlier surgical intervention for CCS may result in better patient disposition and less total charges.

428: Deep Neural Network Analysis of CT scans to Predict Outcomes in a Prospective Database of Severe Traumatic Brain Injury Patients

Matthew W. Pease, MD (Pittsburgh, PA); Dooman Arefan, PhD; Daryl Fields; Julia Billigen; Jane Sharpless; Ava Puccio; Kerri Hockberger; Souvik Roy; Stephanie Casillo; David Okonkwo; Shandong Wu

Introduction: Traumatic Brain Injury (TBI) is the leading cause of death in young adults worldwide. Physicians and other validated models predict long-term outcomes with only moderate success. Models such as IMPACT are designed to guide clinical trial design and are not intended to guide clinical decision-making. Machine Learning (ML) models identify abnormalities in radiographic images with a high degree of accuracy. We applied ML models to CT scans and clinical information from severe TBI to predict mortality.

Methods: 526 severe TBI patients from a prospectively collected database at a single institution from 2002-2018 had a CT scan prior to neurosurgical intervention and complete clinical information. We applied transfer learning and 3D convolutional neural network (CNN) to build a model using CT scans alone for mortality prediction. The CNN model was trained using a novel method to compensate for different CT reconstruction filter kernels. The cohort was chronologically split into 90%, 5%, and 5% for training (year: 2002-2015), validation (year: 2015-2016) and independent test (year: 2016-2018). For the same outcome prediction, we also developed a ML model using only clinical variables, and an augmented prediction model that combined the CT scans and clinical variables using the stacking ensemble method.

Results: The CNN model using CT scans alone predicted mortality in the independent test cohort with an AUC of 0.86 (95% CI: 0.63-0.95) and accuracy of 82%. The clinical variable only model achieved an AUC of 0.80 (95% CI: 0.57-0.92) with accuracy 64%. When CT and clinical variables were combined, AUC increased to 0.88 (95% CI: 0.65-0.96) with accuracy of 82%. The IMPACT model had AUC of 0.83.

Conclusion: CNN models of head CT scans predicted mortality outcome following severe TBI and the combination of CT scans and clinical variables increased prediction performance.

429: From the Fears of World's Worst War Zone: Analysis of 193,618 Neurotrauma Afflicted Patients of Syria

Nida Fatima, MBBS (Boston, MA); Maher Saqqur, MD, MPH; Ashfaq Shuaib, MD; Hani Mowafi, MD; Mahmoud Hariri; Baobao Zhang; Houssam Alnahhas; Basil Bakri, MD; Adam Eldahan; Moustafa Moustafa; Anas Al-Kassem, MD

Introduction: The Syrian Civil War has produced one of the largest humanitarian crises in recent memory. With the transition to the widespread use of aerial bombardment, there has been a mounting toll of trauma patients and significant mortality in Syrian hospitals. The authors aimed to analyze the demographics, spatial and temporal patterns of Neurotrauma patients presented to the Syrian Hospitals.

Methods: Over a period of 25-months, from July 2013–July 2015, a retrospective quantitative secondary analysis of an administrative dataset of 193,618 trauma patients presented to 95 hospitals inside war-affected parts of Syria was conducted.

Results: Of 193,618 Neurotrauma patients, 154,225 (79.6%) were males and 39,393 (20.4%) were females. A complete information about demographics was available for 160,237 encounters (82.8%): 0–2 years: 8,257 (4.52%), 3–12 years: 24,197 (13.2%), 13–18 years: 22,482 (12.3%), 19–60 years: 100,553 (67.3%), and elderly >60 years: 4,746 (2.6%). Shrapnel's (81,946: 42.3%) and blunt/crush injury (71,476: 36.9%) were the dominant mechanism of injury with an increasing proportion of these injuries over time. In-patient mortality was most associated with extremes of age (age<2 years OR: 2.9; age>60 years OR: 2.5), blast head (OR: 13.4), blast-spine (OR: 12.2), gun-shot head (OR: 10.1), and shrapnel-head (OR: 6.2). Postoperative hemorrhage was documented in 6.3% of the patients overall. Bleeding was most commonly associated with vascular (OR: 2.5), critical care (OR: 5.2), and those with incompletely documented procedures (OR: 5.7). There were 2,694 inpatient deaths (4.5% of admitted) and 4,758 patients (8.1%) required transfer to other facilities for definitive care.

Conclusions: Civilians, including children and the elderly are greatly impacted by the War, resulting in significant mortality in the Syrian Hospitals. Our data presents a unique quantitative descriptive analysis of neurotrauma patients that reflect limitation in the data acquisition and patient tracking in the war.

430: A Benzothiazole Aniline Derivative Enhances Neuroplasticity after Traumatic Brain Injury in Rats

Asim Mahmood, MD, FAANS; Yanlu Zhang, MD, MS; Vincent Simmon, PhD; Ye Xiong, MD, PhD (Detroit, MI)

Introduction: The tetra (ethylene glycol) derivative of benzothiazole aniline (SPG101) has been shown to improve dendritic spine density and cognitive memory in a mouse model of Alzheimer's disease (AD). The present study was designed to investigate the therapeutic effects of SPG101 on dendritic spine density and morphology, and sensorimotor and cognitive functional recovery in a rat model of traumatic brain injury (TBI).

Methods: Young adult male Wistar rats were injured with controlled cortical impact (CCI) and randomly divided into experimental and control groups (n=7/group) receiving either SPG101 (30 mg/kg) or a vehicle (1% DMSO in PBS) administered intraperitoneally, respectively. The drugs were administered at 1 h post injury and once daily for the next 34 days. Sensorimotor deficits were assessed using a neurological severity score (NSS) and adhesive removal and footfault tests. Cognitive function was measured by Morris water maze (MWM), novel object recognition (NOR), and 3-chamber social recognition tests. The animals were sacrificed 35 days after injury and their brains were processed for measurement of dendritic spine density and morphology using ballistic dye labeling.

Results: SPG101 treatment significantly improved sensorimotor functional recovery (days 7-35, $p<0.0001$), spatial learning (MWM days 32-35, $p<0.0001$), NOR (days 14 and 35, $p<0.0001$), compared with control and social recognition (days 14 and 35, $p<0.0001$). Histological studies showed that treatment also significantly increased dendritic spine density in the injured cortex ($p<0.05$) and decreased heterogeneous distribution of spine lengths in the injured cortex and hippocampus ($p<0.0001$).

Conclusion: In summary, treatment with SPG101 improves both sensorimotor and cognitive functional recovery, indicating that SPG101 acts as a spinogenic agent and may have potential as a novel treatment of TBI.

431: MRI Tracking of iPS Cells-derived Neural Stem Cells in Animals with Traumatic Brain Injury*Hailiang Tang (Shanghai, China); Jianhong Zhu*

Introduction: Induced pluripotent stem cells (iPS cells) are promising cell source for stem cell replacement strategy applied to brain damage caused by traumatic brain injury (TBI). However, how to trace the fate of iPS cells in host brain is still a challenge.

Methods: In our study, iPS cells were derived from skin fibroblasts using the four classic factors Oct4, Sox2, Myc and Klf4. Then these iPS cells were induced to differentiate into neural stem cells (NSCs), which were incubated with superparamagnetic iron oxides (SPIOs) in vitro. Next, 30 TBI rat models were prepared and divided into 3 groups (n=10). One week after brain injury, group A & B rats received NSCs (labeled with SPIOs) implantation, while group C rats received non-labeled NSCs implantation. After cell implantation, all the rats were performed T2*-weighted magnetic resonance imaging (MRI) scan at day 1, and 1 week to 4 weeks, to track NSCs distribution in rats' brains. One month after cell implantation, all the rats were performed manganese-enhanced MRI (ME-MRI) scan. In group B, diltiazem was infused during the ME-MRI scan period.

Results: (1) iPS cells were successfully derived from skin fibroblasts, expressing the typical antigens including SSEA4, Oct4, Sox2 and Nanog. (2) iPS cells were induced to differentiate into NSCs, which could express Nestin and differentiate into neural cells and glia cells. (3) NSCs were incubated with SPIOs overnight, and prussian blue staining showed intra-cellular particles. (4) After cell implantation, T2*-weighted MRI scan showed these implanted NSCs could migrate to the injury area in chronological order. (5) The subsequent ME-MRI scan detected NSCs function, which could be blocked by diltiazem.

Conclusion: Using in vivo MRI tracking technique to trace the fate of iPS cells-induced NSCs in host brain is feasible.

432: Real-time Secondary Injury Detection in a Pig Model of Traumatic Brain Injury using Bioimpedance*Alicia Everitt (West Lebanon, NH); Brandon Root, MD; Daniel Calnan, PhD, MD; David Bauer, MD; Ryan Halter, PhD*

Introduction: Intracranial pressure (ICP) based monitoring for secondary injury in severe traumatic brain injury (TBI) is limited due to its inability to identify the etiology behind elevated ICP without a CT scan. This study explored the use of a novel bioimpedance monitoring (BIM) system for 1) real-time detection of focal intracranial volume (ICV) changes in an animal model of TBI, and 2) differentiation of ischemic (high impedance) vs. hemorrhagic (low impedance) injury types.

Methods: Eight pigs were instrumented with three intracranial catheters positioned using AxiEM Stealth navigation: 1) a compliance catheter in the left lateral ventricle, 2) a mass effect (ME) and hematoma simulating Fogarty catheter in the left parietal lobe and 3) a coupled ICP monitor and intracranial electrode in the right frontal lobe. The ME balloon was inflated in steps of 100uL every five minutes up to 1.2mL to induce a focal ME. Following deflation, autologous blood was injected in steps of 200uL up to 1.2mL to model hematoma. CT scans were acquired at each intracranial state. Bioimpedance data were collected using our custom BIM system consisting of eight circumferential-positioned dual scalp electrodes, an ICP monitor, intracranial electrodes and custom analog hardware. Four-electrode bioimpedance measurements were sequentially recorded using two current drive electrodes and two voltage pickup electrodes at 2.3mA and 50 kHz.

Results: Impedance correlated to both ICP and ICV, suggesting sensitivity to both intracranial pressure and volume changes. The BIM system detected secondary injury in all cases (p=0.0026) and successfully differentiated between a high impedance (e.g. ischemic) and low impedance (e.g. hematoma) event (p=0.0057). The average detected ICV was 0.28 mL +/- 0.14mL.

Conclusion: The bioimpedance monitoring system successfully detected focal ICV changes and differentiated between modeled injury types. This work suggests the potential for bioimpedance-based monitoring for patients with severe TBI.

433: Development of a Prognostic Scoring System to Predict Risk of Reoperation for Contralateral Hematoma Growth after Unilateral Evacuation of Bilateral Chronic Subdural Hematoma

John J. Y. Zhang (Singapore); Shilin Wang; Aaron Foo; Boon Leong Quah; Ira Sun; Shiong Wen Low; Kejia Teo; Sein Lwin; Ning Chou; Tseng Tsai Yeo; Vincent Nga

Introduction: Bilateral chronic subdural hematoma (bCSDH) is frequently drained unilaterally when the contralateral CSDH is small and asymptomatic. However, reoperation rates for growth of contralateral CSDH can be high. We aimed to develop a scoring system to preoperatively assess risk of contralateral CSDH reoperation in bCSDH patients.

Methods: Data was collected retrospectively across three tertiary hospitals from 2010 to 2017 on all consecutive bCSDH patients aged 21 or above. Predictors of reoperation were identified using backward elimination and multivariate logistic regression. A prognostic scoring system was developed and subsequently applied to the same set of patients for internal validation.

Results: 240 bCSDH patients were analyzed with 98 (40.8%) who underwent unilateral evacuation and 142 (59.2%) who underwent bilateral evacuation. No significant difference was found in clinical outcomes between the unilateral and bilateral evacuation groups. Within the unilateral evacuation group, 4 (4.1%) had a reoperation for contralateral CSDH growth. Reoperation for contralateral CSDH was predicted by preoperative use of anticoagulants (OR=15.0, 95% CI: 1.49 — 169.15, $p=0.017$). Complete resolution of the contralateral CSDH was predicted by its preoperative maximum width, with a cut-off of 9mm producing the highest sensitivity and specificity (OR=4.17 for width $\leq$ 9mm, 95% CI: 1.54 — 11.11, $p=0.004$). Using our prognostic scoring system, reoperation rate for contralateral CSDH was 1.6% in low-risk patients, 3.6% in moderate-risk patients, 16.7% in high-risk patients, and 50.0% in very high-risk patients. With each increase of 1 in the prognostic score, patients were 4 times as likely to undergo reoperation for contralateral CSDH growth (OR=3.98, 95% CI: 1.36 — 13.53, $p=0.013$).

Conclusion: Unilateral evacuation of bCSDH can be as effective as bilateral evacuation, but patients should be carefully selected and followed-up. Our proposed risk score may be used as an adjunct for clinical decision making in the management of bCSDH patients.

434: Delayed-Contrast MRI (DCM) for Depicting Short/Long-Term Subtle BBB Disruption in TBI

Yael Mardor, PhD (Tel-Hashomer, Israel); David Last; David Guez; Ester Shohami; Itzik Cooper; Dianne Daniels; Shirley Sharabi; Abigail Livny-Ezer; Sigal Liraz-zaltsman

Introduction: TBI is a highly complex disorder caused by primary and secondary injury mechanisms. Alterations in gliovascular signaling are not established as a key secondary injury. Moreover, little is known regarding long terms effects of BBB disruption. Here we studied the application of DCM for depicting subtle BBB disruption in moderate TBI mice and the correlation with histology of blood vessels coverage by astrocytes (BVCA).

Methods: 24 mice were followed by DCM 1/8/29/64/98 and 133 days post closed-head injury. BBB maps were calculated from the MRIs and BBB disruption levels in the lesions vicinity were calculated. Extracted brains were sectioned and stained for astrocytes and vessels and the percentage of BVCA was calculated. In addition, 10 TBI mice and 6 controls were scanned 15 months post TBI, and 5 patients were scanned 1 year post TBI.

Results: Significant BBB disruption was depicted in the lesion vicinity in all mice post TBI. Lesion volumes in the BBB maps up to 1 week post TBI were x2.5 larger than enhancing volumes on T1-Gd ($p<0.02$). Disruption levels decreased linearly with time between days 1 and 133 ($r^2=0.93$, $p<0.002$). Significant correlation was found between the disruption calculated from DCM and BVCA for the different time points ($r^2=0.77$, $p<0.05$). At 15 months post TBI, disruption levels in the ipsilateral ventricle were significantly higher for TBI mice vs control ($p<0.03$). Preliminary clinical results in 5 patients show subtle BBB disruption, undetectable by T1-Gd, depicted for all patients. Initial analysis suggests several disruption patterns (local disruption in brain tissue and midline, local blood-CSF disruption, subarachnoid, ventricular and wide-spread).

Conclusion: DCM enables depiction of significant BBB disruption, with higher sensitivity than T1-Gd, up to long times post injury. Correlation between MRI-based disruption levels and BVCA may be explained by alterations in gliovascular signaling resulting from TBI.

435: Traumatic Brain Injury in the United States Army Special Forces

Remi A. Kessler (New York, NY); Raj Shrivastava, MD; Ansh Bhammar, BS; Jonathan Rasouli, MD; Deborah Benzil, MD; Joshua Bederson, MD; Constantinos Hadjipanayis, MD, PhD

Introduction: US Army Special Forces (SF) soldiers, known as Green Berets, constitute 60% of Special Operations casualties, likely due to extraordinary challenges of missions and unconventional warfare tactics. Prevention/assessment of traumatic brain injury (TBI) is a highest priority in military medicine due to its incidence, acute/chronic morbidity, high mortality, and limits of reversibility/treatment. In just 2011, 33,149 US military personnel were diagnosed with TBI - majority being concussions/mild TBI. Despite Department-of-Defense efforts in this domain, demographics of TBI among SF have never been investigated. The goal of this study was to elucidate the incidence and etiologies of neurotrauma affecting this population, given their highest-risk military operations globally and exposure to greatest amount of combat.

Methods: A 162-question study was formulated via collaboration of US board-certified neurosurgeons, retired SF members, and staff of the Green Beret Foundation (GBF). Data on military background, demographics, medical history and exposures were collected. This study was disseminated to thousands of SF soldiers via GBF's extended military network. Inclusion criteria consisted of obligatory 18-Series qualification (SF-designation). Descriptive statistics were employed to present a composite of incidence/etiologies of TBI.

Results: 529 participants met inclusion criteria. 78% reported direct involvement in blasts/explosions. Mild TBI diagnosis was reported by 45% (71% with repeated TBI, with mean 2.7 years between), of whom 93% were directly involved in combat. Common causes were Blast/Explosion/IED (42%) and Parachute/Airborne Operations/Military-Free-Fall (38%). Conversely, 20% reported moderate/severe TBI (32% with repeated TBI), of whom 97% were involved in combat. Common causes included Blast/Explosion/IED (67%) and Parachute/Airborne Operations/Military-Free-Fall (20%). In both TBI severity cohorts, >80% were wearing headgear. Only 23% with moderate/severe TBI were Medevac'ed.

Conclusion: Results demonstrate high incidence of TBI among US Army SF soldiers. Blasts/explosions were the leading cause of both mild and moderate/severe TBI. Given 80% of TBIs occurred while wearing headgear may be reflective of inadequate protective equipment. Low rate of Medevac rescue may suggest a sub-clinical presentation of TBI or that medical rescue was not attainable.

436: The Acutely Injured Cord and Vasopressors: Proceed With Caution in the Frail

James Gregory Malcolm, MD (Atlanta, GA); Brett Tracy, MD; David Gimbel, MD; Rondi Gelbard, MD

Introduction: Vasopressors are recommended to improve mean arterial pressure (MAP) in acute, traumatic spinal cord injury (ATSCI). However, the application to frail patients is unclear. We hypothesize that frail patients receiving vasopressors for MAP goals will have greater morbidity and mortality.

Methods: We performed a retrospective review of patients with ATSCI from 2010-2017 at our level 1 trauma center. We excluded ASIA E injuries, penetrating mechanism, vasopressor use for reasons other than MAP goals and use beyond 7 days. We quantified frailty by tallying each patient's comorbidities (Elixhauser comorbidity method) and stratified patients into no frailty (no comorbidities), mild frailty (1 comorbidity), moderate frailty (2), or severe frailty [SF] (≥ 3). Outcomes included net change in ASIA scores, complications, and mortality. Cochran — Mantel — Haenszel (CMH) tests evaluated categorical data and Kaplan-Meier plots assessed 30-day survival.

Results: There were 186 patients in the cohort; 37.6% (n=70) had no frailty, 30.1% (n=56) were mildly frail, 21.5% (n=40) moderate, and 10.8% (n=20) SF. Median duration of MAP goals was 5 days (IQR 5-5) and was similar between all groups (p=0.4). There was no difference in net ASIA score changes as frailty increased, even when sub-stratified by vasopressor use (p>0.05). On CMH testing, SF patients receiving vasopressors had more unplanned intubations (p=0.007), a greater incidence of troponinemia (p=0.02), and higher mortality (p=0.009) compared to SF patients not receiving vasopressors. Patients with SF had higher mortality (18% vs 4.7%, log-rank p=0.02), which was amplified when evaluating SF patients only receiving vasopressors (24.8% vs 3.6%, log-rank p=0.005).

Conclusion: Vasopressor use was not associated with ASIA score improvement in frail ATSCI patients but correlated with greater morbidity. Given the baseline impaired survivability of severely frail SCI patients and lack of neurologic improvement, we recommend minimizing vasopressor use in this population.

437: The Effect of Ventricular Catheter Type and Drainage System Gentamicin Flushes on Ventriculostomy- Associated Infections

Eric T. Quach, MD (Philadelphia, PA); Anand Kaul, MD; Kadir Erkmen, MD

Introduction: External ventricular drain (EVD) placement is a common neurosurgical procedure for intracranial pressure monitoring and cerebrospinal fluid diversion. There is institutional variation in EVD management with the aim to reduce infections. Historically, our institution has utilized both antibiotic impregnated (AI) and non-AI ventriculostomy catheters depending on presenting pathology. We previously used gentamicin flush within the drainage system, but halted this practice to promote antibiotic stewardship given lack of supporting evidence. During this period, we also began utilizing a non-AI fluoro-oligomeric polymer (FOP) catheter designed to reduce thrombus-related catheter occlusion. We subsequently observed a rise in EVD infections prompting a review of our practices.

Methods: We performed a retrospective review of all EVDs maintained in our institution's neurosurgical intensive care unit from June 2017 through August 2019. Infections were defined as positive CSF cultures. We recorded ventriculostomy catheter types and use of gentamicin flush.

Results: We reviewed 123 EVDs. Prior to the practice change, the EVD infection rate was 2.3%. Infection rate significantly increased to 11.7% ($p < 0.05$) with the practice change. After reverting to our initial practice, the infection rate was 0% ($p < 0.05$). Gentamicin flush was associated with decreased infections ($p < 0.05$) but not when used with AI catheters. FOP catheters were significantly associated with increased infection (41.6%, $p < 0.001$). AI catheters were associated with decreased infection (1.4%, $p < 0.001$). When excluding FOP catheters, non-AI catheters were not significantly associated with increased infections ($p = 0.178$).

Conclusion: We found a significant increase in EVD infections associated with the use of FOP catheters but not with other non-AI catheters. Gentamicin flushes were significantly associated with decreased infections, but further studies are necessary to clarify its role in infection reduction with various catheter types. Our data is consistent with a growing body of literature that an AI ventricular catheter is critical to an infection-reducing EVD protocol.

438: Clinical Depression and Suicidal Ideation Rates Following Concussion

Shane Shahrestani (Yorba Linda, CA); Alexander Ballatori, BA; Shane Shahrestani, MS; Andy Ton, BS; Xiao Chen, BA; Andrew Chan, MD; Gabriel Zada, MD, MS

Introduction: Concussion and TBI have been identified as a potential risk factors for the development of neurodegenerative disorders including Alzheimer's disease and Parkinson syndrome. Although much of the current literature addresses long-term neurodegenerative consequences, limited data evaluates immediate and short-term psychological consequences. The current study evaluates the prevalence of depression and suicide following concussion in the United States.

Methods: Using the 2016 National Inpatient Sample (NIS) database, we conducted a retrospective cohort analysis of 7,253 patients diagnosed with concussion. We further stratified by initial ($n = 6810$) and subsequent encounters ($n = 443$) and analyzed the prevalence of clinically diagnosed depression and suicidal ideation at initial and subsequent encounters. Statistical analysis was conducted using RStudio with Welch Two Sample t-tests.

Results: There were significantly higher rates of clinically diagnosed depression in patients at subsequent encounters compared to the rates at the initial encounter for concussion (20.7% vs. 8.69%, $p < 0.001$). In subsequent patient encounters, 56.5% of the individuals with clinically diagnosed depression were females ($p = 0.045$). There were significantly higher rates of suicidal ideation in patients at subsequent encounters compared the initial encounter for concussion (2.71% vs. 0.54%, $p = 0.006$). There were significant differences in age of individual with suicidal ideation (mean = 27.00 ± 12.56) compared to those without suicidal ideation (mean = 52.91 ± 24.52) at subsequent encounters ($p < 0.001$).

Conclusion: Our data suggests that, following concussion, the rates of clinically diagnosed depression and suicidal ideation increases, women are at greater risk of developing depression, and younger individuals are at greater risk of suicidal ideation.

439: The Burr Hole Location In Chronic Subdural Hematoma Surgery Impacts The Rate Of Revision Surgery

Katharina Klumbies (Heidelberg, Germany); Alexander Younsi, MD; Cleo Habel; Jessica Fischer; Lennart Riemann; Klaus Zweckberger; Andreas Unterberg

Introduction: Chronic subdural hematoma (cSDH) is a common disease in neurosurgery. Typically it occurs in the elderly after mild trauma. Burr hole trepanation is the preferred method of hematoma evacuation. Our objective was to examine whether the location of burr hole trepanation has an impact on the revision rate in cSDH patients.

Methods: We analyzed all cSDH patients who were operated by burr hole trepanation at a single neurosurgical center between 2006-2016 retrospectively. The placement of burr holes (frontal vs. parietal) was reviewed and patients with central or multiple burr holes were excluded. The rate of revision surgery due to remaining or recurrent hematoma within 30 days was compared between patients with frontal vs. parietal burr holes and statistical analysis was performed ($p < 0.05$ was considered significant).

Results: 611 cSDH patients (187 (31%) female / 424 (69%) male; age 75 [69-81] years), with either frontal (50%) or parietal (50%) burr hole trepanation were identified. Both groups presented with a similar clinical status at admission (GCS: 15 [14-15] frontal vs. 15 [14-15] parietal; mRS 2 [2-3] frontal vs. parietal 3 [2-3]) and neither the clinical background (use of anticoagulation, comorbidities) nor radiological characteristics (hematoma diameter, midline shift) differed significantly. The clinical outcome at discharge showed no significant differences either (mRS: 2 [1-3] frontal vs. 2 [1-3] parietal; GOS: 5 [4-5] frontal vs. 5 [4-5] parietal). However, the rate of revision surgery within 30 days was significantly lower in the group with parietal burr holes (16% parietal vs. 26% frontal).

Conclusion: Our data suggest that burr hole placement in the frontal region is associated with a higher revision rate within 30 days compared to parietal burr holes in patients with cSDH. A prospective assessment is needed to verify our current findings.

440: An External Validation of the Surviving Penetrating Injury to the Brain (SPIN) Score

Mark D. Johnson, MD (Cincinnati, OH); Uwe Stolz, PhD; Chris Carroll, MD; George Yang, MD; Norberto Andaluz, MD; Brandon Foreman, MD; Michael Goodman, MD; Laura Ngwenya, MD, PhD

Introduction: The Surviving Penetrating Injury to the Brain (SPIN) score utilizes clinical variables to estimate in-hospital and six-month mortality following civilian cranial gunshot wounds (cGSW). The initial SPIN score had excellent discrimination (area under the ROC curve (AUC) = 0.968), with good discrimination (AUC = 0.880) in a validation study. The goal of our study was to provide an independent, external validation of the SPIN score for in-hospital mortality.

Methods: We retrospectively reviewed six years of data from our institutional trauma registry. SPIN score variables were collected including; gender, transfer status, injury motive, pupillary reactivity, motor Glasgow Coma Score (mGCS) subscore, Injury Severity Score (ISS), and admission international normalized ratio (INR). Multivariable logistic regression identified variables associated with in-hospital mortality. We compared the AUC between models using a non-parametric test for equality.

Results: Of the 282 patients identified, 101 had all SPIN score components available. Our SPIN model had an AUC of 0.962. Continuous mGCS alone had an AUC of 0.932 and the addition of all SPIN score components, did not result in a significant increase in AUC (0.957, $p = 0.26$). Using only mGCS resulted in fewer exclusions due to missing data. The AUC for continuous mGCS (0.932) was significantly higher compared to categorical mGCS (0.891, $p = 0.005$). No additional variable included in the predictive model with continuous mGCS was both a significant predictor of inpatient mortality and increased model discrimination.

Conclusion: The excellent discrimination of the SPIN score, when applied to our cohort, was due to a single variable. The continuous 6-point mGCS may be sufficient as a generalizable predictor of inpatient mortality in patients with cGSW with excellent discrimination and reduced bias due to missing data. Future prospective studies are needed to assess whether our cohort supports use of SPIN score variables for prediction of 6-month mortality.

441: Improved Survival for GBM Patients Treated with DC Vaccine and Adjuvant TLR-3 Agonist in Phase II Clinical Trial**Rosenblum-Mahaley Clinical Research Award**

Joseph Paul Antonios, MD (New Haven, CT); Richard Everson; Aaron Mochizuki; Sara Khattab; Prashant Romiyo; Matthew Sun; Diana Moughon; William Yong; Anthony Wang; Timothy Cloughesy; Robert Prins; Linda Liao

Introduction: We and others have documented immune responses following dendritic cell (DC) vaccination as an active immunotherapeutic treatment for these patients. In this Phase II clinical trial, we randomized malignant glioma patients to receive autologous tumor lysate pulsed DC vaccination with and without adjuvant toll-like receptor (TLR) agonists. TLRs are present on dendritic cells and serve to modulate immune responses.

Methods: Twenty-three patients with WHO grade III or IV glioma were treated with three intradermal injections of autologous tumor lysate-pulsed DC on days 0, 14, and 28 followed by an adjuvant placebo, TLR-7 agonist (Resiquimod), or TLR-3 agonist (Poly ICLC). Mass cytometry (CyTOF) was used to analyze immune cell populations of patient peripheral blood mononuclear cells (PBMC) before and following treatment. Single cell RNA sequencing (scRNAseq) gene expression analysis of systemic PBMCs was utilized to determine functional significance of adjuvant administration.

Results: DC-vaccinated patients that received adjuvant Poly ICLC treatment had a significantly improved median survival of 54 months over placebo (11 months) and adjuvant Resiquimod (17 months) groups ($P < 0.01$). scRNA seq analysis demonstrated increased immune cell activation and expression of proinflammatory genes, as well as peripheral myeloid cell population expansion that was associated with increased survival.

Conclusion: Overall, these findings suggest that adjuvant Poly ICLC treatment improves outcomes with autologous lysate-pulsed DC vaccine treatment via modulation of pro-inflammatory pathways.

442: Protein Decrowding ExM for Discovery of Previously Unidentified Structures and Cell Populations in Gliomas**Ronald L. Bittner Award on Brain Tumor Research**

Pablo Valdes Quevedo, MD (Boston, MA); Jay Yu, BS; Deepak Bhare, PhD; Khalid Shah, PhD; Edward Boyden, PhD; E ChioCCA, MD, PhD

Introduction: Immunohistochemistry is an essential technology for in situ interrogation of protein molecules, but it has a fundamental limitation: proteins that are tightly packed in space cannot get accessed by antibodies, limiting protein epitopes which can be detected. Moreover, current solutions using affinity probes smaller than conventional antibodies are expensive, low yield, and not used clinically. We have developed a new technology - protein decrowding Expansion Microscopy (dExM) - in which expansion of tissues physically separates proteins apart, retains their antigenicity, and makes room for antibodies to access and stain previously inaccessible proteins epitopes (i.e., decrowds proteins)

Methods: FFPE tissue-microarrays of low- and high-grade gliomas underwent the following treatments: immunostaining (pre-expansion tissues); chemical treatment to anchor proteins to a swellable polymer synthesized in situ; denaturation; expansion (pre-decrowding tissues, 4x-expanded, original staining); immunostaining post-decrowding (post-decrowding tissues, 4x-expanded, new staining). Tissues were imaged with super-resolution microscopy and confocal imaging, followed by quantitative image analysis.

Results: We discovered a radical difference in kind in post-decrowding compared to pre-expansion and pre-decrowding staining: 1) new vimentin tubular structures (arrows) between distinct cells that were not previously seen with pre-decrowding staining, and a continuous, rather than punctuate staining pattern (Fig. 1); 2) significantly greater cell regions showing staining co-localization of vimentin(+)GFAP(+) (2.5-fold), vimentin(+)Iba1(+) (2-fold), and GFAP(+)Iba1(+) areas (4.5-fold) (Fig. 2). Our findings reveal structures and cell populations in gliomas that were previously unidentified using conventional techniques.

Conclusion: Our protein decrowding technology is a radical departure from all prior kinds of affinity probe and imaging technologies, which has the potential to be a tool for clinicians and researchers, enabling discovery of new cells, tissue architecture, and possibly improved diagnostics.

443: Oncolytic Viral Delivery into the Surgical Resection Cavity for the Treatment of Glioblastoma in a Murine Model

AANS/CNS Section on Tumors Neuro-Oncology Trainee Award

Sricharan Gopakumar (Houston, TX); Joy Gumin; Marc Daou; Daniel Ledbetter; Malcolm McDonald; Anwar Hossain, PhD; Brittany Parker Kerrigan, PhD; Shawn Hingtgen, PhD; Matthew Ewend, MD; Frederick Lang, MD

Introduction: The oncolytic virus DNX-2401 (Delta-24-RGD) is a novel treatment of GBM. Prior studies have examined intra-tumoral injection of DNX-2401 and intra-arterial delivery of tumor-tropic human mesenchymal stem cells loaded with DNX-2401 (MSCs--DNX--2401) to treat unresected GBM. However, the optimal method for delivering oncolytic virus into the surgical resection cavity for treating residual disease in resected GBM remains unclear. We explore the use of fibrin as a scaffold for delivering DNX-2401 or MSCs-DNX-2401 into the surgical cavity to eradicate residual tumor cells and extend overall survival in a murine model of GBM resection and recurrence.

Methods: U87 cells were transduced with mCherry--Luciferase and implanted into the brains of athymic mice. After fluorescence--guided surgical resection of glioma xenografts, DNX-2401 or MSCs--DNX--2401 were delivered into the resection cavity using fibrin as a scaffold. Serial bioluminescence imaging (BLI) was used to monitor tumor recurrence.

Results: In vivo studies mimicking residual tumor after surgical resection, treatment of the post-resection cavity with MSCs-DNX-2401 suspended in fibrin permitted retention of MSCs-DNX-2401 within the tumor bed. Kaplan--Meier survival analysis revealed statistically significant improved survival after treatment with DNX-2401 in fibrin ($p = 0.0048$, 44% overall survival) and MSCs-DNX-2401 in fibrin ($p = 0.0007$, 40% overall survival) compared to resection only. Median survival with treatment was prolonged to 99 days and 100 days, respectively, compared to 40 days in resected controls and 25.5 days without treatment.

Conclusion: Delivering oncolytic virus DNX-2401 into the surgical resection cavity using fibrin or MSCs in fibrin is capable of eradicating residual GBM and prolonging overall survival. These studies support the clinical translation of this approach in patients undergoing surgical resection of GBM. Future studies utilizing a more invasive tumor cell line may better elucidate the value of intrinsic MSC tumor tropism for eliminating invading GBM foci using this treatment strategy.

444: IDH-Mutant Gliomas Differ in Distribution of Mitochondrial Genomic Alterations

Koray Ozduman, MD, IFAANS (Istanbul, Turkey); Sirin Yuksel, MSc; Cemaliye Akyerli, PhD; Kaya Bilguvar, MD, PhD; Ayca Ersen-Danyeli, MD; Engin Yilmaz, MD, PhD; M Necmettin Pamir, MD

Introduction: IDH1/2-mutations, which are the main driver events in astrocytomas and oligodendrogliomas, are associated with marked alterations in cellular metabolism. We hypothesized that such alterations would exert a purifying selection or evolutionary advantage to certain mitochondrial encoded genes.

Methods: 59 adult hemispheric diffuse gliomas were analyzed. 29 were IDH-mutant (97% lower grade) and 30 were IDH-wt (17% lower grade). Total DNA was isolated from fresh frozen samples and mitochondrial DNA was sequenced using Illumina platform, aligned and analyzed using mitochondrial databases (mtDNA server, MITOMAP). A 10% cutoff was applied for heteroplasmy. Mutation densities (mutations per Mb) in each of the mitochondrial encoded genes were calculated and compared against IDH-mutation status, WHO-grade (Mann-Whitney U, Kruskal-Wallis, bonferoni correction applied). Distribution of mitochondrial haplogroups was comparable (IDH mutant: 76%R, 21%N, 3%L3, IDH-wt: 90%R, 7%N, 3%L3).

Results: Total of 1531 variations (469 unique) were identified. Mutation-density was significantly different between IDH-mut and IDH-wt tumors (25.95mut/Mb, 1.57mut/Mb, $p=0.024$). Significantly higher mutation densities were observed in mt-ATP6, mt-TR, mt-ND6 genes and DLOOP ($p=0.041$, 0.014, 0.025 and 0.030, respectively). mt-TQ, mt-ATP6, mt-TR mutational densities were significantly different between WHO-grade II and WHO gradeIII/IV tumors ($p=0.046$, 0.048 and 0.021). mt-TR mutational density was also significantly different between lower-grade and WHO-grade IV ($p=0.036$).

Conclusion: Mutational densities in several mitochondrial encoded genes differ between IDH-mutant and IDH-wt tumors as well as different WHO grades.

445: Automated Intraoperative Frozen Diagnosis of Brain Tumors Using Machine Learning**Louise Eisenhardt Travel Scholarship**

Siri Sahib Singh Khalsa, MD (Ann Arbor, MI); Todd Hollon, MD; Neil Jairath, BS; Arjun Adapa, BS; Esteban Urias, MS; Karen Eddy; Julianne Szczepanski, MD; Peter Ouillette; Sandra Camelo-Piragua, MD; Daniel Orringer, MD

Introduction: Neurosurgeons rely on rapid histologic diagnosis during brain tumor surgery for surgical decision-making. Although frozen sectioning is available at most surgical hospitals, only 56% of hospitals performing brain tumor surgery in the United States have access to intraoperative neuropathology consultation. Our goal is to develop an artificial intelligence program to automatically diagnose whole frozen slides among the following supratentorial enhancing tumors: metastatic carcinoma, high-grade glioma, lymphoma, and meningioma. To the authors' knowledge, an automated algorithm capable of providing intraoperative brain tumor diagnoses using frozen slides has not been previously published.

Methods: A collection of digitized whole frozen-section slides obtained during brain tumor surgery were divided into 2 million small fields-of-view at full magnification, each of which was labeled as high-grade glioma, carcinoma, lymphoma, meningioma, or non-lesional. These labeled images were used to train a deep machine learning algorithm called a convolutional neural network. An additional algorithm combined these field-of-view diagnoses into whole-slide diagnoses. The automated diagnoses provided by the algorithm on a test set were compared to board-certified neuropathologist interpretation.

Results: 51 whole frozen slides were tested. Among 40 slides correctly diagnosed by the neuropathologist, the automated algorithm correctly diagnosed 11/12 carcinomas, 9/10 high-grade gliomas, 6/7 lymphomas, and 11/11 meningiomas, with an overall whole-slide diagnostic accuracy of 92.5%. In addition, the algorithm correctly diagnosed 9/11 lymphomas that were incorrectly diagnosed by neuropathology at the time of surgery.

Conclusion: We developed a computer program to automatically distinguish between the core differential diagnoses for adult supratentorial enhancing brain tumors, using traditional intraoperative frozen section slides. This algorithm may be beneficial to centers without access to intraoperative neuropathology consultation during brain tumor surgery. A multicenter prospective test of the algorithm's generalizability is currently underway.

446: Successful Clinical Trial of Chronic Convection-Enhanced Drug Delivery via an Implanted Pump

Jeffrey N. Bruce, MD, FAANS, FACS (New York, NY); Eleonora Spinazzi; Andrew Lassman; Fabio Iwamoto; Mary Welch; Matei Banu; Angela Lignelli; Jack Grinband; Peter Sims; Randy D'Amico; Peter Canoll

Introduction: Compared to systemic delivery, convection-enhanced delivery (CED) provides a sizeable advantage for maximizing drug concentrations in a targeted region of the brain. Because CED has relied on external pumps, the duration of infusion has been limited because of infection concerns. To overcome this limitation, we conducted an FDA-approved clinical trial using subcutaneously implanted pumps to provide chronic CED of topotecan to recurrent glioblastoma patients.

Methods: 5 recurrent glioblastoma patients had catheters implanted into the tumor/surrounding brain and connected to subcutaneously implanted pumps that infused topotecan through four cycles over a 30 day period. The catheter and pump were then removed and tumors resected. Multiple biopsies, localized with stereotactic guidance from heterogeneous areas of the tumor and surrounding brain, were performed both prior to treatment at the time of catheter placement and following treatment at the time of tumor resection. Tissue specimens were analyzed with advanced histopathologic and molecular techniques to reveal treatment effects. Advanced MR imaging with co-infusion of gadolinium as a surrogate tracer was used to monitor drug distribution and treatment effects.

Results: All 5 patients tolerated infusions without significant complications. Quality of life and neurocognitive testing verified the safety and tolerability of treatment. MRI non-invasively demonstrated large and stable volumes of drug distribution. Comprehensive molecular and cellular tissue analysis demonstrated decreased proliferative signature in tumor cells with preservation of neurons suggesting non-toxic effect of topotecan even at high local concentrations.

Conclusion: This is the first time that chronic CED through an internalized pump-catheter system has been performed in human patients. In addition to validating the safety and feasibility of topotecan by chronic CED, the trial demonstrated anti-tumor activity that was non-toxic to the normal brain. While successful in gliomas, these findings also have important implications for other CNS diseases where systemic drug delivery limitations compromise treatment efficacy.

447: Survival benefit of lobectomy for glioblastoma: moving towards radical supramaximal resection.

Ashish Shah, MD (Miami, FL); Anil Mahavadi, BS; Long Di, BS; Daniel Eichberg, MD; Veronica Borowy, BS; Evan Luther, MD; Alexa Semonche, BS; Michael Ivan, MD; Ricardo Komotar, MD

Introduction: Extent of resection remains a paramount prognostic factor for long-term outcomes for glioblastoma. As such, supramaximal resection (beyond contrast-enhancement) or anatomic lobectomy have been offered for non-eloquent glioblastoma in an attempt to improve overall survival. Here, we conduct a propensity-matched analysis of patients with non-eloquent glioblastoma who underwent either lobectomy or gross total resection of lesion to investigate the efficacy of supramaximal resection of glioblastoma.

Methods: Patients who underwent initial surgery for gross total resection or lobectomy for non-eloquent glioblastoma (right frontal/temporal/occipital or left occipital) at our tertiary care referral center from 2010-2019 were included for this propensity-matched survival analysis. We utilized inverse probability of treatment weighting (IPTW) with the following covariates (age, location, preoperative KPS) to compare progression-free survival and overall survival.

Results: Seventy-eight patients were identified who underwent initial resection of glioblastoma for non-eloquent glioblastoma from 2011-2019 (GTR=44, lobectomy=34). Using the IPTW, overall survival (30.7 vs. 14.1 mo., $p=0.025$) and progression-free survival (13.2 vs. 9.0 mo, $p=0.021$) were significantly higher in the lobectomy cohort compared to the GTR group. There was no significant difference in pre-op, post-op KPS or complication rates between the two groups.

Conclusion: Our propensity-matched study suggests that lobectomy for non-eloquent glioblastoma confers an added survival benefit compared to lesionectomy alone. For patients with non-eloquent glioblastoma, a supramaximal resection by means of an anatomic lobectomy should be considered as a primary surgical treatment in select patients if feasible.

448: Glioma-Neuronal Interactions: a study of tumor integration and synaptogenesis mediated language plasticity in adult high-grade glioma

Anthony Lee, MD (San Francisco, CA); Saritha Krishna; Sofia Kakaizada; Kyounghee Seo; David Raleigh; Nyle Almeida; David Brang; Srikantan Nagarajan; Mitchel Berger; Michelle Monje; Shawn Hervey-Jumper

Introduction: Little is known about the mechanisms by which gliomas integrate into functional neural networks and influence complex cognitive processes such as language. Glioma-neuron interactions are bidirectional, with increased neuronal activity promoting tumor growth and the latter in turn influencing neuronal excitability and synaptic connections. It remains unknown whether glioma-neuron interactions play a role in maintaining long-range neural networks subserving cognition in humans. We test the hypothesis that glioma-neuron interactions (synaptogenic glioma cells) are enriched within intratumoral high functional connectivity (FC) network hubs, thereby influencing language processing via release of synaptogenic factors into the tumor microenvironment.

Methods: We employed magnetoencephalography imaginary coherence measures of long-range FC to identify intratumoral high (HFC) and low (LFC) functional connectivity network hubs in patients with dominant temporal GBM. Primary patient samples and cultures from HFC and LFC sites were assessed for pre and post-synaptic marker expression, cocultured with murine hippocampal neurons, and induced neuron organoids. Secreted proteins were measured from patient serum and hippocampal neuron condition media. Language assessments were performed in addition to overall survival.

Results: Primary patient samples from HFC regions are enriched for glioblastoma cells with a synaptogenic profile as characterized by pre- and post-synaptic marker expression at both tissue and cellular level (coculture with mouse hippocampal neuron organoid models). RNA sequencing and proteomic analyses from HFC samples revealed a neurogenic signature including TSP1. Overexpression of TSP1 in LFC primary patient cultures rescues the synaptogenic and proliferative phenotype. Glioma integration as determined by intratumoral HFC negatively influenced patient overall survival and language processing.

Conclusion: Glioma-neuron interactions are enriched within intratumoral high network connectivity regions. Glioma-induced neuronal synaptogenesis mediated by TSP1 contributes to the microenvironment in support of tumor network integration which negatively impacts behavior and survival.

449: Treatment of Recurrent Glioblastoma with Activated T cells Against Glioma Stem Cell Antigen Epitopes Leads to Antigen Specific And Cancer Stem Cell Killing

Angelique Sao-Mai S. Do, MD (Los Angeles, CA); Ken Miyaguchi; Hongqiang Wang; John Yu

Introduction: We sought to activate autologous T cells to target the glioblastoma cancer stem cells (CSCs) for patients with recurrent glioblastoma.

Methods: Patients underwent leukapheresis for isolation of peripheral blood mononuclear cells, which were differentiated into DCs in culture, and pulsed with three separate antigen sources: acid-eluted from GBM CSCs, tumor lysate from GBM, or non-glioma CTL and promiscuous helper peptides. T cell markers were measured to evaluate for activation. Interferon-gamma (IFN- γ) Elispot data was collected across three CSC lines to evaluate for antigen specific cytotoxic T cell activity against glioblastoma CSCs after stimulation.

Results: All activation surface markers (CD137, CD69, CD45RO, CD154, and HLA-DR) showed up-regulation in groups at 12 days post activation compared to T0. Elispot data showed that MHC-I eluted peptides, tumor lysate, and CSC epitopes had increases of IFN- γ secretion indicating strong cytotoxic T cell activity compared to no stimulation and non-antigen specific stimulation. At 8 & 13 days, tumor lysate targeting T cells, showed more IFN- γ spots compared to peptide targeting T cells. All groups showed less than 10% increase in killing autologous PHA blasts, which suggests no autoimmune T cell response. Epitope specific targeting showed the most antigen specific killing and the most killing of 3 separate CSC lines.

Conclusion: This data demonstrated antigen-specific recognition of three CSC lines and the ability for potent and long-lasting immune response. Specific CSC targeting CTL epitopes with helper epitopes provided the most potent and specific killing activity. Recurrent GBM patients will be injected IV with autologous T cells activated by DCs with GBM CSC peptides to evaluate the immunogenicity and efficacy of activated T cell infusions to target GBM CSCs.

450: Data-driven Analytics Interrogates Surgical Performance using Novel Haptic Device

Garnette Roy Sutherland, MD, FAANS(L) (Calgary, Canada), FRCSC; Amir Baghdadi, PhD; Hamidreza Hoshyarmansh, PhD; Madeleine Lotbiniere-Bassett, MD; Sanju Lama, MD, PhD; Garnette Sutherland

Introduction: Neurosurgical training continues to be based primarily on apprenticeship model. We have observed that force and motion analysis differentiates surgeons by skill level. Based on end-user requirements, we have developed a unique haptic hand-controller (Excalibur), itself a robot that replicates the force and motion of microsurgery US Patent App. 62/611,024.

Methods: Thirty surgeons performed a peg-in-hole task simulating micro-manipulation using Excalibur and two commercial haptic devices. A modified Kuka end-effector with bipolar forceps, and Leica microscope completed the remote surgical site. Comparisons were made based on subjective performance measures obtained from questionnaires and objective performance features derived from the sensors in the hand-controller. Logistic regression analysis on the significant performance measures (task completion time, number of errors, travel distance, applied force) obtained through MANCOVA tests, was performed to differentiate surgeons by skill levels based on years of experience.

Results: The MANCOVA test results showed that objective features of task completion time ($p=0.02$), number of errors ($p=0.01$), travel distance ($p=0.00$), and applied forces ($p=0.01$) were significant among hand-controllers favouring Excalibur. Experienced surgeons and those with more video game experience preferred Excalibur. Logistic regression model using the above features, classified surgeons by skill level based on their performance using Excalibur. Experienced surgeons worked well within the microsurgery workspace, had increased wrist motion, less error and faster completion time. The trained skill classification model indicated the accuracy of 78%, sensitivity of 67%, and specificity of 83% using the testing group of 9 surgeons.

Conclusion: Excalibur represents an ideal haptic device for integration into a telerobotic system for microsurgery. The technology for the time, provides a quantifiable framework for performance evaluation and training.

451: Vaccination with Irradiated Whole Tumor Cells Pulsed With Phagocytic Agonists, TLR Ligands and Anti-CD40 Antibody Stimulates Antitumor Immune Response Against Metastatic and CNS Tumors

Rogelio Medina (Bethesda, CA); Herui Wang, PhD; Ondrej Uher, MS; John Heiss, MD; Edjah Nduom, MD; Mark Gilbert, MD; Masaki Terabe, PhD; Winson Ho, MD; Jan Ženka, PhD; Karel Pacak; Zhengping Zhuang, MD, PhD

Introduction: Vaccination with irradiated whole tumor cells (rWTC) mixed with immunostimulatory adjuvants has been identified as a promising immunotherapeutic strategy against solid tumors. Optimization of the rWTC vaccine strategy with amphiphilic phagocytic agonists and immunostimulatory adjuvants to target metastatic and CNS tumors has not been explored. Here, we assessed the therapeutic efficacy of an rWTC vaccine, pulsed with a phagocytic agonist (Mannan-BAM), TLR ligands and anti-CD40 antibody (collectively abbreviated as rWTC-MBTA) to control tumor growth and improve survival in mice with metastatic lesions or CNS tumors.

Methods: Syngeneic glioma (GL261) and colon carcinoma (CT26) models were established to assess the rWTC-MBTA vaccine's efficacy in generating immune responses against metastatic lesions and CNS tumors.

Results: In the glioma model, subcutaneous injection of irradiated GL261 cells pulsed with MBTA (rGL261-MBTA) resulted in the complete regression of intracranial gliomas in 87.5% (7/8) of treated animals. In the colon carcinoma model, subcutaneous injection of irradiated CT26 cells pulsed with MBTA (rCT26-MBTA) significantly reduced metastatic CT26 tumor growth rates and induced complete remission (CR) in 28.6% (2/7) of treated animals. Tumor infiltrating leukocyte analyses demonstrated significantly increased CD8⁺ cytotoxic T-lymphocytes (CTL) in metastatic tumors with higher percentages of TNF α and IFN γ positive cells. Therapeutic effect of MBTA was abrogated in CD4⁺ and CD8⁺ lymphocyte depleted mice. Further assessments with MHC I tetramers revealed significantly increased CT26-associated peptide (AH1) specific CTLs in the blood and tumors of rCT26-MBTA Vaccine treated animals. All animals that achieved complete remission in the colon carcinoma model resisted subsequent peripheral and intracranial challenges with CT26 cells, confirming the induction of immunological memory against CT26 tumors.

Conclusion: Collectively, our investigation demonstrates that rWTC-MBTA Vaccines can effectively induce a tumor-specific adaptive immune response that can target metastatic and CNS tumors.

452: GBP2 as a Novel Promoter for Glioblastoma Invasion

Clark C. Chen, MD, PhD, FAANS (Minneapolis, MN); Shuye Yu; Clark Chen; Ming Li

Introduction: Guanylate-binding protein (GBP) is a class of interferon-inducible large GTPase essential for intra-cellular immunity against invading bacterial and viral agents. Many of the functions subserved by GBPs interface with processes essential for tumor immunity and development. Here, we characterize the biological role of GBP2 in glioblastoma, the most common and deadly brain tumor in adults.

Methods: The expression levels of GBP2 were examined by RT-PCR and immunohistochemistry in a collection of glioblastoma patient specimens and the Cancer Genome Atlas (TCGA). Gain/loss-of-function approaches were used to study the effect of GBP2 dysregulation on glioblastoma cell proliferation, migration and invasion.

Results: GBP2 expression is highly elevated in glioblastoma cell lines and in clinical samples. In the TCGA glioblastomas, GBP2 expression is enriched in the mesenchymal subtypes. Additionally, high GBP2 expression is associated with poor prognosis. GBP2 overexpression promoted glioblastoma migration in in vitro and in vivo assays and accelerate tumor-related mortality in independent orthotopic glioblastoma models. GBP2 silencing by RNA interference induced the opposite effects. GBP2 induced increased expression of genes required for canonical cell-migration pathways. This effect was most notable for fibronectin (FN1), where the level of expression was increased by nearly an order of magnitude by GBP2. This induction was dependent on activation of the Stat3 pathway. The effect of silencing GBP2, Stat3, and FN1 were epistatic in terms of cell-migration, suggesting a novel GBP2/Stat3/FN1 pathway for mediating glioblastoma migration/invasion.

Conclusion: Our study defined a novel GBP2/Stat3/FN1 signaling cascade that mediate glioblastoma invasion and suggest GBP2 as an attractive target in glioblastoma therapeutic development.

453: Diagnostic Yield of Biopsy in Corticosteroid Pre-Treated Patients with Primary Central Nervous System Lymphoma

Florian Scheichel (St. Poelten, Austria); Daniel Pinggera; Barbara Kiesel; Tobias Rossmann; Branko Popadic; Melitta Kitzwoegerer; Astrid Dopita; Christian Freyschlag; Georg Widhalm; Karl Ungersboeck; Franz Marhold

Introduction: Corticosteroid treatment (CST) prior to biopsy may hinder histopathological diagnosis in primary central nervous system lymphoma (PCNSL). Therefore, preoperative CST of suspected PCNSL should be strictly avoided if clinically possible. The aim of this study was to analyze the difference in diagnostic yield of PCNSL patients with and without preoperative CST.

Methods: A retrospective study including all patients diagnosed with an intracranial PCNSL between 1/2004 and 9/2018 at four specialized neurosurgical centers in Austria, was performed. Patients with secondary CNS lymphoma, with unclear preoperative corticosteroid status and immunocompromised patients were excluded. Diagnostic yield was defined as successful diagnosis of PCNSL without the need for repeat biopsy.

Results: A total of 146 patients were diagnosed with PCNSL in the study period of whom we could determine the preoperative CST status in 143 patients. There was no statistically significant difference in the diagnostic yield of biopsy in patients with and without preoperative CST with 95.7% (67/70) and 97.3% (71/73) respectively ($p=0.676$). CST was ongoing in 27.3%, paused up to 7 days in 9.4%, paused more than 7 days in 10.8% and no preoperative CST was given in 52.5%. Preoperative tapering and pause of CST led to significant delay of the median timespan from first consultation to surgery for patients without CST or ongoing CST to patients with paused CST of 17.5 days and 23.5 days, respectively ($p=0.035$).

Conclusion: No statistical difference in the diagnostic yield of biopsy in PCNSL patients with and without preoperative CST was found. Tapering and pause of preoperative CST led to significant delay of surgery and subsequently diagnosis and therapy which might result in worse outcome. In our opinion, surgeons therefore should try to keep the diagnostic delay to a minimum as the diagnostic yield still seems to be sufficiently high in patients with preoperative CST.

454: Immunogenomic Responder Phenotype from a Phase I Trial of Anti-LAG3 or Anti-CD137 Alone and in Combination with Anti-PD-1 in Patients with Recurrent GBM

Christina Chen-Jackson, MD (Baltimore, MD); Christina Jackson, MD; John Choi, MD; Anna Piotrowski; Tobias Walbert; Manmeet Ahluwalia; Burt Nabors; Serena Desideri; Patrick Wen; Stuart Grossman; Drew Pardoll; Michael Lim

Introduction: Immune checkpoint inhibitors (ICIs) are not uniformly effective in glioblastoma treatment. Immunogenomic determinants may identify patients who are most likely to benefit from these therapies. Therefore, we compared the immunogenomic phenotype of a responder to combination anti-LAG-3 and anti-PD-1 therapy to non-responders.

Methods: We performed T cell receptor (TCR) sequencing and gene expression analysis on pre-treatment, post-chemoradiation, and post-immunotherapy tumor specimens of glioblastoma patients treated with anti-LAG3 in combination with anti-PD-1 after first recurrence (NCT02658981, ongoing). We evaluated T cell clonotypes and immunophenotype of serially collected peripheral blood mononuclear cells (PBMCs) during treatment using multi-parametric cytometry.

Results: To date, six patients have been enrolled in the initial anti-LAG-3 and anti-PD-1 cohort. One patient demonstrated complete response, one had stable disease, and four had progressive disease by radiographic evaluation. The responder demonstrated substantially higher TCR clonality in the resected tumor at initial diagnosis compared to non-responders (mean 0.028 vs. 0.005). Shared tumor infiltrating clonotypes with pre-immunotherapy PBMCs exhibited an increase in frequency from initial resection (6.8%) to resection at recurrence (20%). The responder's tumor at initial resection exhibited increased gene signatures of PD1low CD8+ T cells, chemokine signaling, and interferon gamma pathways. On PBMC phenotypic analysis, the responder demonstrated significantly higher percentage of CD137+ CD8+ T cells (median 8.38% vs 3.24%, $p=0.02$) and lower percentage of Foxp3+CD137+ CD4+ T cells compared to non-responders (median 18.5% vs. 38.5%, $p=0.006$). Interestingly, dynamic analysis of PBMCs showed that the responder demonstrated lower percentage of PD1+ CD8+ T cells pre-immunotherapy (median 2.5% vs. 12.4%, $p=0.002$), and a persistent decrease over treatment course while non-responders showed no consistent pattern.

Conclusion: Our preliminary results demonstrate significant differences in tumor and peripheral blood immunogenomic characteristics between responder and non-responders to anti-LAG3 and anti-PD-1 therapy. These immunogenomic characteristics may help stratify patients' response to combination ICIs.

500: From Madness to a Modern Useful Surgery: The Journey of the Transorbital Corridor to Enter the Neurosurgical Armamentarium

Vesalius Award

Lena Mary Houlihan (Phoenix, AZ); Evgenii Belykh; Xiaochun Zhao; Michael O' Sullivan; Mark Preul

Transorbital surgery has gained recent notoriety due to its incorporation into endoscopic skull base surgery. However use of this surgical corridor has pervaded throughout the 20th century, utilized by multiple disciplines for both clinical and experimental purposes to great success, although its historical origin is both medico-ethically controversial and chequered. Knapp introduced experimental orbital surgical technique in 1874, with Kronlein's procedure introduced in 1889. While Italian psychiatrist Fiamberti is credited with completing the original transorbital prefrontal leucotomy in 1937, Freeman revolutionized psychosurgery (1946) by completing seemingly successful transorbital leucotomies promoting its minimally invasive and benign surgical characteristics. As Freeman's legacy came under disrepute, so did the transorbital brain-access corridor, resulting in its stunted evolution. Rivalry ensued as Dandy in Neurosurgery and Berke in Ophthalmology clashed heads on methods of tackling intracranial and intraorbital pathologies. Dandy, steadfast in his conviction, believed in the craniotomy as the superior surgical technique: 'It is rarely possible before operation to be certain whether or not a tumor lies within the cranial cavity.....Even for tumors confined to the orbit alone, this approach has been found far superior to those hitherto used by ophthalmologists.' Ironically similar to the 1930s, a transorbital brain approach began in 1970 with experimental surgeries in animals. Historical analysis of present aspirational goals in modern skull base surgery echoes principles established through an approach first described almost 150 years ago; minimally invasive, minimal morbidity, with priority of patient satisfaction. The progression of the transorbital approach reflects not only psychosocial influences on medical therapy, as well as the competition of surgical pioneers for supremacy, but it also describes the diversification of skull base techniques, the impact of microsurgical mastery on circumferential neurosurgical corridors, the influence of technology on modernizing skull base surgery and the advancing trend of the multi-disciplinary approach towards surgical excellence.

501: Objectivity, Photography and Performative Culture in the Emergence of the Modern Neurological Examination

Alexander Forcht Dagj, AB, MPhil (Newton, MA); T Forcht Dagj, MD, MPH, MBA, DMedSc, FAANS

Introduction: While the explicitly performative nature of surgery and the surgical amphitheatre is widely appreciated, the high-thespian roots of the early neurological examination are less so. We discuss the origins and historical significance of formal performance in neurological examination, including the demonstration of clinical signs, the emphasis on seeing, and the adoption of photography by Duchenne, Charcot and Babinski, the founding triad of 19th century French neurology.

Methods: We analysed three sentinel works: Duchenne's *Mecanisme de la physionomie humaine ou Analyse électro-physiologique de l'expression des passions applicable à la pratique des arts plastiques* (1862). Charcot's *Nouvelle iconographie de la Salpêtrière* (1882) and Londe's *La Photographie medicale* (1893).

Results: The modern neurological examination emerged in the mid-19th century but did not become standardized until the early 20th. Objectivity and proper seeing emerged as critical concerns. The new art of photography was adopted by Duchenne to record investigations and choreographed demonstrations of muscular activity and emotion during galvanic stimulation of the face. The camera was construed as an objective witness to a medical theater in which both neurologist and patient played to an audience. Many of the performative features of the classical neurological examination are attributable to this time. While Duchenne's photographs were celebrated by the *Ecole des Beaux-Arts*, he was deemed eccentric by medical colleagues. Still, both performance and photography were enthusiastically adopted by Duchenne's student, Charcot, who suffered no such disparagement, and eventually rose to greater fame. Indeed, Charcot, as well as his student Babinski, were avid performers. Charcot frequently invited non-medical members of the Paris intelligentsia to observe his examinations and hypnotic sessions, while Babinski directed a significant theatrical performance, *Les Détraquées* (The Unhinged).

Conclusion: Performative clinical demonstration endured as a prominent characteristic of neurological culture, traceable historically to these roots.

502: The Influence of the Boer Wars on Cerebral Abscess Management*Keenan M. Boulnemour (Kalamazoo, MI); Chris Sloffer, MD*

Warfare has always proven to be fertile ground for surgical advancements, and changes in warfare leads to new challenges in the management of the resulting injuries. The Boer Wars of 1899-1902 can be described as the first modern war, due in part to its being the first major conflict to utilize a modern rifle delivering a projectile with a smaller caliber and higher velocities. These higher velocities resulted in greater kinetic energy delivered to the target. The resulting wounds frequently had bone fragments deeply embedded in the brain. These fragments could serve as a nidus for infection, though outright sepsis was rare. In some ways, the higher velocity projectiles with their small, straight tracts into the brain dragged less debris into the wounds than the larger, slower velocity weapons that they replaced. Soldiers with cranial wounds that arrived alive to medical care were either managed symptomatically, and with watchful waiting, or via trephine. Surgical approaches often involved digital exploration and debridement of brain tissue and bone fragments from the wound. The appropriateness of each approach was debated both before and during the conflict. There were brief philosophical differences in how each side of the conflict dealt with their wounded. One documented difference notably compares the approaches to initial head wounds by the German Corps in other conflicts of the era to the British medical service during the Boer Wars. Treatment varied widely but recurring symptoms due to infection were commonly documented. With time, and after the war, it became better accepted that trephining [could] be done with the utmost freedom, and with the greatest advantage to the patient. The Boer Wars therefore provided the field of neurosurgery with a breakthrough in the management of penetrating head trauma and cerebral abscesses.

503: A Hundred Years Later: The History of Ray Chapman and the Pitch that Killed*Pranay Soni, MD (Cleveland, OH); Ghaith Habboub, MD; Edward Benzel, MD; Richard Schlenk, MD*

Introduction: Nearly a hundred years have passed since one of the most tragic accidents in baseball history. In a time before helmets were mandatory, when pitchers were all but encouraged to throw high and tight, Ray Chapman became the only player in MLB history to suffer a fatal injury during a game.

Methods: A historical review was conducted using published literature and online searches.

Results: At the top of the fifth inning, Cleveland Indians' Ray Chapman came out to face pitcher Carl Mays of the Yankees. The ball hit Chapman's skull so hard that Mays initially thought it came off Chapman's bat. He threw the ball to first base for the out, but Chapman collapsed to the ground. A lucid interval followed, Chapman even attempting to walk off the field. He was rushed to St. Lawrence Hospital, where he underwent an emergency operation. A New York Times article read, the brain had been so severely jarred that blood clots had formed. The shock of the blow had [deeply cut] the brain not only on the left side of the head where the ball struck but also on the right side where the shock of the blow had forced the brain against the skull. Chapman died a few hours after the surgery, casting a grim shadow over the city of New York and over all of baseball throughout the nation.

Conclusion: The Brooklyn Dodgers are credited as being the first team to wear protective caps in 1941, and it was neurosurgeon Walter Dandy who contributed to their design. It nearly took a second fatal injury, this time to Don Zimmer in 1953, for the MLB to formally mandate helmets in the batter's box. And while head injuries do still occur in baseball, we hope to avoid another tragedy like Ray Chapman.

504: Sir Charles Bell Life and the Art of Science*Diego Dereck Luy (Pittsburgh, PA); Stephanie Casillo; Nitin Agarwal; Ezequiel Goldschmidt*

Introduction: Sir Charles Bell, a Scottish-born surgeon, had many passions in life, including artistry and neuroscience. These passions culminated in An Essay on the Anatomy of Expression in Painting, which was read by Queen Victoria, and The Anatomy of the Brain, which he read before the Royal society. Until his death, Bell compiled numerous accolades including professorships and knighthood. Among his most lasting achievements are his discoveries regarding the nervous system including spinal nerve root arrangements, Bell's phenomenon, Bell's nerve, Bell's spasm, and the Bell-Magendie/Bell's Law.

Methods: Details on Bell's scientific and artistic ventures were extensively reviewed. Bell's "The Nervous System of the Human Body" and Gordon-Taylor's biography on Charles Bell were the primary sources, in addition to a number of historical pieces focusing on physicians of the nineteenth century.

Results: After receiving his medical degree, Bell achieved feats including purchasing part of the Great Windmill Street School of Medicine, studying gunshot wounds of the Napoleonic Wars, operating at the battle of Waterloo, and knighthood into the Guelphic Order. Bell published various works on the nervous system including The Anatomy of the Brain. Apart from criticizing other researchers for their lack of tact and anatomical knowledge, he discovered that spinal nerves came in

pairs with a motor ventral and a sensory posterior root, the long thoracic nerve, several cases on facial palsies, and a new form of facial spasm. Today, they all have their name.

Conclusion: Sir Charles Bell debunked popular beliefs of the nervous system by the combination of the scientific method and the beauty of his paintings. His full understanding of the anatomy of the brain resulted in a new appreciation of the relationship between structure and function.

505: From the Historical Examples of Drs. Osler, Cushing and Van Wagenen: Lessons on the Importance of Mentorship in Contemporary Neurosurgery

Anthony S. Larson (St. Paul, MN); Stephen Haines, MD; Webster Pilcher, MD, PhD; Taylor Piva, MA; Andrew Grande, MD

Introduction: Excellent mentorship remains indispensable in order to become a proficient neurosurgeon. The historical relationships between William Osler, Harvey Williams Cushing and William Perine Van Wagenen are well-known in the neurosurgical world. However, the mentor-mentee relationships between these medical giants are not widely appreciated. We describe and exemplify such relationships and subsequently extract important and applicable principles from them.

Methods: We reviewed relevant primary and secondary sources, including published literature, biographies and personal correspondence pertaining to the mentor-mentee relationship that existed between Cushing, Osler and Van Wagenen.

Results: In founding the field of neurological surgery while at Johns Hopkins Hospital, the brilliant yet volatile Dr. Harvey Cushing received guidance from his mentor, Dr. William Osler. Through our review, it is undeniable that Dr. Osler's personal and professional guidance was vital to young Cushing's success as the founding father of modern neurosurgery. Likewise, Cushing's tutelage of Van Wagenen at Peter Bent Brigham Hospital enabled Van Wagenen to become one of the leaders of a second generation of neurosurgeons, and thus perpetuate the existence of Cushing's high standards of neurosurgical excellence.

Conclusions: These historical mentor-mentee relationships demonstrate four critical features of successful mentorship: Accurate recognition of talent, guidance, arrangement of opportunity, and sustenance of mentorship. These actions have been consistently demonstrated as components of effective mentorship in contemporary literature, thereby implicating that these historical relationships continue to serve as valuable examples of exceptional mentorship. Proper mentorship remains indispensable for younger neurosurgeons to thrive and live up to the high standards within the field of modern neurosurgery.

506: The Neuroanatomy of Albert L. Rhoton, Jr.: An Analysis of Origin, Evolution, and Application

Evgenii Belykh, MD, PhD (Phoenix, AZ); Xiaochun Zhao, MD;; Dara Farhadi, BS; Jubran Jubran, BS; Lena Houlihan, MD; Ronald Smith, PhD; Mark Preul, MD

Incorporation of perspective into art and science altered investigation of the brain. About 1504 Leonardo began to model the ventricles in 3D, while a few years later Vesalius illustrated radically novel brain dissections. Willis' 1604 *Cerebri Anatome* illustrated by Wren remarkably revealed the brain undersurface, and Bell's 1802 stylishly accurate images of the brain demonstrated its color. In the 1930s Klingler revealed complex white matter tracts. About 1968 Albert Rhoton (1932-2016) would begin to earn his place among the eminent neuroanatomists by focusing his lens on microanatomy to harness the potential for greater knowledge of microneurosurgery and microneurological anatomy to improve the care of [his] patients. While his biography and images are well-known, analysis of the composition of Rhoton's publications and work to identify progression, impact, and trends in his research has not been accomplished. From 508 publications, 413 works were analyzed by various regions, surgical approaches, subjects, methods utilized, forms of multimedia, and subspecialty. Specific analysis of 268 original papers (54% pure anatomical descriptions, tumor 23%, vascular 21%, functional 9%, spine 1%; not including 2002 cranial anatomy book chapters, 2007 temporal bone anatomy book, non-anatomical studies): before 2002, 134 papers (50%; 4 papers/year) published; after 2002, 10 papers/year published, with a trend toward subspecialty-oriented studies. 31% of studies included artistic drawings, 8% 3D photos, 5% endoscopic photos; 3D photography increased chronologically. The three most common studied approaches were frontotemporal(18%), retrosigmoid(15%), and endonasal(13%); three most common studied anatomical regions were basilar(34%), paraclinoid(25%), and supraclinoid arteries(24%). Using meticulous, comprehensive, and surgical perspective evolving with advancing technical demands of neurosurgery, Rhoton taught detailed neuroanatomy never before seen, inspired students and contemporaries, making him arguably and historically the most influential anatomist of the modern neurosurgical era. We want perfect anatomical dissections, because we want perfect surgical operations.

507: Renaissance Neuroanatomy and Secular Philosophy in the Sistine Chapel

Luis E. Savastano, MD (Cambridge, MA); Daniel Nijensohn, MD, PhD

Introduction: Michelangelo's frescos in the Sistine Chapel have been traditionally considered to represent the catholic dogma of the Creation. However, studies have suggested that Michelangelo concealed anatomical information of human brains in these drawings. This study was conducted to analyze and interpret these frescos in the appropriate historical, anatomical and philosophical context.

Methods: Philosophical and brain function theories during the Renaissance were reviewed to contextualize Michelangelo's work in time and space. Anatomical representations and dissection techniques of that specific timeframe, available to Michelangelo were identified and reproduced in ten cadaveric human brains. Anatomical specimens were used as art models to analyze the Sistine Chapel's frescos in light of contextual anthropocentric philosophical ideas.

Results: Galen's Ventricular Theory of brain function was still dominant during the Renaissance, as evidenced by Da Vinci's folios. Michelangelo performed human dissections together with anatomist Colombo, who trained under Vesalius, author of *De humani corporis fabrica*. This work includes extensive neuroanatomical iconography embodying Galen's theory. We replicated Vesalius' dissections to generate neuroanatomical models. We support the following contextual interpretations: 1) Separation of light from darkness: represents the dorsal brainstem, known to control arousal and when damaged, to cause coma; 2) Creation of the Sun and the Moon: represents the eyes, optic nerves and chiasm, the organ of sight, known to result in blindness if damaged; 3) Creation of Adam: representation of the mid-sagittal section of the human brain depicting the ventricular system, providing mankind with the ability of thought; 4) The Last Judgement: a coronal section of a brain with lateral and third ventricles provides the substrata to interpret and judge the environment.

Conclusion: We conclude that Michelangelo already perceived a critical relationship between the Brain, God, and Man's spirit and coded a new manifesto in the Sistine Chapel.

508: Reconstructive surgery of peripheral nerve injuries during the Chaco war, Paraguay-Bolivia 1932-1935

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

Introduction: The Chaco War was a conflict between Paraguay and Bolivia, from 09/09/1932 to 06/14/1935. It was the most important war in South America during the twentieth century. In the three-year period, Bolivia mobilized 250,000 soldiers and Paraguay 120,000, who faced fighting in which there were large numbers of casualties (60,000 Bolivians and 30,000 Paraguayans). The historian Juan Miguel Balcazar described it: the Chaco War was a true field of experimentation for surgery. That all doctors had to become surgeons to save the wounded and sick.

Methods: A descriptive analysis and bibliographic review of the book "REPAIR SURGERY FOR INJURIES OF THE PERIPHERAL NERVES", written by the physician Abelardo Ibañez Benavente, and published by the Bolivian Government 1936, was performed.

Results: 176 cases of nerve injuries in 151 patients are described, where upper limb injuries predominate. Nerve lesions are described with the terms "contusion" and "complete or incomplete section". In 126 pages Dr. Ibañez Benavente describe the diagnosis, the surgical and clinical follow-up of war wounds, treatment against infections, the exploration of wounds and the definitive surgical approach, emphasizing the end-to-end suture and neurolysis.

Conclusion: We present a beautiful monograph with the description of 176 peripheral nerve surgeries during the Chaco War, considering this work as revolutionary for its time (1932-1936) taking into account the limitations of anesthesia, the discovery and use of antibiotics and even knowledge of the nerve injury Seddon (1943) and Sunderland (1951)

509: Effects of External Low Intensity Focused Ultrasound in a Swine Model of Common Peroneal Nerve Injury.

Julie G. Pilitsis, MD, PhD, FAANS (Albany, NY); Abigail Hellman, BA; Teresa Maietta, BS; Alicia Clum; Kanakaharini Byraju; Erin Jeannotte, BS; Nataly Raviv, MD; Michael Staudt, MD, MSc; Goutam Ghoshal, PhD; Clif Burdette, PhD; Jiang Qian, MD

External, non-invasive, low intensity focused ultrasound (liFUS) shows potential for treatment of chronic neuropathic pain. liFUS treatment improves sensory thresholds in a rodent common peroneal nerve injury model (CPNI). Here, using a novel large animal model, we further validate and extend the use of liFUS neuromodulatory therapy for chronic pain. CPNI was developed and evaluated in male farm pigs by ligating the left peroneal nerve. Post-surgical baseline nociceptive thresholds and social/motor behaviors were recorded one week later. External liFUS, targeting the left L5 dorsal root ganglion (DRG), was applied and responses were re-assessed. A liFUS dose response curve was performed, the optimal treatment dose determined, and DRG samples assessed for histopathological change. Following surgery, animals demonstrated significant increases in sensitivity to both mechanical and thermal stimuli (ANOVA, $p < 0.05$: von Frey filaments, VFF ($n=12$) and Medoc Pathway ($n=6$), respectively); leg guarding was also present. liFUS treatment (power 25-30W, 3-4 minutes, coolant rates of 20-26ml/min): 1) significantly increased common peroneal nerve conduction velocity for up to 30 minutes ($p < 0.05$), 2) significantly reduced mechanical nociceptive sensitivity for up to 4 days ($p < 0.001$), in 11 of 12 animals, and 3) significantly reduced thermal nociceptive sensitivity for 24 hours ($p < 0.05$), when compared to pre-liFUS responses. Similarly, after treatment, elevated post-CPNI motor scores returned to pre-surgical baseline levels for the remainder of the study in 11 of 12 animals. Fluoro-jade, or eosin/hematoxylin, stained DRG tissue showed no evidence of neuronal degeneration or nerve damage after liFUS treatment. We report the first neuropathic pain model in farm pigs. In addition, we demonstrate that external liFUS treatment of the L5 DRG reverses mechanical and sensory allodynia, and does not produce pathological tissue damage. Future work will focus on an 'all-in-one' device using FUS to non-invasively administer and monitor therapy in anticipation of clinical trials.

510: Duration of Trigeminal Neuralgia Symptoms does not Influence Pain Free Outcomes after Microvascular Decompression

Matthew W. Pease, MD (Pittsburgh, PA)

Introduction: While medical treatment is generally favored until Trigeminal Neuralgia (TN) symptoms become refractory, microvascular decompression (MVD) provides more consistent pain relief and fewer side effects than medications. The optimal timing of microvascular decompression for TN is unknown. The purpose of this study was to evaluate whether the duration of symptoms affected pain-free outcomes in MVD.

Methods: We analyzed outcomes from 208 consecutive TN (classical and nonclassical) patients undergoing MVD by a single surgeon between 2011–2016. Median follow up was 40.4 months (range 1-86).

Results: 105/206 patients were completely pain-free at last follow up for 3 and 5 year rates of 72.5% and 70.3%, respectively. Multivariate analysis was not significant for pain duration > 1 year ($p=0.214$) or as a continuous variable. We then performed recursive partitioning analysis and identified 3 classes of patient outcomes. Groups one and three had three-year pain rates of approaching 95% and had neurovascular compression and classical pain, versus 5.3% for patients without neurovascular compression, and atypical pain. The duration of pain symptoms was not significant in any grouping.

Conclusions: In both a multivariate and recursive partitioning model, duration of pain was not related to outcomes after MVD. This suggests that delaying surgery for additional medication trials is safe, and operating on patients with long-standing pain does not reduce the chances for a successful operation.

511: Neuron-Glial Inflammasome Enhanced Reversal by DTM-SCS Relative to High Rate and Low Rate SCS in a Neuropathic Pain Model

William J. Smith (West Lebanon, NH); David Cedeño, PhD; Courtney Kelley, MS; Dana Tilley, PhD; Ricardo Vallejo, MD, PhD

Introduction: Microglia-specific and Neuron-specific genes involved in inflammation, known as the inflammasome, have been elucidated via single-cell RNAseq. Our group recently reported that Differential Target Multiplexed SCS (DTM-SCS), where different pulsed signals are combined to target different cell types, produced a larger impact on pain-related biological processes compared to low-rate (LR) or high-rate (HR) SCS. This study compares the ability of DTM-SCS, HR-SCS, and LR-SCS to restore the unbalanced neuron-glial inflammatory response in a neuropathic pain model.

Methods: Microglia-specific and neuron-specific inflammasomes were compiled and compared to our RNA-sequencing results. Changes in inflammasome due to a pain model (SNI) compared to Naïve animals were characterized. In order to evaluate the effects of SCS, the Naïve group was considered a treatment, allowing for comparison between DTM-SCS, HR-SCS (1,200Hz), LR-SCS (50Hz), and Naïve, relative to SNI, via Pearson correlations.

Results: 132 microglia-specific and 242 neuron-specific inflammasome genes were identified in our dataset. SNI decreased expression in 68% of neuron-specific genes and increased expression in 57% of microglia-specific genes. DTM-SCS and HR-SCS showed significant positive correlations with Naïve in the microglia-specific ($R=0.58$, $R=0.53$ respectively) and neuron-specific inflammasomes ($R=0.77$, $R=0.28$ respectively). LR-SCS showed a significant positive correlation in the microglia-specific ($R=0.18$) inflammasome only. DTM-SCS restored 79% of microglia-specific and 78% of neuron-specific genes towards Naïve expression levels, more than HR-SCS (53% and 66%) or LR-SCS (55% and 50%). DTM-SCS restored >80% of genes recovered by HR-SCS or LR-SCS plus an additional 63 genes.

Conclusion: Our results show that pain creates an imbalance in the inflammasome, upregulating neuron-specific genes and downregulating microglia-specific genes, supporting recent research regarding neuron-glial interaction in mediating chronic pain. DTM-SCS was the most effective at rebalancing both inflammasomes, modulating gene expression in a manner that most closely resembles the inflammasome of Naïve animals and restoring genes unaffected by HR-SCS or LR-SCS.

512: Clinical Characterization of Thin Bone Overlying the Superior Semicircular Canal

Michelle Hong (Los Angeles, CA); Taranjit Kaur; Leslie Hwang; Meachelle Lum; Courtney Duong, BS; Isaac Yang, MD; Quinton Gopen, MD

Superior semicircular canal dehiscence (SSCD) is a rare disorder that causes vestibular and auditory symptoms resulting from a dehiscence in the middle cranial fossa floor overlying the superior semicircular canal (SSC). Patients with thin bone overlying the canal without true dehiscence can also experience these symptoms. Currently, many institutions do not perform surgeries on symptomatic thin bone patients and only considers surgical intervention with true dehiscence. We aim to provide more data on thin bone patients to characterize their symptoms and explore surgical intervention for symptom alleviation. This retrospective study examines temporal bone CT scans from 256 SSCD patients to determine whether they had true dehiscence or thin bone. A threshold of 0.5mm was used for thin bone classification. There were 37 bilateral thin bone patients (BiThin), 33 unilateral thin bone and normal bone patients (ThinNormal), and 73 unilateral thin bone and dehiscence patients (ThinDehisc). We then examined consult notes pre- and post-operatively to characterize their clinical presentation. In BiThin patients, pulsatile tinnitus recovery post-surgery is affected by bone thinness pre-surgery ($p=0.02$). Additionally, the sex of BiThin patients affects whether they present with hearing loss pre-surgery ($p=0.03$) and post-surgery ($p=0.001$). Age of BiThin patients correlates with dizziness and headache presentation pre-surgically ($p=0.05$). Bone thinness also affects the presentation of autophony ($p=0.02$) and vertigo ($p=0.07$) in ThinNormal patients. In this study, BiThin and ThinNormal patients were highlighted assuming that their symptoms were caused by thin bone without confounding by a true dehiscence. Pulsatile tinnitus, autophony, and vertigo are directly affected by bone thinness. Thus, bone thinness can be used as a relative indication of symptom severity. The results also show that age and sex could affect thin bone patient presentation. This could be taken into account when assessing whether a patient would benefit from thin bone surgical correction.

513: Microgravity Induces Genetic Alterations in the Neuropathic Pain Network in Mice Undergoing Fracture Healing In Space

Stephen Kyle Mendenhall, MD (Indianapolis, IN); Nabarun Chakraborty; Aarti Gautam; Paul Childress; Bintu Sowe; Allison Hoke; Lily Nef; Rasha Hammamieh; Melissa Kacena

Introduction: Spaceflight imposes significant stress on flight crews, resulting in complex adaptation processes to counteract the physiological and psychological strains. Pain encompasses an extensive list of biological networks associated with nociception, neurotransmission, neuroreception, somatosensation, and inflammation. The aim of this research was to examine the distinct effects of microgravity on the processing of pain from segmental bone defect (SBD) surgery.

Methods: Nine-week-old, male C57BL/6J mice were used in this NASA study. Four days prior to spaceflight launch, a 2 mm defect was created in the right femoral shaft and was replaced by a synthetic graft to maintain the defect size. Mice were euthanized approximately 4 weeks post-surgery. Bones were analyzed by micro-computed tomography. Transcriptomic analysis was performed on brain tissues to identify differences in gene expression between spaceflight, ground, and control groups. IPA (Ingenuity Pathway Analysis) was then performed for functional annotation and pathway enrichment analysis.

Results: Image analysis revealed that spaceflight mice suffered impaired bone healing compared to ground controls. Microarray analysis found more genes significantly altered in the surgery groups vs. control groups (2,212 vs. 657); where <95% of genes were exclusively altered in the surgery group due to microgravity. The neuropathic pain network was significantly altered in microgravity, along with a cluster of signals linked to neuromodulators such as GABA, glutamate, corticotrophin, and cortisol. Activated synaptic transmission and potentiation was coupled with inhibited sensation and nociception in spaceflight.

Conclusion: These data suggest the adaptation of pain sensitization to stress induced by spaceflight. Brain region specific information is recommended to capture a comprehensive picture. Our research is poised to describe the impact of microgravity on pain perception. Further understanding of how the brain modulates pain will serve as a platform for future studies on optimizing the management of pain during space missions.

514: A Retrospective Analysis of High Opioid Use Patients Undergoing a Preoperative Pain Program Prior to Spine Surgery

Lindsey B. Ross, MD (Los Angeles, CA); Wittnebel Karl, MD; Jeanne Black, PhD; Keith Seigel; Terrence Kim, MD; Sang Kim, MD; Eli Baron, MD; Alexander Tuchman, MD; Mark Vrahas, MD; j. Patrick Johnson, MD

Introduction: Back pain is the most disabling disorder worldwide and is the most common reason an individual seeks a visit to the doctor (Hoy). We spend over 250 billion dollars treating back in the United States and we primarily use opioids to do so (BMUS). Previous studies have shown that after spine surgery, chronic opioid users have worse patient outcomes, increase their long-term opioid use and spend more healthcare dollars (Devin, Lee, Wick, McAnally). The Preoperative Pain Program (PPP) is a treatment program aimed at optimizing high opioid use patients undergoing elective spine surgery. We hope to show that high opioid users who participate in PPP will have improved patient outcomes following spine surgery.

Methods: This is a retrospective data analysis from spine patients treated at our center. High opioid users, >80 MED were enrolled in PPP. Opioid reduction at 10% weekly. Primary outcomes include 30-day re-admissions/ER visits and LOS. Secondary outcomes include complications, 90-day re-operation rate and discharge disposition.

Results: 330 patients underwent treatment in the PPP with 80 of those patients with sufficient follow up data. Reoperation rates were 6X lower in the PPP group. PROMIS scores were collected, showing no significant increase in pain level despite an average opioid reduction of over 30%.

Conclusion: We have laid the ground work for future research assessing the efficacy of a PPP to improve surgical outcomes for high opioid users. The feasibility of decreasing opioid doses before major spine surgery is demonstrated, without undue hardship for patients. We hope that this initial study will serve as a template for other health centers seeking to improve spine surgery outcomes through opioid reduction, as well as a basis for further research on specific opioid weaning targets and lead times associated with maximal benefit.

515: Percutaneous Trigeminal Ganglion Stimulation for Intractable Facial Pain

Pavlos Texakalidis (Atlanta, GA); Muhibullah Tora; Tanner McMahon; Alexander Greven; Casey Anthony; Nicholas Boulis

Introduction: Facial pain syndromes can be refractory to medical management and often need neurosurgical interventions. Neuromodulation techniques, including percutaneous trigeminal ganglion (TG) stimulation, are reversible and have emerged as alternative treatment options for intractable facial pain. Our objective was to report the complication rates and analgesic effects associated with TG stimulation and identify potential predictors for these outcomes.

Methods: A retrospective chart review of 59 patients with refractory facial pain who underwent TG stimulation was conducted. Outcomes following trial period and permanent stimulation were analyzed. Patients with >50% pain relief during trial stimulation received permanent implantation of the stimulation system.

Results: Successful trial stimulation was endorsed by 71.2% of patients. During the trial period, one TG lead erosion was identified. History of trauma (facial/head trauma, oral surgery) was the only predictor of a failed trial compared to pain of idiopathic etiology (OR: 0.15; 95%CI: 0.03-0.66). Following permanent implantation, approximately 29.6% and 26.5% of patients were diagnosed with lead erosion and infection of the hardware respectively. TG lead migrations occurred in 11.7% of the patients. The VAS score showed a statistically significant reduction of 2.49 (95%CI: 1.37-3.61; $p=0.0001$) at an average of 10.8 months following permanent implantation.

Conclusion: TG stimulation is a feasible neuromodulatory approach for the treatment of intractable facial pain. Facial/head trauma and oral surgery may predict a non-successful trial stimulation. Future development of specifically designed electrodes for stimulation of the TG, and solutions to reduce lead contamination are needed to mitigate the relatively high complication rate.

516: PiPeD Revascularization: A Novel Surgical Technique for Treatment of Anterior Cerebral Territory Ischemia in Pediatric Moyamoya. Case Series with Long-term Clinical and Radiographic Follow-up

Edward Robert Smith, MD, FAANS (Boston, MA); Alaa Montaser, MD, PhD; Jessica Driscoll; Hudson Smith; Tina Mounlavongsy; Emily Day; Madeline Karsten; Darren Orbach, MD, PhD; Edward Smith

Introduction: Isolated anterior cerebral territory ischemia in pediatric moyamoya is rare. Surgical treatment is complicated by limited graft choices, with the small number of case series focused on complex, higher-risk operations (omental flap transfers, large interhemispheric rotational grafts), direct bypass (often untenable in children due to vessel size) or multiple burr-holes (of limited efficacy outside of infants). Here we describe a novel approach of PIAL-Pericranial-Dural (PiPeD) revascularization, building on the principles of pial synangiosis but unique in using pericranium and dura as the primary vascular supply and employing a larger craniotomy with arachnoid dissection to provide robust full-territory revascularization in all ages without the attendant risks of more complex procedures.

Methods: Retrospective single-center series with institutional review board approval. Surgical indications included anterior circulation arteriopathy with evidence of co-localized stroke or slow flow (ivy sign on FLAIR). A large craniotomy is prepared, utilizing a pedicled pericranial graft, stellate dural opening and extensive arachnoid dissection, with subsequent synangiosis using 10-0 nylon.

Results: A total of 20 operations were performed in 18 patients (age 1-22 years, average 8.7; 12 female/6 male). Complications included 1 stroke (5%), 1 superficial infection (5%), with no hemorrhage, seizures or deaths. Follow-up was available in 14/18 patients (3 international patients lost to follow-up, one patient less than 3 months out; average 23.6 months, range 6-40). Radiographic engraftment was present in 93.8% (15/16) and no new strokes were evident on MRI (0%, 16/16) on long term follow-up, despite radiographic progression of disease.

Conclusion: This novel surgical approach is simple, but differs from what is currently described in the pediatric literature in its focus on arachnoid opening, donor site graft flexibility and ability to revascularize a larger territory with a craniotomy. Extensive follow-up demonstrates that it confers durable, long-term radiographic and clinical protection from stroke in pediatric moyamoya patients.

517: Design of an Implantable, Programmable and Wireless-Based Ventriculoperitoneal (VP) Shunt System with Intracranial Pressure Monitoring using Mixed Signal CMOS Circuit Approach

International Travel Scholarship

Lean Angelo Ang Silverio (Davao City, Philippines); Angelito Silverio, PhD

Introduction: Hydrocephalus happens due to the unbalanced production and absorption of CSF in the ventricles of the brain. ICP build-up may occur due to CSF accumulation leading to functional impairments. VP shunt is the common treatment involving drainage of excess CSF. However, this poses issues like obstructions and over-drainage. Clogged shunt accounts for most complications and is addressed using revision surgery. Methods to detect shunt clogging include imaging, catheterization, and micro-sensing in the subarachnoid or ventricles. Present VP shunts have magnetically adjustable thresholds but don't have feedback. Presently, surgeons don't have quantitative shunt thresholding and clog notification.

Methods: The system consists of MEMS pressure sensor interface, valve controller, and transceiver. It incorporates low-noise amplifier (IA) that extracts ICP while attenuating background noises; window comparator (WC) that proportionally controls the valve thru a pressure integrator; programmable reference that sets the upper (VUP) and lower (VLOW) thresholds; clogged shunt logic that flags clogging based from the accumulated pressure; transceiver for remote setting of VUP and VLOW, digital ICP transmission, and clogged-valve notification.

Results: The system was designed using 0.18 μ m CMOS. The front-end is able to interface with piezo-resistive micro-sensors. The IA has wide dynamic range, large gain (70 dB) and low noise efficiency factor (NEF=2.28). The threshold reference has an output non-linearity within half of the pressure resolution limiting quantization error. When the pressure is above VUP, the shunt valve is driven; otherwise, "shuntfail" is flagged. Over-draining occurs when shuntfail and low accumulated pressure persist. If the accumulation rate remains high despite shunting, clogged valve is detected. The system consumes 500uW of dynamic power.

Conclusion: The design of a VP shunt system featuring a novel method for shunt malfunction detection and digital programming of shunting threshold is presented. The circuits have been optimized for implantable applications.

518: A Multicellular Model of Medulloblastoma Suggests a Microenvironment-Driven Phenotype

Nardin Samuel, MD, PhD (Toronto, Canada); Alexander Landry; Julian Spears; Zsolt Zador

Introduction: An emerging strategy in the treatment of various tumors involves targeting the microenvironment. To date, there is limited knowledge of the immune and stromal composition in medulloblastoma microenvironment, and the extent to which these cells contribute to tumor phenotype. To address this gap, the aim of the present study was to investigate multicellular networks of medulloblastoma subgroups to identify distinct features of tumor microenvironment.

Methods: Publicly available gene expression dataset on 763 medulloblastoma samples were used to implement the ESTIMATE algorithm to derive cell fractions from tumor bulk transcriptomics. Weighted gene co-expression network analysis (WGCNA) was used to identify gene clusters (modules) that are likely co-expressed to serve uniform functions. Hierarchical clustering of genes enabled identification of distinct modules that were subsequently mapped to gene ontology (GO) terms to infer the shared biological mechanisms. Multicellular networks within the functional annotation of the mammalian genome (FANTOM) catalogue was utilized to select candidate ligand-receptor pairs for further study.

Results: Molecular subtypes of medulloblastoma showed differences in stromal and immune fractions, consistent with distinct microenvironments. We identify 14 gene clusters with significant meta-gene associations between medulloblastoma subtypes. Of these, 6 demonstrated highest or lowest median meta-gene expression in SHH subtype. Gene expression clusters revealed by WGCNA were most significantly correlated with SHH medulloblastoma subgroup and annotated to immune related processes. These networks were used to identify several receptor- ligand pairs specific to SHH tumours, including COL4A2-CD93 activating pericytes, fibroblasts, neutrophils.

Conclusion: Our findings demonstrate distinct microenvironment and multicellular network configurations in SHH medulloblastoma. The selective activation of immune and stromal cell-population may be linked to this medulloblastoma phenotype, with potential implications on novel therapy. These results highlight the concept of targeting multicellular networks in understanding biology and exploring treatments for SHH medulloblastoma.

519: Gene Therapy for the Treatment of Primary L-Aromatic Amino Acid Decarboxylase Deficiency in Children

Nalin Gupta, MD, PhD, FAANS (San Francisco, CA); Toni Pearson, MBBS; Jill Imamura-Ching; Waldy San Sebastian; Amy Viehovever, MD; Ana Grihalvo-Perez; Neha Seth; YeongHo Seo; Miguel Pampaloni; Paul Larson; Krystof Bankiewicz

Introduction: Aromatic L-amino acid decarboxylase (AADC) deficiency is a rare genetic disorder that causes deficient synthesis of dopamine and serotonin. Infants present with hypokinesia, oculogyric crises (OGC), dystonia, and motor delay. Restoration of AADC activity could correct deficient dopaminergic activity and attenuate the associated motor impairments. We evaluated the safety and tolerability of a viral vector expressing AADC delivered into the substantia nigra (SN) and ventral tegmental area (VTA) of patients with AADC deficiency.

Methods: Six children underwent convection enhanced delivery (CED) with AAV2-hAADC to bilateral SN and VTA locations. There were two dose cohorts (3 subjects in each): 1.3 x 10¹¹ vg, and 4.2 x 10¹¹ vg. The infusate volume was 80 µL/hemisphere (SN 50 µL, VTA 30µL). Safety, AADC activity (FDOPA PET, CSF neurotransmitters), gross motor function, and non-motor disease symptoms were assessed in detail at baseline, 1, 3, 6, 12 and 18 months after treatment.

Results: Infusion of AAV2-hAADC was well-tolerated and achieved a target coverage of 98% and 70% of the SN and VTA. Subjects showed transient involuntary movements (dyskinesia) that peaked 6-8 weeks after gene transfer. Dopamine metabolism (HVA) was increased in all subjects and FDOPA uptake was enhanced within the SN/VTA and the striatum. By Month 2, OGCs had completely resolved in 5 of the subjects. All subjects achieved gains in head control and voluntary movement at 6-18 months. Two subjects attained the ability to sit independently, weight-bear fully while standing, take steps with support, and reach and grasp with both hands.

Conclusion: Midbrain gene delivery in children (4-9 years old) is feasible and safe. There is evidence of enhanced dopamine metabolism, accompanied by resolution of oculogyric crises (OGCs), marked improvement of mood and sleep, and gain of motor function and developmental milestones.

520: Head Growth And Ventricular Size Following Shunting Or Endoscopic Third Ventriculostomy (ETV) In Infants With Aqueductal Stenosis: Further Insights From The International Infant Hydrocephalus Study (IIHS)

Ian Craig Coulter (Toronto, Canada); Abhaya Kulkarni; Spyros Sgouros; Shlomi Constantini

Introduction: Head circumference (HC) and ventricular size measurements are part of the clinical assessment of infants with hydrocephalus and are often utilized in conjunction with other clinical and radiological parameters to determine treatment success. We aimed to assess the effect of ETV and shunting on craniometric measurements during the follow-up of a cohort of infants with aqueductal stenosis.

Methods: We conducted a post hoc analysis of data from the International Infant Hydrocephalus Study (IIHS) - a prospective, multicentre study of infants (<24 months old) with hydrocephalus secondary to aqueductal stenosis treated with either an ETV or shunt. The following craniometrics were measured during a 5-year follow-up period: HC, HC centile, HC z-score and frontal-occipital horn ratio (FOR). Data were compared in an analysis of covariance, adjusting for baseline variables including age at surgery and sex.

Results: Of 158 enrolled patients, 115 underwent an ETV, whilst 43 received a shunt as their primary treatment. Both procedures led to improvements in the mean HC centile position and HC z-score, a trend which continued until the fifth year of assessment. A similar trend was noted for FOR which was measured 12 months and 3 years following surgery. Although the values were consistently higher for ETV compared to shunt, the differences in HC value, HC centile and HC z-score were not significant. ETV was associated with a significantly higher FOR compared to shunting at 12 months (0.52 vs 0.44; p=0.002) and 3 years (0.46 vs 0.38; p=0.03) of follow-up.

Conclusion: Both treatments led to improvements in HC centile, HC z-score and FOR measurements during long-term follow-up of infants with hydrocephalus secondary to aqueductal stenosis. Head size was not significantly different between the treatment modalities during follow-up, however ventricle size was greater in those undergoing ETV when measured at 1 and 3 years following treatment.

521: One-stage High-density Focal Stereo-array SEEG-guided Radiofrequency Thermocoagulation For The Treatment Of Giant Hypothalamic Hamartoma in Children

Min Wang (Shanghai, China); Rui Zhao; Yuanfeng Zhou; Hao Li

Introduction: The size of giant hypothalamic hamartomas is beyond the scope of thermal coagulation or laser damage, and the treatment effect is not good, multiple operations are often required. To investigate the value of one-stage stereo-array radiofrequency thermocoagulation based on stereotactic electroencephalography (SEEG) in giant hypothalamic hamartoma in children.

Methods: We analyze the clinical data of 6 patients with giant hypothalamic hamartoma (Delalande type 4 or the mass is attached to the hypothalamus or floor of the third ventricle with a wide interface) who underwent stereotactic electrode implantation from November 2017 to July 2019. After multidisciplinary discussion, we design high-density focal stereo-array electrodes implantation. SEEG-guided bipolar coagulations were performed between two contiguous contacts of the same electrode, or between two adjacent contacts of different electrodes.

Results: Among the 6 patients, 3 were male and 3 were female, with an average age of 5.08 ± 4.73 years (range, 1.4-12 years); the average duration of follow-up was 15.63 ± 3.16 months. One patient had previously undergone open surgery. Five patients (5/6) had gelastic seizure and generalized tonic clonic seizure. The number of implanted electrodes range from 3 to 7, with an average 5.33. One patient had diabetes insipidus after the operation, and all children had neither fever nor new hormone metabolisms disorder after the operation. 4 patients had Engel I classification outcomes (free from disabling seizures), 2 patients had Engel classification outcomes.

Conclusion: It is safe and effective to treat the giant hypothalamic hamartoma in children by one-stage high-density focal stereo-array SEEG-guided radiofrequency.

522: Evaluation and Treatment of Children with Radiation-Induced Cerebral Vasculopathy

David S. Hersh, MD (West Hartford, CT); Kenneth Moore; Vincent Nguyen; Lucas Eljovich; Asim Choudhri; Jorge Lee-Diaz; Raja Khan; Brandy Vaughn; Paul Klimo Jr.

Introduction: Steno-occlusive cerebral vasculopathy is an infrequent delayed complication of ionizing radiation. It has been well-described with photon-based radiation therapy, but less so following proton beam radiotherapy. Here, we report our recent institutional experience in evaluating and treating children with radiation-induced cerebral vasculopathy.

Methods: Eligible patients were age 21 or younger with a history of cranial radiation who also subsequently developed vascular narrowing by magnetic resonance arteriography significant enough to warrant a cerebral angiogram, with or without ischemic symptoms. The study period was January 2011–March 2019.

Results: Thirty-one patients met study inclusion criteria. Eighteen (58%) were male with a median age of 12 years. Proton-based radiation was used in 20 patients (64.5%) and photon-based radiation in 11 patients (35.5%). Patients were most commonly referred for workup as a result of incidental findings found on surveillance cancer imaging ($n=23$; 74.2%). Proton-beam patients had a shorter median time interval from radiation-to-catheter angiogram (24.1 months; IQR, 16.8–35.4 months) than photon radiation patients (48.2 months; IQR, 26.6–61.1 months; $p = 0.04$). Eighteen total revascularization procedures were performed in 15 patients. One surgical patient suffered a contralateral hemispheric infarct 2 weeks after revascularization; no child treated medically (aspirin) has had a stroke to date. Median follow-up was 29.2 months (IQR, 21.8–54.0 months) from the date of the first catheter angiogram to last clinic visit.

Conclusion: All children who receive cranial radiation from any source, particularly if the parasellar region was involved and the child was young at the time of treatment, require close surveillance for the development of vasculopathy. A structured and detailed evaluation is necessary to determine optimal treatment.

523: Disulfiram and Copper Combination Therapy Targets NPL4, Cancer Stem Cells and Extends Survival in a Medulloblastoma Model

Riccardo Serra (Baltimore, MD); Tianna Zhao, MD, PhD; Noah Gorelick, MD, PhD; Joshua Casaos, MD; Sakibul Huq, BS; Arba Cecilia, BS; Antonella Mangraviti, MD; Renyuan Bai, PhD; Alessandro Olivi, MD; Henry Brem, MD; Eric Jackson, MD; Betty Tyler, BA

Introduction: Medulloblastoma (MB) is the second most common brain malignancy among children and has recently been classified into four molecular subtypes, WNT-driven, Shh-driven, Group 3 and 4. The aim of this study was to assess the effects of the combination of Disulfiram (DSF), an FDA-approved inhibitor of Aldehyde Dehydrogenase (ALDH), and Copper (Cu++) on two animal models of Group 3 MB.

Methods: The cytotoxic and anti-cancer stem cell (CSC) effects of DSF and the combination of DSF/Cu++ were evaluated with clonogenic assays, flow cytometry with AnnV/PI, PI/Ki67, Aldefluor®, anti-CD133 antibody, immunofluorescence, and western blotting using established cell lines - ONS76, UW228, D425med and D341 - representing MB's main molecular subtypes. In vivo survival, tumor volume, and nuclear protein localization protein-4 (NPL4) expression were assessed in different models of Group 3 MB.

Results: Significant in vitro cytotoxicity was demonstrated at nanomolar concentrations of DSF. DSF/Cu++ induced cell death (increased AnnV/PI, cleaved-Poly(ADP-ribose)polymerase fraction, and Apoptosis Inducing Factor) through NPL4 accumulation in cell nucleus and intracellular buildup of poly-ubiquitylated proteins. DNA damage was also detected with western blotting and H2AX foci on immunofluorescence. Flow cytometry analysis demonstrated a significant reduction in ALDH and CD133-positive cells following DSF/Cu++ treatment. DSF/Cu++ prolonged survival, reduced tumor volume, and increased nuclear NPL4 expression in D425 and D341 tumors in vivo.

Conclusion: DSF/Cu++ demonstrated a potent therapeutic effect on Shh-driven and Group 3 MB cell lines by inducing apoptosis and targeting cancer stem cells, and prolonged survival in different models of Group 3 MB. Our data suggest that this combination may serve as a novel treatment, alone or with existing therapies, for pediatric MB.

524: Impact of timing of ventriculoperitoneal shunt and intra-abdominal surgery on shunt infection rates during the first year of life

Stephen Cannada Harward II, MD (Durham, NC); Jordan Komisarow; Sarah Hodges; Jess Rames; Henry Rice; Carrie Muh; Herbert Fuchs; Timothy George; Gerald Grant

Introduction: Patients requiring placement of a ventriculoperitoneal shunt (VPS) during the first year of life often have other comorbidities necessitating additional intra-abdominal surgeries during this first year. Some have suggested that the temporal proximity and sequence of these procedures may increase risk of subsequent VPS infection; however, data supporting such suggestions have proven limited and inconsistent. Our group investigated the effect of surgery timing on VPS infection rates with the hypothesis that having an intra-abdominal procedure prior to VPS insertion would increase risk of subsequent VPS infection.

Methods: We performed a retrospective review of all children during the first year of life who underwent both a VPS and an intra-abdominal procedure at a single institution between January 1, 2000 and January 1, 2018. We examined the impact of timing as well as sequence of surgeries (VPS first versus intra-abdominal procedure first) on VPS infection rates within 1 year of the last procedure. We additionally examined the effect of gestational age, birth weight, and placement of a prior ventricular reservoir on VPS infection.

Results: We identified 86 total patients undergoing both procedures with 37 having the intra-abdominal procedure first versus 49 having the VPS first. Patients who had the intra-abdominal procedure first had a significantly higher rate of infection — 30% (11 of 37 patients) — compared to those who had the VPS first — 6% (3 of 49 patients). Further analysis failed to attribute this difference in VPS infection rate to differences in gestational age, birth weight, or time between the procedures.

Conclusion: In our study, for patients needing both a VPS and an intra-abdominal surgery, procedure sequence greatly impacted one's subsequent risk of shunt infection. These data suggest that if possible, the VPS should be performed prior to any intraabdominal procedure.

525: Injury Mechanisms and Severity in Pediatric Traumatic Brain Injury Patients Admitted To the Ward or Intensive Care Unit – The European Perspective

Alexander Younsi, MD (Heidelberg, Germany); Lennart Riemann; Ahmed El Damaty; Klaus Zweckberger; Andreas Unterberg

Introduction: Traumatic brain injury (TBI) used to be leading cause of death and disability in children. It includes a range of different pathologies and differs considerably from adult TBI. Analyzing and understanding injury patterns of pediatric TBI is essential to establishing preventive efforts as well as to improving clinical management.

Methods: The multi-center, prospectively collected core and registry databases of the Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI) study were screened and TBI patients were included when younger than 18 years and admitted to the regular ward (admission stratum) or intensive care unit (ICU stratum). Patient demographics, injury mechanisms, clinical findings, brain CT imaging details, and outcome (GOSE at 6-months follow-up) were analyzed. Results from the core study were compared to the registry dataset which includes larger patient numbers but no follow-up data.

Results: 227 patients in the core dataset and 687 patients in the registry dataset were included in this study. In the core dataset, road-traffic incidents were the most common cause of injury overall and in the ICU stratum, while incidental falls were most common in the admission stratum. Brain injury was considered serious to severe in the majority of patients and concurrent injuries in other body parts were very common. Intracranial pathologies were detected in 60% of initial brain CTs. Intra- and extracranial surgical interventions were performed in one-fifth of patients. The overall mortality rate was 3% and the rate of unfavorable outcomes 10%, with those numbers being considerably higher in the subgroup of ICU patients. Injury characteristics from the core study could be confirmed in the registry dataset.

Conclusion: Road-traffic incidents and incidental falls are the most common injury mechanisms of pediatric TBI in Europe. Preventive efforts are still needed to decrease the incidence of this serious condition in children.

526: The Incidence of Post Traumatic Epilepsy after TBI: A TRACK-TBI Study

John Fredrick Burke, MD (San Francisco, CA); Ramon Diaz-Arrastia, MD, PhD; Geoffrey Manley, MD, PhD; Nancy Temkin

Introduction: Post traumatic epilepsy (PTE) is a sequela of traumatic brain injury (TBI) and is an independent risk factor for poor functional outcome. Moreover, trauma has been estimated as the etiology of up to 5% of symptomatic epilepsy in the United States. These estimates are based on studies done decades ago, prior to the widespread use of modern neuroimaging. Further, there are no large prospective studies documenting the incidence of PTE after the full spectrum of head injury.

Methods: TRACK-TBI represents a multi-center prospective database with over 2700 head injured patients. All patients undergo follow up at 6- and 12-months; during this time, we administered an NINDS epilepsy screening questionnaire, designed to identify patients with potential PTE symptoms. Of those patients who screened positive, we further queried about the frequency and last occurrence of seizures. Patients with a new diagnosis of a seizure disorder, and who had a seizure more than seven days after their original injury, were grouped into the PTE+ cohort.

Results: 2,698 patients with both 6- and 12-month follow up after TBI were included in the study. Of these, 11.51% screened positive using the NINDS questionnaire. The risk of PTE varied as a function of the Glasgow Coma Scale (GCS), with patients presenting with GCS scores less than 8 having over a 6% rate of PTE at 6 months and over a 12.5% rate at 12 months. For patients presenting with GCS scores between 13-15, the rate of PTE was 0.9% at 6 months, and 1.4% at 12 months.

Conclusion: The incidence of PTE in the TRACK-TBI cohort is consistent with prior studies. Although the current study is currently limited by the length of follow up, it is the largest source of prospective data on PTE. The availability of MR imaging and blood biomarkers during the acute, post-acute, and chronic stage from TRACK-TBI participants make this cohort useful for studies of novel mechanisms of epileptogenesis.

527: Intrathecal Opioid Pump for Treatment of Abdominal Pain in Chronic Pancreatitis: Retrospective Case Control**William H. Sweet Young Investigators Award**

Andrew S. Koivuniemi, MD (Indianapolis, IN); Andrew Koivuniemi, MD, PhD; Kelly Grott, MD; Raheleh Rahimi Darabad, MD

Introduction: Chronic pancreatitis (CP) is an inflammatory condition characterized by severe abdominal pain and both exocrine and endocrine pancreatic insufficiency. In the United States pancreatitis was estimated to be responsible for a significant cost burden estimated at 3.7 billion dollars per year and the incidence is rising. Total pancreatectomy with islet cell transplantation offers a definitive treatment of abdominal pain, but carries with it an increased risk of mortality and increased risk of insulin dependence. Intrathecal opioid pumps are a relatively new alternative therapy in chronic pancreatitis patients.

Methods: We performed an institutional retrospective review of chronic pancreatitis patients treated with intrathecal opioids to evaluate long-term pain control. Inclusion criteria: diagnosis of chronic pancreatitis and age > 18. Primary outcomes were oral morphine equivalent (OME) doses required for pain control after intrathecal pain pump placement. Secondary outcome was pain score (scale 1-10). The follow up times were at 2 weeks, 1 month, 3 months, and 1 year after intrathecal pump placement. Statistical analysis was with an ANOVA mixed model.

Results: At baseline, 77/80 study participants were taking oral opioids daily, compared to only 5/74 at one year. Median (IQR) OME at baseline were 120 (45, 240) mg/day while at all other time points (2 weeks, 1 month, 3 months, and 1 year) oral morphine equivalents were 0 (0,0) mg/day (p-value= 0.0001). Median (IQR) pain scores were 8 (6, 9) at baseline and 4 (2, 7), 4 (2, 7), 4 (3, 6), 4 (2, 6) at 2 weeks, 1 month, 3 months, and 1 year respectively (p-value = 0.0001).

Conclusion: Intrathecal pain pumps successfully decrease pain scores (on VAS 0-10) and virtually eliminated the use of oral opioids.

528: The Crippled Brain That Prolonged The Civil War: General Joseph Hooker's Traumatic Brain Injury At Chancellorsville

Matthew Thomas Helton, MD (Little Rock, AR); T. Pait, MD

Introduction: Lincoln appointed General Joseph Hooker to command the Army of the Potomac in January, 1863. Fighting Joe instituted needed reforms. April, 1863, Hooker possessed 130,000 men compared to Lee's 60,000. The Union had more food, clothing, and ammunition. On a decisive day of the Chancellorsville Campaign, as Hooker stood on his headquarters porch, a cannonball struck the pillar against which he was leaning. He was hurled to the floor, stunned, and senseless. Unconsciousness followed a lucid interval requiring rest. Half of the Army was not thrust into battle, resulting in retreat, as Hooker was not capable of commanding. The Potomac Army was unable to capture Richmond.

Methods: First-person accounts and documents were used to recount the Battle of Chancellorsville. Presented is the detriment Hooker's concussion had on leadership by using current military guidelines for traumatic brain injury diagnosis and return to duty requirements.

Results: Hooker's Army missed the opportune time to attack. The order was never received as Hooker suffered a traumatic brain injury; he regained consciousness followed by nausea and vomiting, consistent with signs of concussion. Under current military protocol, Hooker would not be allowed to return to participation. During this crucial period, a reporter stated, the precious hour passed, while our army was without a head. The Chancellorsville Campaign resulted in Union retreat.

Conclusion: Hooker suffered a disabling traumatic brain injury, preventing him from giving orders and changing the battle's outcome. Had the General not sustained a concussion, perhaps the Civil War would have ended earlier.

529: Different Principles Govern Multiple Scales of Brain Folding

Arka N. Mallela, MD, MS (Pittsburgh, PA); Hansen Deng, MD; Alan Bush, PhD; Ezequiel Goldschmidt, MD, PhD

Introduction: Brain folding is the centerpiece of human brain development. Understanding this process is key to furthering our knowledge of cortical and vascular development and the functional parcellation of the cortex. While multiple hypotheses seek to explain brain folding — including differential cellular growth, volume constraints, and mechanical instability — these heuristic models do not explain the global geometry of the brain or the consistent pattern of sulci and gyri characteristic of the adult human brain. Here, we utilize a large cohort of in utero fetal MRIs to study changes in the cortical topography. The result is an accurate timetable that accounts for large - and small-scale brain folding.

Methods: Using a digital fetal brain atlas constructed from in utero brain MRI of 81 healthy fetuses, we performed week-to-week nonlinear registration utilizing Advanced Normalization Tools. We additionally algorithmically segmented key sulci and components of the subarachnoid space and analyzed global volumetric growth, growth of sulci and neighboring gyri, and modeled restricted brain growth. Finally, using Jacobian determinant analysis we identified spatiotemporal patterns of brain folding.

Results: Brain volume growth follows a logistic growth curve that corresponds to different phases of gyrification; volume constraints are not a plausible mechanism for brain folding. Folding of the Sylvian fissure involves closure, where separate lobes overgrow an existing subarachnoid space. In contrast, every other sulcus folds by deepening, creating a new subarachnoid space. These are fundamentally different processes. Finally, our Jacobian analyses identify three different phases of folding corresponding to interlobar folding, large sulci folding, and secondary sulci folding.

Conclusion: Our analysis demonstrates that multiple spatially and temporally distinct processes fold the brain. These findings have direct implications for understanding vascular anatomy and modeling and genetics of cortical development. This demonstration that not all sulci are formed equally challenges our current perception of this process.

530: Large-Scale, Projection-Specific Functional Representations of Cognitive Decisions

Philip L. Gildenberg Resident Award

Xiaonan (Richard) Sun, MD, PhD (Manhasset, NY); Simon Musall, PhD; Steven Gluf, MS; Anup Khanal, MS; Anne Churchland, PhD

Introduction: Cognition and emotion are constructed from multitudes of quantifiable psychological processes, which can aid in the diagnosis and classification of neuropsychiatric disorders. Understanding the pathways supporting these processes will be critical in the development of targeted neuromodulation. To resolve the complexities of cognition, psychophysics enable reproducible measures of a subject's response to sensory stimuli. In this study, we investigate the mechanisms of decision-making, implicated in various movement and psychiatric disorders. We approached this by developing a mouse decision behavior model and recorded large-scale neural activity from projection-specific subpopulations.

Methods: We first developed a viral intersectional strategy combining a retrograde virus (CAV2) and a blood-brain-barrier-permeable AAV9 variant (AAV-PHP.eB) to express genetically-encodable calcium indicators (GECIs) in widespread, cortico-striatal or cortico-thalamic projections. Neural activity imaging during behavior was performed using widefield fluorescence or two-photon microscopy. Mesoscale activity was characterized using visual retinotopic mapping. We trained mice on a two-alternative forced choice (2AFC) task by presenting a stochastic, lateralized auditory stimulus. We fitted tracked behavior and task parameters against high-dimensional neural data using a generalized linear model.

Results: Mouse decision behavior reached near-perfect performance after 7 days whereas a sigmoid psychometric function correlates the proportion of correct choices with stimulus intensity. Mesoscale retinotopy confirmed high levels of GECI expression by mapping visual stimulus-specific responses to discrete primary and multiple secondary visual areas. Cortex-wide as well as cellular-resolution imaging during decision-making demonstrated projection-specific spatial and temporal patterns of neural activity.

Conclusion: We reveal diverse cognitive and behavioral representations within a given cortical region: neuronal subpopulations independently encode unique elements of behavior. We currently aim to determine circuit-specific causality using optogenetic inactivation and to model additional cognitive variables through behavioral manipulations (e.g. contingency reversal). By assigning pathways (i.e. prefrontal-thalamus projection) to behavioral metrics, we hope to define the neural substrates of decomposed neurological functions, which will complement the evolution of targeted neurotherapies.

531: Predicting Determinants of Variation in Episode-of-care Bundled Payments for Adult Spinal Deformity Surgery

Robert Florin, MD Resident Award

Zachary Adam Medress, MD (Stanford, CA); Kunal Varshneya; Adrian Rodrigues; Parastou Fatemi, MD; Martin Stienen; Corinna Zygourakis, MD; Atman Desai; Jon Park, MD; Stephen Skirboll, MD; John Ratliff, MD; Anand Veeravagu, MD

Introduction: Episode-of-care bundled payments (EBP) amalgamate reimbursements for preoperative, inpatient, and postoperative care into a single bundled payment in order to promote care coordination and reduce costs. EBP has been introduced in simple spinal fusion and decompression operations but has not been expanded to adult spinal deformity (ASD) surgery. Given the substantial resource utilization associated with ASD surgery, ASD may become a target for

expansion in future iterations of the bundled care improvement initiative (BPCI).

Methods: We performed a large retrospective observational study using the MarketScan database in order to generate 30, 60, and 90-day bundled payment projections for episodes of care centered around ASD surgery. Multivariable analysis was performed to identify the impact of pre-operative, operative, and post-operative characteristics on bundled payment values for ASD surgery.

Results: We identified 10,862 operations that met our inclusion criteria. The average index hospitalization payment was \$99,976, and mean total projected bundled payments were \$163,752, \$167,108, and \$169,520 for 30-, 60-, and 90-day bundles, respectively. On multivariable regression analysis, pre-operative characteristics including advanced age, osteoporosis, and baseline paraparesis significantly increased projected bundle payments. Technical aspects of ASD surgery including utilization of a combined anterior and posterior approach increased projected bundle payments, whereas use of recombinant bone morphogenetic protein did not affect projected bundled payments. Discharge to an inpatient rehabilitation facility was associated with a 15.8% (95% C.I. 10.2-21.8, $p < 0.005$) increase in 90-day bundle value. Postoperative complications including hematoma, venous thrombo-embolism, infection, and neurologic injury significantly increased projected bundled payments.

Conclusion: Baseline preoperative characteristics, surgical approach, discharge destination, and post-operative complications significantly impacted bundle values for 30-, 60-, and 90-day episodes of care centered around ASD surgery. Based on these data, we predict that expansion of the BPCI to include ASD surgery would have important ramifications for patient selection, approach type, and practice patterns.

532: Basal Ganglia Cavernous Malformations: Surgical Approaches and Long Term Outcomes

Yiping Li, MD (Stanford, CA); Jason Kim; Gary Steinberg, MD, PhD

Introduction: We report our experience in resecting basal ganglia cavernomas (BGCM) to gain insight into this infrequent disease subtype.

Methods: We retrospectively reviewed a prospective database of all deep-seated cerebral cavernomas treated between 1987-2019 and included those with radiographic diagnosis of BGCM.

Results: Our search yielded 44 patients with BGCM. Headache was the most common presenting sign (53.4%). Lesion location involved the caudate in 21.4% compared to 78.6% of cases within the lentiform. Caudate BGCMs were larger upon presentation, more likely to present to the ependymal surface with intraventricular hemorrhage and hydrocephalus ($p < 0.05$). Dizziness and diplopia were also more common when involving the caudate. Due to anatomic location, caudate BGCMs were preferentially treated via interhemispheric approach and less likely to suffer worsening perioperative deficits compared to lentiform cohort ($p < 0.05$). Ten patients (25.6%) were clinically worse after surgery postoperatively, four (10.2%) of whom continued to suffer permanent morbidity at last follow-up. Long-term good outcome (mRS 0-1) was achieved in 74.4% of cases compared to 69.2% upon presentation. Relative to baseline mRS, 89.8% of patients were improved or unchanged at last follow-up. The mean length of postop follow-up is 11 months (range 0.1-252 mos). Outcomes after surgery did not differ between surgical approaches; however, hemiparesis presentation and lesions involving the globus pallidus or posterior limb were more likely to suffer from neurological deficits during the immediate perioperative period. Patients whose surgeries were performed awake were more likely to suffer from neurological decline at early as well as late follow-up. When adjusting for awake craniotomy as a potential confounder of lesion location, BGCM involving the posterior limb was predictive for developing early postop deficits, but this finding did not persist at long term follow-up.

Conclusion: Surgery is a safe and effective in managing BGCMs, with an estimated long-term permanent morbidity rate of 10%.

533: Natural History of a Mouse Model of Intracranial Aneurysm Formation and Rupture Highlights Sex and Strain Differences in Outcome

Takeshi Yanagisawa, MD (Boston, MA); Yuichi Murayama, MD; Aman Patel, MD; Cenk Ayata, MD

Introduction: Intracranial aneurysm formation and rupture risk are in part genetically determined. To examine the role of genetic background and sex, we compared three wild-type mouse strains commonly used in cerebrovascular studies in a model of intracranial aneurysm formation and spontaneous rupture.

Methods: Intracranial aneurysms were induced in four different groups of mice (CD-1 male, C57BL/6 male, C57BL/6 female and 129/Sv male) by a single stereotaxic injection of elastase into the cerebrospinal fluid at the skull base, combined with systemic deoxycorticosterone acetate-salt hypertension. Neurological deficits and mortality were recorded. Aneurysms and subarachnoid hemorrhage grades were quantified post-mortem, either after spontaneous mortality or at 21

days if the animals survived. In a separate cohort, proinflammatory mediator expression was measured by quantitative RT-PCR and arterial blood pressures were measured via the femoral artery.

Results: We found striking differences in aneurysm formation, rupture and post-rupture survival rates among the groups. 129/Sv mice showed the highest rates of aneurysm rupture (80%), followed by C57BL/6 female (36%), C57BL/6 male (27%), and CD-1 (21%). The contingency of aneurysm rupture and the presence of unruptured aneurysms significantly differed among all three strains, as well as between male and female C57BL/6 (c2). The same hierarchy was observed upon Kaplan — Meier analysis of both overall survival and deficit-free survival among the three mouse strains ($P < 0.001$). Subarachnoid hemorrhage grades were also more severe in 129/Sv than all other groups. For all endpoints, CD-1 male mice showed the highest resistance to aneurysm rupture and the mildest outcomes. Higher mean blood pressures in the 129/Sv strain provided an explanation for the higher incidence of and more severe aneurysm ruptures, but TNF α , IL-1b and CCL2 expressions did not differ among the groups.

Conclusion: The outcome of elastase-induced intracranial aneurysm formation and rupture in mice depends on genetic background and shows sexual dimorphism. Our results highlight the congruence between the outcomes in this experimental model and the clinical aneurysmal subarachnoid hemorrhage.

534: Neutrophils Contribute to Intracranial Aneurysm Pathogenesis in an Estrogen-dependent Manner

Devan Patel (Gainesville, FL); William Dodd, BS; Koji Hosaka, PhD; Brian Hoh, MD, MBA

Introduction: Although epidemiological studies of intracranial aneurysms (IA) suggest sex differences with women having a higher prevalence and postmenopausal women having the highest risk of aneurysm rupture, the precise underlying mechanisms are not fully understood. Estrogen has been shown to attenuate neutrophil migration after vascular injury but this phenomenon has not been investigated in IA despite growing evidence that inflammation is critical to IA pathogenesis. Here, we investigated the role of neutrophils in murine aneurysm formation and rupture in the context of estrogen deficiency.

Methods: Using C57BL/6 mice, IA were created in estrogen-deficient females (bilateral ovariectomy), normal estrogen-producing females, and normal males. Briefly, aneurysms were induced through a combination of hypertension, hemodynamic alterations, and intracranial elastase injection as previously described. Animals were randomized to receive injections of either rabbit anti-polymorphonuclear antibody to induce neutrophil depletion or rabbit serum control. Three weeks after the elastase injection, or earlier if neurological symptoms were present, mice were euthanized and assessed for aneurysm formation and rupture by blinded investigators.

Results: In normal females, neutrophil depletion did not affect aneurysm formation or rupture compared to control (formation: 66.7% vs. 83.3%, $p=1.00$; rupture: 75.0% vs. 80.0%, $p=1.00$). In estrogen-deficient females, neutrophil depletion did not affect aneurysm formation but did decrease aneurysm rupture compared to control (formation: 75.0% vs. 86.6%, $p=0.65$; rupture: 50.0% vs. 92.3%, $p=0.03$). In males, neutrophil depletion decreased aneurysm formation but did not affect aneurysm rupture compared to control (formation: 33.3% vs. 83.3%, $p=0.03$; rupture: 33.3% vs. 70.0%, $p=0.51$).

Conclusion: Neutrophils contribute to aneurysm rupture in estrogen-deficient females and to aneurysm formation in males, but do not affect aneurysm formation or rupture in normal females. These results are novel in implicating neutrophils in estrogen deficiency-associated aneurysm pathophysiology. Further studies are necessary to elucidate the mechanism by which estrogen modulates neutrophil recruitment and activity in IA formation and rupture.

535: Bradycardia and Asystole in Patients Undergoing Symptomatic Chronically Occluded Internal Carotid Artery Recanalization

Joseph Scott Hudson, MD (Pittsburgh, PA); Mario Zanaty, MD; Victoria Wadman; Daichi Nakagawa; Daizo Ishii; Jorge Roa, MD; Sami Al Kasab, MD; Kaustubh Limaye, MD; Pascal Jabbour, MD; Harold Adams; Edgar Samaneigo, MD, MS; David Hasan, MD

Introduction: Reports have emerged describing the successful endovascular recanalization of the chronically occluded internal carotid artery (COICA). The impact this restoration of flow has on the sensitive carotid sinus baroreceptors has not been previously described. In this manuscript, we present the largest COICA surgical series to date, with a specific focus on perioperative heart rate abnormalities.

Methods: Patient demographics were obtained, and the COICAs were radiographically classified based on the anatomic distribution of the stenosis and collateral flow. Thirty-six patients had a total of 37 COICA revascularization procedures.

Results: A total of 23 patients had intraprocedural bradycardia during balloon angioplasty. Three patients went into transient asystole during the procedure, and 2 of these patients had symptomatic bradycardia with ischemic cerebral changes, 1 of which required permanent pacemaking. All other patients had immediate resolution of their bradycardia,

asystole, and neurologic symptoms immediately following balloon deflation and pharmaceutical management. There was a statistically significant difference in the observed proportion of bradycardic patients among COICA classifications ($P = 0.014$). There was no statistically significant difference in mean age between patients with bradycardia and those without (aged 63.36 vs. 67.71 years, $P = 0.2265$).

Conclusion: Bradycardia associated with angioplasty of the carotid bulb was observed in the majority of patients receiving COICA revascularization. A small percentage of these patients were symptomatic. Our results suggest that carotid sinus baroreceptors remain active while residing in a complete arterial occlusion, and close monitoring is necessary during balloon angioplasty of the proximal COICA.

536: A Retrospective Analysis of EVD Infection Rates Following Stroke and Other Related Brain Injuries: Comparison of Emergency Room and ICU/OR Setting

Harshit Terala (Monroe, NY); David Altschul; Mousa Hamad; Andre Boyke; Christopher Lin; Jinyuan Liu; Rony Thomas; Rose Fluss; Santiago Unda

Introduction: The setting where an External Ventricular Drain (EVD) can be placed has been proposed as a potential predictor for EVD related infections (ERIs). We hypothesize ER setting is an iatrogenic factor that contributes to EVD infections due to its environmental contamination. Thus, the purpose of this study was to analyze the incidence of infections in patients following placement of EVD in either the Emergency Room (ER) or the Intensive Care Unit (ICU)/Operating Room (OR) at a single Comprehensive Stroke Center.

Methods: Retrospective analysis of post-procedure infection rates in 710 patients with EVDs placed on site between 2010 and 2018 was performed. We analyzed cases between sex, age, stroke and non-stroke related and further requirement of conversion EVD to ventriculoperitoneal (VP) shunt.

Results: Significant decrease in EVD related infection (ERIs) rates following the shift in EVD placement from ER to ICU/OR (from 13% to 7.7%, $p=.03$) among all ages, sex and type of brain injury. Furthermore, our data displays the rate of conversion of EVDs to VP shunts is independent of the setting where EVD was placed, but increases in patients who develop ERIs. 23.1% of stroke patients that developed an ERI required a conversion to VP shunt while 67.3% of non-stroke patients that developed an ERI required further VP shunt ($p<.001$). Non-stroke EVD patients with infections are more likely to require VP shunt.

Conclusion: This is one of the larger retrospective studies conducted on EVD related infections. ERIs were significantly higher when EVDs were placed in the ER. Moreover, our results highlight the relation between ERIs and further requirement of conversion EVD to VP shunt. These figures highlight the importance of focusing on infection rates, and the implications CSF infection has on the long-term care of patients.

537: Multicenter Prospective Assessment of Outcomes and Complications Associated with Severe Adult Scoliosis Surgery in 146 Patients with Minimum 2-Year Follow-up

Thomas Buell, MD (Charlottesville, VA); Thomas Buell; Justin Smith; Christopher Shaffrey; Virginie Lafage; Renaud Lafage; Han Jo Kim; Eric Klineberg; Frank Schwab; Shay Bess; Christopher Ames; ISSG

Introduction: Few reports focus on surgery for severe adult scoliosis.

Methods: A prospective multicenter database of adult spinal deformity (ASD) patients was reviewed. Enrollment required: scoliosis $\geq 20^\circ$, sagittal vertical axis (SVA) ≥ 5 cm, pelvic tilt $\geq 25^\circ$, and/or thoracic kyphosis $\geq 60^\circ$. Patients with severe scoliosis (thoracic Cobb $\geq 75^\circ$ or thoracolumbar/lumbar Cobb $\geq 50^\circ$) and minimum 2-year follow-up were assessed.

Results: Of 178 patients, 146 (82%, mean age=54 years, 92% women, 88 thoracolumbar, 50 lumbar, 8 thoracic) had minimum 2-year follow-up (mean=3.1 years). Almost 30% had prior fusion, 6% were active/past smokers, 16% had osteoporosis, and 77% had at least one comorbidity. Surgical details included: posterior-only (58%) or anterior-posterior approach (42%), SPO (65%), 3CO (14%), TLIF (23%), ALIF (37%), sacropelvic fixation (76%), upper thoracic UIV (64%), and mean posterior fusion of 13.2 levels. Coronal plane parameters improved significantly, including global alignment (3.8 to 2.8 cm, $p<0.001$), thoracic Cobb (83° to 55° , $p=0.013$), thoracolumbar Cobb (67° to 33° , $p<0.001$), and lumbar Cobb (61° to 27° , $p<0.001$). Overall sagittal alignment also improved significantly, most notably for severe lumbar curves (SVA: 6.7 to 2.5 cm, $p<0.001$; PI-LL 18° to 3° , $p<0.001$). Outcomes improved significantly, including ODI (39 to 26, $p<0.001$), SF-36 PCS (35 to 41, $p<0.001$) and SRS-22r (2.9 to 3.8, $p<0.001$). 191 complications were reported (92 minor/99 major), and 94 (64%) patients had at least one complication. The most common complications included dural tear (12%), pleural effusion (12%), rod fracture (11%), radiculopathy (8%) and proximal junctional kyphosis (7%). 34 reoperations were performed in 27 (18%) patients, with most common indications of rod fracture/pseudarthrosis ($n=8$), deep wound infection ($n=6$) and neurological deficit ($n=5$).

Conclusion: Surgery for severe adult scoliosis is associated with significant improvement in radiographic alignment and outcomes measures. Although associated complication rates are high, these appear to be comparable to reports of less severe scoliosis.

538: Impact of Nsaid Use after Lumbar Fusion Surgery on Fusion Rate and Complications

Sheeraz Qureshi (New York, NY); Yahya Othman; Abduljabar Alhammoud, MD; Avani Vaishnav, MBBS; Steven McAnany, MD; Sravisht Iyer, MD; Todd Albert, MD; Catherine Himo Gang, MPH

Introduction: The purpose of this study is to compile data presented in literature regarding the efficacy of incorporating NSAIDs in the postoperative course for patients undergoing spine surgery, in particular its impact on pain levels, opioid use, complications and hospital length of stay.

Methods: This is a meta-analysis and systematic review. A literature search was conducted using the backbone search [spinal surgery] [Nsaid] [complications]. Criteria for inclusion were: use of NSAIDs for postoperative pain management of spinal surgery, comparison between NSAID and NSAID-free cohort, and reporting on any of pain scores, hospital opioid use, hospital length of stay, complications rate, and operative outcomes.

Results: Out of 799 studies, 19 studies met the inclusion criteria. A total of 1522 patient were included in this analysis. The studies included randomized controlled trials, Prospective and retrospective cohorts. Operations included discectomies, laminectomies and fusions. Most commonly regimens included the NSAID Ketorelac, as in injection given immediately post operatively. Patients that received NSAID analgesia postoperatively had significantly lower VAS pain scores at 1h and 12h post operatively. This group also had a significantly lower opioid consumption and shorter hospital length of stay. 7 Fusion studies reported on arthrodesis, showing a significantly lower odds of fusion after NSAIDs use, however after subgrouping according to smoking, this difference proves to be no longer significant.

Conclusion: Incorporation of NSAIDs into the postoperative regimen for analgesia in patients undergoing spine surgery is an effective approach in reducing hospital length of stay, patient reported pain scores, hospital opioid use, and has no increased risk of complications. Furthermore, use of NSAIDs in the non-smoking population does not seem to affect arthrodesis rates in patients undergoing spine surgery.

539: Cost-Effectiveness of Balloon Kyphoplasty and Vertebroplasty, Compared with Conventional Medical Management, among Patients with Osteoporotic Vertebral Compression Fracture from a US Medicare Perspective

Thomas J Hopkins (Durham, NC); Simon Eggington; Michelle Quinn; Christine Nichols-Ricker

Introduction: To date, no published study has evaluated the cost-effectiveness (C/E) of balloon kyphoplasty (BKP) or vertebroplasty (VP) in patients with osteoporotic vertebral compression fracture (VCF) from a US Medicare perspective. This study evaluates the C/E of surgical treatment vs. CMM using a Markov modelling approach.

Methods: We developed a model to compare C/E of BKP versus CMM, and VP versus CMM, over a patient's lifetime. Cost (Medicare payment) data were based on an analysis of Medicare claims data, with propensity-score matching performed for BKP & VP vs. controls (CMM). Mortality inputs were based on US life tables, modified to account for age at initial fracture, presence of subsequent fracture(s), and relative risk of mortality by treatment. Separate ICERs were calculated for inpatient vs. outpatient surgical treatment location to account for individual clinical profiles presenting to each. Probabilistic sensitivity analysis was performed to explore the impact of uncertainty in all inputs on results.

Results: The ICERs for surgical treatment relative to CMM in an inpatient setting were \$43,455 (BKP versus CMM) and \$39,774 (VP versus CMM). For surgical treatment in an outpatient setting, the corresponding ICERs were \$10,992 (BKP versus CMM) and \$12,293 (VP versus CMM). Probabilistic sensitivity analysis suggested that model results were robust and that both BKP and VP would be considered C/E vs. CMM at a US willingness-to-pay threshold of \$50,000 per QALY in 80% and 100% of 500 model simulations, respectively. The most sensitive parameters in the model included the quality of life estimates and the hazard ratios for the treatment effect on mortality.

Conclusion: These results suggest that both BKP and VP are C/E interventions from a US Medicare perspective, compared with CMM, in patients with VCF in both an inpatient and outpatient setting. This conclusion supports those from economic analyses conducted in other countries.

540: Influence of approach on Spinopelvic Correction with Lumbar interbody: A Multi-level Meta-Analysis and Systematic Review

Jennifer Z. Mao, MBA (Buffalo, NY); Timothy O'Connor, MD; Elena Pezzino, BS; Muhammad Waqas, MBBS; Asham Khan, MD; Junyu Nie; Justice Agyei, MD; Alexander Fritz, BS; John Pollina, MD; Jeffrey Mullin

Introduction: Lumbar interbody fusions (LIF) are used for the stabilization of painful motion segments, providing indirect decompression, and restore lumbar lordosis in corrective deformity surgery. LIFS can be performed from an anteriorly (ALIF), transforaminal (TLIF), posterior (PLIF) and lateral (LLIF/DLIF/XLIF) approach. Studies have reported the change in spinopelvic parameters. However, the degree of correction between approaches have yet to be investigated.

Methods: A systematic review was conducted based on PRISMA guidelines of English articles from 2009 to 2019 from EMBASE, PUBMED, and Cochrane databases. Lumbar lordosis, segmental lordosis (SL), disc height (DH), pelvic tilt, pelvic incidence, sacral slope was extracted. (Table 2) SPSS (V26) and R metanalysis tool pack were used for data analysis. Forest plots were generated to evaluate the effect size and study heterogeneity.

Results: 69 articles (n = 4544) were selected for full text review (Table 1). Quantitative analysis was conducted on 34 studies (Table 2), with mean follow-up time of 27.87 ± 17.40 months and spinopelvic measurements reported in Table 3. Meta-Analysis showed significant improvement at follow up for: SL (Figure 1) and DH (Figure 2) in ALIF, TLIF, and Lateral approaches. ALIF (SMD = 0.42°; I² = 0%; p = 0.001), TLIF (SMD = 0.71° I² = 74%; p = 0.037), and lateral approaches (SMD = 0.52°; I² = 0%; p = 0.029), significantly maintained LL from preop to final follow up. (Figure 3) On multivariate linear mixed effect modeling, when comparing the effects of the three approaches, TLIF and ALIF held significance. (Table 4) Of the three approaches, ALIF had the greatest effect on lumbar lordosis. Whereas, lateral approaches lost significance.

Conclusion: All approaches demonstrated significant improvement of segmental lordosis and disc height at final follow up. ALIF and TLIF improve lumbar lordosis with a greater effect in the former. Further research correlating improved lordosis with clinical outcomes needs to be done.

541: Incidence and Risk Factors of Mechanical Complications Following Osteotomies for Correction of Moderate to Severe Cervical and Cervicothoracic Deformities: Series of 83 Patients with Minimum 1-Year Follow-up

Darryl Lau, MD (San Francisco, CA); Rushikesh Joshi, BA; Alexander Haddad, BA; Vedat Deviren, MD; Christopher Ames

Introduction: Rigid inflexible sagittal cervicothoracic deformities often require multilevel or high-grade osteotomies in order to achieve adequate correction. The rate and risk factors of hardware failure in the long-term is not well defined. This study aims to define the incidence of mechanical complications and identify risk factors for failure.

Methods: A retrospective review of consecutive cohort of patients that underwent cervical and cervicothoracic deformity correction from 2010 to 2018 was performed. Inclusion criteria was cervical kyphosis > 20 degrees and/or cervical sagittal vertical axis (cSVA) > 4cm. Mechanical complications of interest were: junctional kyphosis/failure, implant failure/rod fracture, and pseudarthrosis. Multivariate analysis was used to identify risk factors for outcomes at 1- and 2-year follow-up.

Results: A total of 83 patients had at least 1-year follow-up, and 51 of 73 (69.9%) had 2-year follow-up. Mean age was 63.4 years, and 61.0% of patients were female. Over half (53.0%) of the patients underwent three column osteotomy. Overall, preoperative and postoperative measures significantly improved: cSVA (6.2 vs. 4.6 cm, p<0.001), cervical lordosis (6.3 vs. -8.3 cm, p<0.001), cervical scoliosis (6.5 vs. 2.2 degrees, p<0.001), and T1 slope (41.7 vs. 36.3 degrees, p=0.007). Mechanical complication rate at 1-year was 28.9%: junctional failure (18.1%), implant failure (16.9%), and pseudarthrosis (10.8%). At 2 years, mechanical complication rate was 35.3%: junctional failure (21.6%), implant failure (21.6%), and pseudarthrosis (15.7%). Reoperation rate at 1-year and 2-years were 24.1% and 27.5%, respectively. Higher body mass index (BMI) and presence of preoperative cervical scoliosis were independently associated with higher odds of mechanical failure (p=0.020 and p=0.014) and reoperation (p=0.043 and p=0.014).

Conclusion: Mechanical complications are relatively high at 1- and 2-years following cervical and cervicothoracic deformity correction. High BMI and presence of preoperative scoliosis predispose patients for hardware failure. Large multicenter prospective studies are needed.

542: Next Generation Sequencing of Cerebrospinal Fluid to Improve Diagnostic Sensitivity, Detect Spatial Heterogeneity, and Predict Outcomes for Advanced Lung Cancer Patients with Leptomeningeal Carcinomatosis

Tej Azad, MD (Baltimore, MD); Shigeki Nanjo, MD, PhD; Jacob Chabon; Michael Jin; Ian Connolly; Ryan Ko; Christopher Yoo; Michael Iv; Seema Nagpal; Melanie Gephart; Ash Alizadeh, MD, PhD; Maximilian Diehn, MD, PhD

Introduction: Cerebrospinal fluid tumor-derived DNA (CSF-tDNA) detection is a less invasive method of monitoring neoplastic processes of the central nervous system (CNS). We hypothesize that detection of CSF-tDNA in patients with advanced lung cancer would improve the sensitivity of leptomeningeal carcinomatosis (LM) diagnosis and predict response to targeted therapy.

Methods: We applied a lung cancer-specific sequencing panel (CAPP-Seq) to 85 CSF, blood, and tissue samples from 25 patients with advanced lung cancer who underwent lumbar puncture (LP) for suspected LM. A cohort subset (N=12) was drawn from a prospective study where serial LPs were performed during treatment with osimertinib for refractory LM.

Results: CSF-tDNA variant allele fractions (VAFs) were significantly higher than plasma circulating tumor DNA (ctDNA) VAFs (median CSF-tDNA, 30.3%; median ctDNA, 1.8%; $P < 0.0001$). We further observed a positive correlation between CSF-tDNA VAFs and ctDNA VAFs (Spearman's ρ , 0.45; $P = 0.02$). For LM diagnosis, cytology was 100% specific and 82.6% sensitive. CSF-tDNA maintained 100% specificity but achieved 91.3% sensitivity. CSF-tDNA was strongly prognostic for overall survival (HR = 7.3; $P = 0.02$). Among patients with progression on targeted therapy, resistance mutations, such as EGFR T790M and MET amplification, were common in peripheral blood but were rare in time-matched CSF, suggesting differences in resistance mechanisms based on location. In the osimertinib cohort, patients with CNS progression had increased CSF-tDNA VAFs at follow up LP. Post-osimertinib CSF-tDNA was strongly prognostic for CNS progression (HR = 5.6, $P = 0.01$).

Conclusion: Detection of CSF-tDNA in lung cancer patients with suspected LM is feasible and may have clinical utility. CSF-tDNA may improve the sensitivity of LM diagnosis, enable improved prognostication, and drive therapeutic strategies that consider spatial heterogeneity of resistance mechanisms.

543: Cerebrospinal Fluid-Responsive Factor SERPINA3 Promotes Proliferation, Migration and Invasion of Glioblastoma

Montserrat A. Lara Velazquez (Jacksonville, FL); Natanael Zarco, PhD; Anna Carrano, PhD; Jordan Phillips; Paula Schiapparelli, PhD; Emily Norton; Stephanie Jeanneret; Teresita Corona Vazquez; Jose Segovia, PhD; Kaisorn Chaichana, MD; Alfredo Quinones Hinojosa, MD; Hugo Guerrero Cazares, MD, PhD

Introduction: Glioblastoma (GBM) is the most aggressive brain tumor in adults with high recurrence rate and poor survival. Anatomical location of the tumor is an important factor for prognosis. Periventricular GBMs exhibit worse survival than tumors distal to the lateral ventricles (LV). A hypothesis for this outcome is the proximity of these tumors to the cerebrospinal fluid (CSF). Chemotactic signals present in the CSF regulate cells migration and differentiation profile during normal development. CSF-responsive factors can play a role orchestrating cancer cells aggressiveness. We showed that the overexpression of SERPINA3 mediated by CSF is a contributing factor to GBM malignancy.

Methods: We used human GBM derived Brain Tumor Initiating Cells (BTICs) and CSF. Transcriptome changes upon CSF stimulation were determined by RNA expression array. BTICs migration response to CSF was evaluated by Boyden chamber assay. We determined the impact of SERPINA3 expression in glioma patients using TCGA databases. We also evaluated the biological effects of SERPINA3 on BTICs migration, invasion, proliferation, and cellular stemness through loss and gain of function experiments.

Results: We observed that GBM CSF induced an increase in cell migration and identified SERPINA3 as one of the genes with highest overexpression in response to GBM CSF. In primary samples and TCGA data we observed SERPINA3 and its transcript alpha 1-antichymotrypsin correlate directly with brain tumor grade and indirectly with GBM patient survival. Silencing of SERPINA3 induced a decrease in cell proliferation, migration, invasion, and cellular stemness, while SERPINA3 overexpression increased cell migration and invasion. Mice orthotopically-injected with SERPINA3-knockdown (KD) cells showed a prolonged overall survival. We also detected a decrease phosphorylated expression of MAPK, and a decrease metalloproteinases (MMPs) activity.

Conclusion: We showed that SERPINA3 as a factor induced by CSF-stimulation plays a key role in GBM malignancy, and its inhibition results in a better outcome using GBM preclinical models.

544: Laser Interstitial Thermal Therapy Followed By SRS Increases Time to Progression of Recurrent Brain Metastases Initially Treated With SRS

Matthew M. Grabowski, MD (Cleveland, OH); Eric Sankey, MD; Ethan Srinivasan, BS; Elizabeth Howell, BS; Alex Scott, BS; Michael Olufawo, BS; Balint Otvos, MD, PhD; Albert Kim, MD, PhD; Gene Barnett, MD, MBA; Eric Leuthardt, MD; Alireza Mohammadi, MD; Peter Fecci, MD, PhD

Introduction: Improved survival among patients with brain metastases (BM) has been accompanied by a rise in tumor recurrence after stereotactic radiosurgery (SRS). Traditionally, these patients have had limited treatment options. Laser interstitial thermal therapy (LITT) has evolved as an effective treatment for SRS failures and an alternative to resection. While patients undergoing resection of recurrent BM typically undergo repeat SRS, no study has examined the benefit of post-LITT SRS for recurrent BM.

Methods: A multicenter, retrospective study was performed of BM patients who underwent LITT for biopsy-proven tumor recurrence following SRS. Patients were stratified by planned, adjuvant SRS vs. no SRS. Radiographic tumor progression was determined by Response Assessment in Neuro-oncology criteria. Outcomes were compared by post-LITT SRS status.

Results: Thirty-seven patients met eligibility criteria, with a median follow up of 7.3 months (range:1.3-30.5). Median age was 60 (range:38-86), with a median KPS of 80 (range:60-100). Diagnoses included lung (57%), breast (14%), colon and melanoma (8% each), and esophageal (5%) cancers, among others. Twelve (32%) patients underwent post-LITT SRS. Median time to progression was increased in the post-LITT SRS group (>21.3 vs. 7.5 months). Age, tumor histology, and post-LITT SRS status were predictors of tumor progression. In a univariate Cox proportional hazards analysis, patients not treated with SRS after LITT were 3.6 times more likely to have progression of their index lesion ($p=0.037$). When controlled for patient age and tumor histology, patients not treated with SRS after LITT were 10.7 times more likely to have progression ($p=0.013$). Of those patients undergoing post-LITT SRS who experienced later radiographic progression, all were subsequently diagnosed with recurrent tumor.

Conclusion: These data suggest that adjuvant, post-LITT SRS for treatment of biopsy-proven BM recurrence after SRS is warranted. Prospective trials should be designed to further validate the utility of adjuvant SRS after LITT.

545: Spheno-orbital Meningiomas: Genetic Alternations and Long-Term Outcomes

Hongda Zhu, MD, PhD (Shanghai, China); Lingyang Hua, MD, PhD; Jiaojiao Deng, MD; Ye Gong, MD, PhD

Introduction: Spheno-orbital meningiomas (SOM) are considered to be surgically challenging. This retrospective study analyzes clinical characteristics, genetic alternations and long-term outcomes in this population.

Methods: A total of 176 patients who underwent resection of SOM in our institution (2001 — 2018) was conducted. The median follow-up was 85.4 months (range 1-182 months). Array-based comparative genomic hybridization analysis and targeted sequencing of 15 known meningioma driver genes were performed on 38 most recent SOMs.

Results: One hundred twenty-eight (73%) patients presented with primary and 48 (27%) with recurrent disease. Gross total resection (GTR) was achieved in 122 (69%) patients. Thirty-three patients received postoperative adjuvant radiation. Tumor recurrence occurred in 51 (29%) cases at last follow-up. The most common histology was meningothelial (61%), followed by fibroblastic (20%) and transitional (4%) subtypes. Among 26 patients with atypical or anaplastic histology, 19 were recurrent ones. The authors identified recurrent NF2 mutations (and/or Chr22q Loss) in 8 (21%) patients, KLF4K409Q mutations in 4 (11%) patients, mutations in TRAF7/PI3K pathway in 10 (26%) patients, mutations in Hedgehog signaling in 4 (11%) patients, POLR2A mutation in 2 patients, CREBBP and TERTp mutations in 1 patient respectively. No mutation was found in SMARCB1, SMARCE1 or BAP1 from this cohort. NF2 associated SOMs had reduced progression-free survival (PFS) and overall survival (OS) compared with NF2 wild-type patients (Kaplan-Meier analysis, PFS, $P=.001$; OS, $P=.021$). Cox proportional hazards regression model demonstrated GTR and WHO grade were significantly associated with PFS ($P<.001$ and $P=.023$, respectively).

Conclusion: SOMs are a distinct category of meningiomas due to their increased difficulty and morbidity of treatment. A radical resection can provide a significantly improved clinical outcome in the long-term period. NF2 mutations (and/or Chr22q Loss) tend to have negative impact on patients' outcome.

546: Spatial Distribution of Polycomb Repressive Complex 2 (PRC2)-Associated Genes and Therapeutic Targeting of EZH2 in Glioblastoma

Lauren Elana Rotman, MD (Birmingham, AL); Lauren Rotman, MD; Daisuke Yamashita, MD, PhD; Galal Elsayed, MD; Gustavo Chagoya, MD; Joshua Bernstock, MD, PhD; Adeel Ilyas, MD; James Mooney, MD; Shinobu Yamaguchi; Svetlana Komarova, PhD; James Markert, MD; Ichiro Nakano, MD

Introduction: Glioblastoma (GBM) contains two distinct tumor-initiating cell populations (TICs) with unknown intratumoral distribution. Understanding TIC distribution is important for targeting heterogeneous tumor cells. Polycomb repressive complex 2 (PRC2) is involved in epigenetic regulation of gene expression impacting tumor initiation and recurrence. Enhancer of Zeste homologue 2 (EZH2), the essential component for activation of PRC2, has been shown to be upregulated in GBM. Which of the TICs are dependent on the EZH2-mediated signaling remains largely unknown. Herein, we conducted an analysis of PRC2 associated gene expression in core and edge GBM tissues in order to assist in elucidating which TICs are dependent on EZH2 mediated signaling and where these cells are spatially distributed within GBM tissues.

Methods: Following IRB approval and informed consent, we isolated tumor core and edge tissue samples from three GBM patients. GBM (neuro)sphere culture models were established from these samples and were xenografted into mouse brains. RNA sequencing analysis (RNA-seq) and immunohistochemistry (IHC) were performed. Validation was done using additional GBM tissue samples and publicly-accessible GBM bioinformatics data.

Results: RNA-seq data exhibited EZH2 upregulation in tumor core as compared to edge tissues. IHC and Ivy GAP database assessment supported this. Survival outcomes analysis revealed significantly worse survival in patients with elevated EZH2 expression using Rembrandt ($p=0.002$) and Glioma-French ($P<0.001$) datasets. Testing EZH2 inhibition in the GBM sphere models using Tazemetostat and CPI-1205 resulted in increased potency to reduce growth of the tumor core-derived GBM sphere cultures as compared to tumor edge.

Conclusion: EZH2 was found to be upregulated in core TICs as compared to the edge, and was associated with poorer survival. Given that many of the current surgical treatment for our GBM patients fail to completely eliminate the tumor core lesions, these findings may guide new investigative and therapeutic approaches for GBM.

547: Wireless Intracranial Pressure Monitoring: Technical Challenges and Applications

Sandeep Bhangoo, MD, FAANS (Mason City, IA); Mike Muhonen, MD; Jason Liauw, MD; Kevin Hughes, MS; Nick Hu; David Beck, MD

Introduction: Use of intracranial pressure (ICP) monitoring has been limited to acute indications in an ICU setting because of the need of a continuous connection from the skull to an external device. Yet, there are technical challenges to creating a wireless monitor. These include ease of insertion with minimal trauma, powering the device post-implantation, calibration and minimizing measurement drift. Despite these challenges, the development of a wireless monitor has lead to new diagnostic applications in multiple sub-fields of neurosurgery.

Methods: Eight patients (Ages 17-77) received a wireless ICP implant. Pathologies included trauma, hydrocephalus, NPH, pseudotumor cerebri, and intracranial hemorrhage. Patients were monitored for adverse events related to the implant.

Results: Mean implant duration was 32.5 days (range 5-75). One patient (ICH) expired in 5 days secondary to the severity of the injury. To date, no other implant has been removed. Post-implant monitoring revealed that a pseudotumor cerebri patient with intractable headaches had intracranial hypotension which resolved following a valve change. Another patient with suspected hydrocephalus on imaging was monitored for an extended period and found to have no increased ICP thus being spared an unnecessary shunt. A third patient with persistent intracranial hypotension confirmed by the monitor was found to harbor an occult CSF leak. Finally, two patients with NPH were shown to have intracranial hypotension that was treated by titrating the settings on their adjustable shunt valves. One previously had a post-shunt subdural hematoma.

Conclusion: Wireless ICP monitoring has potential uses in acute and chronic settings. A functioning monitor can be queried in the clinic, the ER or general floor as opposed to simply in the ICU. This can lead to new applications for clinical research and therapy not only in trauma but hydrocephalus, pseudotumor cerebri, neuro-vascular and neuro-oncology.

548: Penetrating Gunshot Wounds to the Head: 10 Years of a Single Institutional Experience

Daniel Wolfson (Nashville, TN); Fakhry Dawoud, BS; Ranbir Ahluwalia, BS; Patrick Kelly, MD; Aaron Yengo-Kahn, MD

Introduction: Gunshot wounds to the head (GSWH) are common, devastating, and often require neurosurgical intervention. The current study describes our ten-year experience at a Level I trauma center.

Methods: Over ten years (01/2009-06/2019) of institutional data were queried for GSWH with dural penetration. Patient records were reviewed for demographics, admission parameters, and sequelae. Patients surviving longer than 48 hours after hospital arrival were classified as initial survivors. At most recent follow-up, Glasgow Outcome Scale scores of 4-5 were considered good outcomes.

Results: Over the study period, there were a median of 28 annual GSWH from 2009-2013 and 27 from 2014-2018, with 14 in 2019 to date. Of 297 GSWH patients, in-hospital mortality was observed in 68.4% of patients with 45.8% initial survivors. Of these, 69.1% lived to hospital discharge and 1.5% died within 6 months of discharge as a result of their injuries. Bullet track was mostly bifrontal or unihemispheric (45.5%). Of 63 (21.2%) patients receiving computerized tomography angiography, 46% experienced vascular injury. Mean international normalized ratio on arrival was 1.74 with 29.3% of patients receiving corrective measures. Neurosurgical interventions included 52 (17.5%) patients who underwent craniotomies/craniectomies and 4.7% who received external ventricular drains, 3.0% receiving intracranial pressure monitors, and 1.7% receiving both. Among initial survivors, median length of stay was 7 days with 4 ICU days. Median follow-up time after discharge was 3.4 months at which time 50.7% were classified as good outcomes. Cranioplasty was performed in 20.6% while 2.2% received ventriculoperitoneal shunts. Complications of the injury included infections related to their wound (12.5%) and seizures (6.6%).

Conclusion: GSWH are relatively frequent with high mortality and poor outcomes, less than half survive longer than 48 hours, but over half of GSWH victims that survive longer than 48 hours experience good outcomes. Survivors often require intensive neurosurgical care.

549: Hypernatremia and Creatinine Clearance as Predictors of Mortality in Acute Subdural Hematomas

Nicolas Khattar, MD (Louisville, KY); Andrew Donovan, BS; Jacob Shpilberg, BS; Kevin John, BS; Aaron McPheters, BS; Quan Do, BS; Emily Sieg, MD, MS

Introduction: Hypernatremia and kidney injury have been previously associated with worse outcomes and increased early mortality in patients with severe traumatic brain injury (TBI). Timing of the disturbances in sodium and renal homeostasis have not been directly correlated to any outcome measures.

Methods: Between 2013 and 2018, a total of seventy-four patients presenting with severe TBI and acute subdural hematomas were treated at a level one tertiary care trauma center. We retrospectively reviewed their records to evaluate the relationship between laboratory variables and outcome.

Results: Thirty-four patients died in hospital (45.9%) with a median GCS of 3 [3-6] at admission compared to 7 [4-7] in the survival group. Patients in the deceased group had elevated sodium ($p=0.003$), decreased BUN/Cr ($p<0.0001$), and decreased CrCl ($p<0.0001$) compared to the surviving population. Elevated sodium was first noted in patients that died at 24-36 hours ($p=0.00016$) with persistent elevation until 84-96 hours. Decreased CrCl was first seen between 0 and 12 hours ($p=0.0035$), 60 and 72 hours (0.027) as well as 72 and 84 hours ($p=0.03$). Linear regression models showed that sodium levels were inversely proportional to CrCl in both groups, with a more striking change in the group of patients that survived ($p=0.0261$). Patients in the mortality group displayed an inverse relationship between sodium and BUN/Cr ratios; however, this relationship was directly correlated in the patients that survived ($p=0.0001$).

Conclusion: Hypernatremia is strongly associated with increased in-hospital mortality, with persistent elevations in sodium first noted after 24-36 hours. In our cohort, hypernatremia was inversely proportional to creatinine clearance and could represent an underlying mechanism of action of the worsened outcomes. This new outlook may help improve the outcomes of patients with severe TBI.

550: Osteoconductive Bone Adhesive versus Plates and Screws for Cranial Flap Fixation in an Ovine Model

Kevin T. Foley, MD, FAANS (Memphis, TN); Eric Woodard, MD; Jonathan Slotkin, MD; Cassandra Mayotte, MBA; Abigail Baldwin; Michael Brown; Brian Hess, MBA

Introduction: This study investigated the use of a bioresorbable, osteoconductive bone adhesive comprising tetracalcium phosphate and phosphoserine (TTCP-PS) for cranial bone flap fixation compared to conventional titanium plates and screws.

Methods: Bilateral craniotomies were performed in 41 sheep. The cranial flaps were replaced and the gaps between the surrounding bone and flap edges (kerfs) were either completely filled with TTCP-PS (T1 group), half-filled with TTCP-PS (T2 group), or left empty and the flaps fixated by plates and screws (C group). At twelve weeks, one year, and two years postoperatively, the extent of bone healing, local tissue effects, and remodeling of the TTCP-PS were analyzed using macroscopic observations, histopathology, and histomorphometry. Flap fixation strength was evaluated by biomechanical testing at twelve weeks and one year postoperatively.

Results: No adverse tissue effects were observed. At 12 weeks, bone flap fixation strength was statistically greater ($p=0.007$) when fixated with T1 ($1,689\pm574$ N) compared to the C group (663 ± 385 N). Flaps fixated with plates and screws frequently loosened or migrated, but those fixated with TTCP-PS had no loss of fixation. T1 had the best overall performance based on histomorphometry and biomechanical testing. At 2 years, the kerfs filled with TTCP-PS had evidence of osteoconduction and replacement of TTCP-PS by bone with nearly complete osteointegration. Only 13 of 32 kerf sections examined in the control group healed and osteolysis was evident around many of the bone screws.

Conclusion: Osteoconductive, bioresorbable bone adhesive appeared to have multiple advantages over standard plate and screw bone flap fixation, including biomechanical superiority, more complete bony healing across the flap kerfs, and minimization of bone flap and/or hardware migration and loosening. These properties of TTCP-PS may improve human cranial bone flap fixation and cranioplasty.

551: Four Standard Clinical Variables Are Sufficient To Predict An Unfavorable Outcome After Surgical Treatment Of Chronic Hematoma Patients

Alexander Younsi, MD (Heidelberg, Germany); Moritz Scherer; Lennart Riemann; Cleo Habel; Jessica Fischer; Andreas Unterberg; Klaus Zweckberger

Introduction: Chronic subdural hematomas (cSDH) are expected to become the most frequent neurosurgical disease by the year 2030. Although often perceived as a benign condition, considerable rates of mortality and poor outcome have been reported. We, therefore, evaluated factors associated with an unfavorable outcome after surgical treatment of cSDH patients by developing a predictive model using machine-learning.

Methods: Consecutive patients treated for cSDH with surgical evacuation between 2006-2018 at a single institution were retrospectively analyzed. Potential demographical, clinical, imaging and laboratory predictors were assessed and a decision-tree predicting unfavorable outcome (GOS 1-3) was subsequently developed using the Classification and Regression Tree (CART) algorithm. Hereby, the complexity parameter was set at 0.02 and at least 25 observations were required at every split or node. Out-of-sample model performance was evaluated using repeated cross-validation (5-fold with 200 repetitions).

Results: 755 eligible patients were analyzed. The median age was 75 (IQR 68-81) years and 69% were males. The mortality rate was 1.6% and the rate of unfavorable outcome was 14.3%. The developed decision-tree to predict unfavorable outcome had 5 splits and included the following 4 clinical variables (in descending order of calculated importance): GCS, comorbidities, Hb, and age. After cross-validation, the following model performance metrics were obtained: a model accuracy of 0.88 (0.85-0.90), sensitivity of 0.35 (0.19-0.51), and specificity of 0.96 (0.94-0.99).

Conclusion: GCS, comorbidities, Hb, and age were identified as the most important clinical predictors for an unfavorable outcome in cSDH patients after surgery. The developed model was simple and still displayed a high accuracy and very high specificity, the sensitivity was however rather low. Our results might help clinicians to better assess the prognosis in patients with cSDH.

552: Poliovirus Oncolytic Activity in Medulloblastoma is Mediated by Oxidative Stress

Eric M. Thompson, MD, FAANS (Durham, NC); Eric Thompson; Wafa Hassen, PhD; Meredith McDonald, BS; Daniel Picard, MS; Michael Brown, PhD; Elena Dobrikova; Matthias Gromeier

Introduction: PVSRIPO is an oncolytic polio:rhinovirus currently in a Phase I clinical trial for recurrent medulloblastoma in children. However, the mechanism of tumor cell killing of PVSRIPO is unknown. The purpose of this work is to define the mechanism of medulloblastoma cell death induced by PVSRIPO.

Methods: Cell viability assays were performed on 5 low-passage medulloblastoma cell lines (8A, 283, 435, 458, 556). Plaque assays (a measure of viral production) were performed. Unsupervised hierarchical clustering (HCL) of mRNA expression data was performed to elucidate differences in cellular process in these cell lines. To elucidate the mechanism of 283 resistance to PVSRIPO, Caspase 3/7 apoptotic assays, DCFDA flow cytometry assays of reactive oxygen species (ROS) formation, annexin flow cytometry assays of cellular viability/apoptosis/necrosis, anti-oxidant glutathione (GSH) assays, and viability assays of PVSRIPO in combination with pro- and anti-oxidant agents were performed.

Results: 283 was significantly ($P < 0.05$) more resistant to PVSRIPO-induced lethality than the other cell lines. PVSRIPO plaque assay demonstrated significantly delayed viral propagation in 283 cells as evidenced delayed protein expression of 2C, a key component of viral RNA synthesis. HCL of Gene Ontology data sets of demonstrated profoundly reduced 283 mRNA expression of oxidative stress pathway genes compared to the other cell lines. Accordingly, 283 had significant higher ($P < 0.05$) baseline levels of GSH. Further, 283 demonstrated significantly less ($P < 0.05$) apoptosis and ROS production in reaction to PVSRIPO compared to other cell lines. In non-283 medulloblastoma lines, the addition of GSH rescued PVSRIPO-induced lethality and the addition of the pro-oxidants, BSO and erastin, significantly ($P < 0.05$) increased lethality in all medulloblastoma cells.

Conclusion: PVSRIPO cause oxidative stress in medulloblastoma, resulting in cell death. Future in vivo and clinical studies will utilize pro-oxidant agents in combination with PVSRIPO to further enhance efficacy.

553: Inhibiting Complement Activation Prevents Severe Brain Injury and Post-Hemorrhagic Hydrocephalus in New Model of Germinal Matrix Hemorrhage

Mohammed Alshareef, MD (Charleston, SC); Ali Alawieh, MD, PhD; Khalil Mallah, PhD; Tyler Vasas, BSE; Ramin Eskandari, MD, MS; Stephen Tomlinson, PhD

Introduction: Germinal matrix hemorrhage (GMH) is a common neonatal pathology often leading to post-hemorrhagic hydrocephalus (PHH) and periventricular leukomalacia (PVL). The complement cascade is implicated in secondary injury and chronic inflammation in the injured and stressed brain. We investigated the role of complement activation in propagating secondary following murine GMH while using a novel clinically-relevant therapeutic strategy that has potential for human translation

Methods: Neonatal GMH was induced by collagenase injection in the subventricular zone of 4-days-old mice. We performed a randomized treatment study using CR2-Crry, a novel complement inhibitor. Through Nissl, and immunofluorescent staining for microglia/macrophage, complement deposition, and astrocytosis, regional tissue loss (infarction), ventriculomegaly and inflammatory response was evaluated. Neurocognitive motor function and survival analysis was obtained on all animals up to 45 days of life. An infarct grading system was developed (grade 1-5) for severity of infarction and ventricular involvement.

Results: A significant reduction in proportion of high-grade infarcts, bilateral ventricular involvement, and PHH (grade 5) was observed in CR2-Crry-treated mice compared to vehicle (7% vs. 65% respectively, $p < 0.005$). There was an overall reduction in C3d deposition with concurrent reduction in astrogliosis and microglial/macrophagic activation. Survival of CR2-Crry treated animals was 90% at 21 days compared to 30% in vehicle group ($p = 0.03$). Neurocognitive decline was higher in vehicle group compared to treatment as measured by Barnes maze, passive avoidance, and gait analysis.

Conclusion: There are currently no medical therapies for GMH aimed to reduce brain injury volume and prevent PHH. Targeting the neuroinflammatory pathway leading to gliosis and PVL is a viable option requiring reproducible models and therapeutic compounds. We have developed a novel and highly translatable GMH model to test anti-complement therapy. We found that site-targeted complement inhibition mitigates effects of the secondary injury with increased survival and reduced rates of PHH and PVL

554: Safety and Feasibility of Focused Ultrasound Mediated Blood Brain Barrier Opening in a Murine Model of Brainstem Glioma

Zachary K. Englander, MD (New York, NY); Hong-Jian Wei, PhD; Antonios Pouliopoulos, PhD; Pavan Upadhyayula, BS; Chia-Ing Jan, MD, PhD; Eleonora Spinazzi, MD; Peter Canoll, MD, PhD; Jeffrey Bruce, MD; Neil Feldstein, MD; Stergios Zacharoulis, MD; Elisa Konofagou, PhD; Cheng-Chia Wu, MD, PhD

Introduction: Diffuse intrinsic pontine glioma (DIPG) is a devastating pediatric cancer with limited treatment options and poor survival. Drug delivery is a major therapeutic obstacle in this disease, as the blood brain barrier (BBB) limits the distribution of intravenous therapies to the brainstem. Focused ultrasound (FUS) is an exciting new technology that, when combined with the administration of microbubbles, can effectively open the BBB permitting the entry of drugs across the cerebrovasculature. Given that the utility of FUS in brainstem tumors remains unknown, the purpose of our study was to determine the safety and feasibility of this technique in a preclinical murine pontine glioma model.

Methods: A syngeneic orthotopic model was established by stereotactic injection of PDGF-B+PTEN^{-/-}p53^{-/-} murine glioma cells into the pons of B6 albino mice, and visualized with MRI on post-injection day 13. A single-element, spherical-segment FUS transducer (center frequency=1.5MHz) driven by a function generator through a power amplifier (acoustic pressure=0.7MPa) was used with concurrent intravenous microbubble injection (FUS+MB) to sonicate the tumor and its margins on post-injection day 14. BBB opening was confirmed with gadolinium-enhanced MRI. All mice underwent Konziela inverted screen testing before and after FUS to measure strength. Three mice were sacrificed post-FUS for histological analysis and the remaining four animals were serially monitored for survival.

Results: In all mice that underwent FUS (n=4, mean tumor volume=3.9µl), there was no measured deficit in strength testing. Additionally, there was no difference in overall survival between control mice (n=2, mean=22.5 days) and treated mice (n=2, mean=27 days)(p=0.072). Lastly, histopathological assessment of treated mice (n=2) with H& E revealed no evidence of hemorrhage or necrosis within the brain parenchyma.

Conclusion: FUS+MB is a safe and feasible technique to open the BBB in a preclinical pontine glioma model. Further studies to assess efficacy of FUS-mediated drug delivery in these tumors are underway.

555: Evaluation of pre-and post-operative Ambulatory Oxygen Consumption in Patients Who Have Undergone Selective Dorsal Rhizotomy (SDR) For Lower Extremity Spasticity

Rasha Gamaleldin Elbadry Ahmed, MBCh (Aurora, CO); Sarah Graber, CCRP; Kim Cowie; Joyce Oleszek, MD; Amy Bodkin; James Carollo; Charles Wilkinson, MD

Introduction: Selective dorsal rhizotomy (SDR) has been shown to reduce spasticity and improve gait in ambulatory children with spastic diparetic cerebral palsy. After SDR and intensive postoperative therapy patients often are faster, fall less, and have greater ability to keep up with their peers. Formal gait analysis is essential in quantifying postoperative improvement after SDR, and we routinely perform gait studies 1 year post-SDR in ambulatory patients. One measure of gait efficiency that we have been using recently is ambulatory oxygen consumption volume (VO₂). In this study, we evaluate the hypothesis that ambulatory VO₂ improves (is lower) after SDR.

Methods: We reviewed the records of all patients who underwent SDR from 2009 through 2018, excluding those without preoperative and 1-year postoperative gait studies incorporating ambulatory VO₂ measurements. All VO₂ measurements were weighted for body mass and speed. Changes in ambulatory VO₂ were compared to barefoot gait speed (BGS) and Gait Deviation Index (GDI; a composite measure of gait kinematics) as measures of gait improvement.

Results: Of 47 patients who underwent SDR, only 7 had both preoperative and 1-year postoperative gait studies incorporating ambulatory VO₂. There were 5 males and 2 females with diparetic (6) or triparetic (1) spasticity. The average age at SDR was 7.9 years. Post-operatively, average VO₂ decreased by 8%, from 0.39 ml O₂/kg-m to 0.35 ml O₂/kg-m. Average BGS increased by 12% from 47.9 m/min to 53.3m/min. Average GDI improved by nearly 1 standard deviation from 63.9 to 72.4. There were nonsignificant trends for BGS (p=0.72) and GDI (p=0.17) to increase as VO₂ decreased.

Conclusions: Ambulatory VO₂ may be a useful adjunct measurement in evaluating improvement in gait after SDR. Evaluation of more patients undergoing preoperative and 1-year-postoperative ambulatory VO₂ will determine how useful it is.

556: Low Benefit to Routine Imaging After Pediatric Shunt Revision

Alexander Frans Christiaan Hulsbergen (Utrecht, Netherlands); Francesca Siddi, MD; Malia McAvoy, MSc; Benjamin Lynch, BA; Madeline Karsten, BA; Marike Broekman; William Gormley; Mark Proctor, MD

Introduction: Postoperative routine imaging is common after pediatric ventricular shunt revision, but the benefit of scanning in the absence of symptoms is unknown. This study aimed to assess how often routine imaging results in a change in clinical management in this setting.

Methods: The charts of the Boston Children's Hospital were retrospectively reviewed for all consecutive cases of pediatric shunt revision between July 2013 and July 2018. Postoperative imaging was classified as routine (i.e. in absence of symptoms, complications or other direct indications) or non-routine. Reinterventions within 30 days were assessed in these groups.

Results: Out of 387 included cases, postoperative imaging was performed in 297 (76%), which was routine in 244 (63%) and non-routine in 53 (14%). Ninety cases (23%) underwent any shunt-related reintervention after postoperative imaging, including shunt redial (n = 36, 9%), shunt tap (n = 10, 3%), and return to operating room (OR; n = 58, 15%). Of the 244 cases receiving routine imaging, 52 (21%) underwent any re-intervention, including 30 returns to OR (12%). Three reinterventions (all return to OR) were triggered by imaging findings in a routine scan in the absence of symptoms; this constituted 0.8% of all cases or 1.3% of cases receiving a routine scan. Alternative reasons for re-intervention in the routine imaging group were postoperative complications (n = 15), reappearance of symptoms (n = 17), shunt redial after dislodgement by MRI (n = 15), or shunt redial for other reasons unrelated to imaging findings (n = 2).

Conclusion: We found a low yield to routine scanning after pediatric shunt revision, with only 0.8% of cases undergoing a change in management based on routine imaging findings. Moreover, a routine scan without abnormal findings did not guarantee an uneventful postoperative course. Clinical monitoring can be considered as an alternative in asymptomatic, uncomplicated patients.

557: Brain Metabolic Changes and Clinical Efficacy of Transcutaneous Afferent Patterned Stimulation for Essential Tremor Patients

Abhijeet Singh Barath (Rochester, MN); Charles Blaha, PhD; Aaron Rusheen; Adam Loudermilk; Hoon-Ki Min, PhD; Val Lowe, MD; Erika Ross, PhD; Sooyoon Shin, PhD; Kate Rosenbluth, PhD; Apoorva Rajagopal, PhD; Kendall Lee, MD, PhD

Introduction: Transcutaneous afferent patterned stimulation (TAPS) targeting the median and radial nerves has been shown to be effective for treatment of essential tremor (ET). This study investigated the efficacy and regional brain metabolism effects of TAPS therapy over three months of use.

Methods: This is an ongoing interventional, single-group study enrolling 20 patients who were approved to undergo deep brain stimulation (DBS) surgery for treatment of ET. All enrolled patients were instructed to use TAPS therapy on their dominant hand for 40 minutes twice daily for 90 days. Therapeutic efficacy was quantified using improvements in Tremor Research Group Essential Tremor Rating Assessment Scale (TETRAS) and Bain & Findley Activities of Daily Living (ADL) scale from pre to post TAPS on day 1 and 90. Changes in regional brain metabolism were evaluated using 2-deoxy-2-[18F]fluoro-D-glucose (FDG) uptake PET-CT scans on day 1 (no stimulation), 2 (stimulation during FDG uptake), and 90 (no stimulation). Preliminary results of the first 5 patients completing the study are presented.

Results: Lateral postural, kinetic and forward postural tremor subcomponents of TETRAS improved significantly ($p < 0.05$) and tremor amplitude decreased by 59% (day 1) and 32% (day 90) from pre to post-stimulation. All subsets of TETRAS, Archimedes spiral task and Bain and Findley ADL hand subset for the stimulated hand trended to improvement. Metabolism decreased in motor cortex and cerebellum contralateral to the side of stimulation at day 90 compared to day 1 ($p < 0.05$, uncorrected).

Conclusion: Longitudinal TAPS therapy in ET patients is associated with improvement in tremor and ADL and decreased metabolism in contralateral motor cortex and cerebellum, suggesting a mechanism by which TAPS induces neuronal plasticity. Further clinical and bench side studies are warranted to investigate the mechanism of tremor relief observed with this therapy.

558: Topographical Organization of the Cortico-subthalamic Hyperdirect Pathway Related to the Speech Network

Ahmed Jorge, PhD (Pittsburgh, PA); Ahmed Jorge; Witold Lipski, PhD; Dengyu Wang; Donald Crammond; Robert Turner; R. Mark Richardson, MD, PhD

Introduction: Speech production and modulation is dependent on basal ganglia-thalamocortical networks. Given the importance of the hyperdirect cortical-subthalamic (STN) pathway in basal ganglia function, we investigated whether evoked potentials consistent with antidromic activation were observed in speech-related opercular cortical areas following STN stimulation.

Methods: 20 patients with Parkinson's disease underwent STN (n=17) or GPi (n=3) DBS surgery and temporary placement of one to two 63-channel ECoG arrays located over cortical areas including pars triangularis, pars opercularis, premotor, primary motor (M1), primary sensory (S1), supramarginal gyrus (SMG), and superior temporal gyrus (STG). Stimulation at 1Hz for 30s was performed at different sites within the STN or GPi. Cortical evoked potentials (cEPs) were processed and compared to a 30 second baseline period; significant peaks rising above baseline were considered significant. STN stimulation sites and their corresponding cEPs locations were averaged to obtain the center of the cEP as a function of STN location

Results: We identified 9450 distinct voltage-time traces across cortical areas and multiple STN stimulation locations that exhibit a significant short-latency antidromic cEP (latency=2.9±0.8 ms). Similar cEPs were not observed after GPi stimulation. In addition, there was a positive relationship in cEP locations as a function of STN stimulation site (Spearman rho=0.81, p-val=0.02), that is, stimulations closer to the center of the STN motor region elicited higher amplitudes in M1, S1, SMG and STG, while stimulations closer to the center of the associative region of STN elicited higher amplitudes in premotor, pars opercularis and pars triangularis.

Conclusion: We provide evidence for the presence of a hyperdirect pathway from speech-related opercular cortex to STN, with conservation of cortical topography. These findings suggest that cortex may communicate speech perception and planning information directly to STN.

559: Novel Microelectrode Technologies Reveal Unique Electrophysiologic Dynamics in Epilepsy

Jimmy Yang, MD (Boston, MA); Angelique Paulk, PhD; Daniel Cleary, MD, PhD; Brian Nahed, MD, MSc; Pamela Jones; Daniel Cahill, MD, PhD; Eric Halgren, PhD; G. Rees Cosgrove, MD; Ziv Williams, MD; Shadi Dayeh, PhD; Sydney Cash, MD, PhD

Introduction: Interictal discharges and high frequency oscillations (HFOs) are neurophysiologic markers of epilepsy that may represent irritative cortex and provide evidence of a seizure onset zone. In this study, we capitalize on recent progress in electrode technologies by fabricating custom PEDOT:PSS microelectrodes for intraoperative use in order to better understand microscale dynamics of these neurophysiologic markers.

Methods: PEDOT:PSS devices with spatial resolution up to 50 µm were used in 21 subjects to record from the cortical surface intraoperatively. As part of their clinical care, a subset of patients was administered an intervention to either provoke or dampen the appearance of interictal epileptiform discharges. Data analysis was subsequently performed with custom MATLAB scripts. Interictal discharges and HFOs were both first automatically detected using separate algorithms, followed by visual review.

Results: Interictal discharges that were seen across the entire array were detected in 94% of the subjects. On the other hand, local events, defined as those seen over <50% of the microelectrode array, were only seen in 67% of the subjects. By tracking the peaks of the interictal discharges across individual microelectrodes, it was found that different populations appeared to travel in specific paths across the array. Similar trends were found in detections of HFOs. Overall, HFOs that could be detected over the majority of the microelectrode array were found in 94% of the subjects, while local events were only detected in 75% of the subjects. Through clustering of detections, it was found that specific combinations of individual electrodes would detect HFOs at the same time.

Conclusion: Using new technologies of PEDOT:PSS microelectrode arrays, markers of epileptiform activity can be identified at high spatial and temporal resolution. Overall, this data may suggest micro-domains of irritable cortex and may therefore offer insight into the underlying epileptic and pathologic networks.

560: Revisiting the Selective Vestibular Neurotomy for Intractable Ménière's Disease in the Era of Endoscopy

Fabrizio Salvinelli (Rome, Italy); Fabio Greco; Francesco Capuano; Lucia Giovanna Maria di Somma; Erika Carrassi; Gianluca Bizzocchi; Maurizio Iacoangeli

Introduction: Vestibular neurectomy is considered a quite effective salvage-procedure to control intractable vertigo associated with Meniere's disease while preserving hearing and facial nerve function. However, it is still a potentially very dangerous procedure in terms of mortality and morbidity for a benign disease. The gold standard for the treatment of severe vertigo associated to Meniere's disease is transtympanic gentamicin injection and the extradural endolymphatic sac decompression surgery. We present our experience with the selective vestibular nerve neurectomy for intractable Meniere Syndrome.

Methods: Twenty-two patients with disabling, intractable vertigo associated to Ménière's disease treated by a combined micro-endoscopic selective vestibular neurotomy between May 2017 and May 2019 were evaluated. All patients come from a failure of a previous extradural surgical decompression of the endolymphatic sac. Demographics, clinical signs and symptoms, quality of life, thresholds of hearing, and adverse events were documented at baseline, 1 week, 1, 3, 6, 9, 12 18 and 24 months after surgery.

Results: At the maximum present follow-up of 2 years, vertigo disappeared in 20 out of 22 patients and improved in one case. In the other case probably we did not sectioned completely the nerve. In all cases, intraoperative neurophysiological monitoring and direct stimulation of nervous fibers allowed the selective identification of the facial and cochlear nerve. No major complications occurred, one case presented skin infection.

Conclusion: The modern endoscopic technique and the intraoperative advanced neuromonitoring seem to be able to allow a precise, complete and very selective vestibular neurotomy, preserving at the same time, the cochlear and facial nerve functions. We believe that the surprisingly quite high success rate is due to the completeness of the vestibular nerve deafferentation of almost all its fibers. The main concern is the duration over the time being the follow-up still quite short.

561: Unilateral Laser Amygdalohippocampotomy Ameliorates PTSD Symptoms and Biomarkers

Jon T. Willie, MD, PhD, FAANS (Atlanta, GA); Kelly Bijanki; Sanne van Rooij; Rebecca Fasano; Daniel Drane; Tanja Jovanovic

Introduction: Post-traumatic stress disorder (PTSD) is a severe psychobiological disorder associated with hyperactivity of the amygdala, particularly on the right side. Symptoms include unwanted re-experiencing of the event, hyperarousal and emotional distress or physical reactivity when confronted with trauma reminders, avoidance of trauma-related stimuli, and negative alterations in cognition and mood. Up to 50% of patients do not respond to trauma-focused psychotherapy with or without medications. We predicted that right laser amygdalohippocampotomy for medically-refractory medial temporal lobe epilepsy (MTLE) would improve comorbid PTSD.

Methods: Two patients with well-documented chronic PTSD subsequently developed late-onset right MTLE. Each underwent unilateral stereotactic laser interstitial thermal therapy of the amygdala and anterior hippocampus. Prospective clinical and neuropsychological measures were collected in Patient 1. Additional prospective standard measures of PTSD symptoms and biomarkers (fear potentiation of the startle reflex, functional MRI responses to fear-inducing stimuli, and emotional declarative memory) were collected in Patient 2.

Results: Both patients experienced not only reduced seizures, but also profoundly abated PTSD symptoms. Patient 1 reported immediate postoperative abatement of aggression and hypervigilance in response to triggers. He experienced meaningfully improved Beck Depression and Anxiety inventories at 6 and 12 months. Patient 2 experienced a meaningfully improved depression inventory at 6 and 12 months and -31% and -68% reductions in the Clinician-Administered PTSD Scale at 6 and 12 months, which was driven by greatest reductions in hyperarousal (-90%) and negative alterations in cognition and mood (-83%) at 12 months. PTSD-related biomarkers in Patient 2 showed robust improvements in fear potentiated startle reflex, functional MRI responses in ventromedial prefrontal and dorsal anterior cingulate cortices and left amygdala, and emotional declarative memory.

Conclusion: To our knowledge, this is the first prospective investigation of the effects of amygdala ablation on PTSD. These observations support the emerging hypothesis that the right amygdala particularly perpetuates the signs and symptoms of PTSD, and suggests that focal unilateral amygdalohippocampotomy can provide clear therapeutic benefit.

562: Ex-Vivo Multi-Electrode Analysis Reveals Spatiotemporal Dynamics of Ictal Behavior at the Infiltrative Margin of Gliomas

Brian Gill (New York, NY), MD; Farhan Khan, BS; Xiaoping Wu, MD; Alexandre Sosunov, MD, PhD; Alexander Goldberg, BS; Tejaswi Sudhakar, BS; Athanassios Dovas, PhD; Matei Banu, MD; Guy McKhann II, MD; Peter Canoll, MD, PhD; Catherine Schevon, MD, PhD

Introduction: The precise relationship between the electrophysiologic and histopathologic changes that occur at the margins of glioma remains poorly understood. Here we present findings from microelectrode array (MEA) recordings with ex-vivo murine glioma slices, relating the spatial seizure structure to the underlying histological milieu.

Methods: MEAs were used to study electrophysiologic changes in ex-vivo slices from a PTEN/p53 deleted, PDGF-B-IRES-Cre driven mouse model of high-grade glioma. Standardized methods were applied to identify and localize seizure-like events (SLEs). A 0.16 mm² area was defined around each electrode, the histology within this region was classified as tumor, infiltrative cortex, or peritumoral cortex, based on the following criteria. Areas with many NeuN+ neurons and rare YFP+ glioma cells were classified as peritumoral, areas with many YFP+ glioma cells intermingled with many NeuN+ neurons were classified as infiltrative, and areas with many YFP+ glioma cells and rare NeuN+ neurons were classified as tumor.

Results: 222 peritumoral, 78 infiltrated, and 98 tumor sites were sampled across all tumor-bearing slices. All three histologic regions showed significant increases in firing rates when compared to control slices (7.98, 14.52, 11.65 vs 4.39, p-value < 0.0001). Tumor-bearing slices demonstrated increased proclivity for SLEs, with 40 events in tumor-bearing slices and only 5 in control slices (p-value = 0.0105). Seizure foci comprised areas from all histologic regions. The onset electrode was found to be at the infiltrative margin in 50% of cases and in the peritumoral cortex in 36.9% of cases. Peritumoral seizure onset electrodes were on average 0.45 mm from the nearest electrode in the tumor or infiltrated cortex (range 0.4-1.2 mm).

Conclusion: Using an ex-vivo MEA based approach we have shown that tumor-bearing slices have greater seizure proclivity than controls, contain multiple noncontiguous seizure foci, and have SLEs arising predominantly from the infiltrating margins of the tumor.

563: Local Combination Therapy of Poly-ADP-Ribose-Polymerase-Inhibitor Olaparib and Temozolomide-Etoposide From a Biodegradable Paste Potentiates Radiotherapy and Prolongs Survival

Riccardo Serra (Baltimore, MD); Stuart Smith, MD, PhD; Jonathan Rowlinson; Noah Gorelick; Gareth Veal; Kevin Shakesheff; Richard Grundy; Henry Brem; Ruman Rahman; Betty Tyler

Introduction: Olaparib, a PARP (poly-ADP-ribose-polymerase) inhibitor tested in combination with radiation (XRT) and temozolomide, has shown promising results in several Glioblastoma (GBM) clinical trials. To minimize toxicities and increase local drug concentrations, we assessed delivery of Olaparib from our PLGA/PEG thermo-sensitive biodegradable paste in an intracranial rodent model of GBM.

Methods: Proliferation, clonogenic, and cell-viability were assessed on 9L, U251, and U87 lines to evaluate the efficacy of Olaparib alone and with etoposide, temozolomide, and XRT. Western blotting, immunofluorescence, and flow cytometry with AnnexinV/PI and PI were performed to characterize apoptosis and cell cycle. mRNA-sequencing of patient-derived lines obtained from 5-ALA positive/negative margins and immunohistochemistry of >100 tumor samples were used to quantify PARP and AIF expression. An in vivo study was performed on F344 rats implanted with intracranial 9L xenografts (n = 77), as well as immunohistochemistry and mass spectrometry on brain samples.

Results: Olaparib showed substantial antiproliferative, clonogenic, and cytotoxic activity against all lines, and cell apoptosis was demonstrated with AnnexinV/PI staining. Western blotting for Apoptosis-Inducing Factor, cleaved-PARP and H2AX, a DNA damage marker, shed light on the molecular targets of Olaparib, and higher mRNA expression of PARP and AIF in 5-ALA positive GBM margins provided evidence for effective translatability to human patients. Furthermore, Olaparib/XRT, alone and in combination with temozolomide or etoposide, showed a statistically significant improvement in overall survival when compared to controls and standard therapy. Combination therapies also achieved long-term survival at rates >50% of the treated cohort.

Conclusion: Novel treatments for GBM are strongly needed to improve patient survival and quality of life. Interstitial chemotherapy was proven to be a safe and effective approach to increase tumor killing and minimize toxicities. In this study, an intracavitary combination of Olaparib/XRT showed a promising increase in survival, paving the way for future translation to clinical application.

564: Resting-state fMRI Detects Alterations in Whole Brain Connectivity Related to Tumor Biology in Glioma Patients

Veit Stoecklein, MD (Munich, Germany); Sophia Stoecklein; Franziska Galiè; Ren Ren; Marcus Unterrainer; Nathalie Albert; Friedrich-Wilhelm Kreth; Niklas Thon; Birgit Ertl-Wagner; Joerg-Christian Tonn

Introduction: Systemic infiltration of the brain by tumor cells is a hallmark of glioma pathogenesis which may cause disturbances in functional connectivity. We hypothesized that aggressive high-grade tumors cause more damage to functional connectivity than low-grade tumors.

Methods: We designed an imaging tool based on resting-state functional MRI to individually quantify abnormality of functional connectivity and tested it in a prospective cohort of patients with newly diagnosed glioma.

Results: 34 patients (WHO II: 13; WHO III: 6; WHO IV: 15; mean age 48,7 years) were analyzed. Connectivity abnormality could be observed not only in the lesioned brain area but also in the contralateral hemisphere with a close correlation between connectivity abnormality and aggressiveness of the tumor as indicated by WHO grade. IDH 1 mutation status was also associated with abnormal connectivity, with more alterations in IDH 1 wildtype tumors independent of tumor size. Finally, deficits in neuropsychological performance were correlated with connectivity abnormality.

Conclusion: Here, we established an individually applicable resting-state fMRI marker in glioma patients. Analysis of the functional connectome using this marker revealed that abnormalities of functional connectivity could be detected not only adjacent to the visible lesion but also in distant brain tissue, even in the contralesional hemisphere. These changes were associated with tumor biology and cognitive function. The ability of our novel method to capture tumor effects in non-lesional brain suggests a potential clinical value for both individualizing and monitoring glioma therapy.

565: Modeling the Genetic, Transcriptomic, and Cell Surface Antigen Heterogeneity of Glioblastoma Using Patient Derived Tumor Organoids

Daniel Zhang (Philadelphia, PA); Fadi Jacob; Ryan Salinas, MD; Phuong Nguyen; MacLean Nasrallah, MD; Steven Brem, MD; Donald O'Rourke, MD; Guo-Li Ming, MD, PhD; Hongjun Song, PhD

Introduction: Glioblastoma exhibits enormous cellular heterogeneity at both the macroscopic level across distant anatomic regions of the tumor and at the microscopic level between close-by neighboring cells, all of which contribute substantially to treatment resistance with standard of care therapies as well as with novel targeted agents and immunotherapies. Although tumor heterogeneity has been increasingly well appreciated given recent technological advancements, the specific mechanisms and processes by which this heterogeneity gives rise to this disease's clinical behavior remains poorly understood, largely due to the lack of suitable laboratory tumor models that adequately recapitulate this essential feature of glioblastoma.

Methods: We have developed a method of generating glioblastoma organoids (GBOs) from fresh tumor tissue obtained directly from surgical resection and maintaining them in culture for more than 1 year. We also leverage massively parallel multi-omic analyses and next generation sequencing approaches to interrogate the mutational status, transcriptome profile, and cell surface antigen abundance in glioblastoma tissue and GBOs down to the single cell level.

Results: We have generated GBOs from more than 50 patients with IDH wildtype primary glioblastoma with some GBOs from different anatomic regions of the same patient's tumor. GBOs recapitulate the somatic genomic landscape and transcriptome profile of their corresponding parent tumors, indicating the genetic fidelity of this tumor model. Driver mutations and unique cell surface antigens, such as EGFRvIII, are also present at similar abundances and distributions compared to the parent tumor, suggesting that these GBOs preserve the heterogeneity of targetable cellular pathways and tumor-specific markers within the tumor. Importantly, these GBOs also contain important aspects of the tumor microenvironment, such as the presence of non-neoplastic cells including endothelial cells, tumor associated macrophages, and T cells.

Conclusion: GBOs preserve complex tumor heterogeneity within an in vitro culture system, creating new opportunities for extended manipulation and functional study to understand the emergent biological and clinical behavior of this disease.

566: Exploiting Inherent DNA Damage Repair Defects in IDH1/2 Mutated Gliomas with the CNS-Penetrant PARP Inhibitor BGB290

Christopher S. Hong, MD (New Haven, CT); Amrita Sule; Jason Beckta; Ranjini Sundaram; Ranjit Bindra

Introduction: Our group recently demonstrated that IDH1/2-mutated gliomas exhibit intrinsic homologous recombination (HR) defects mediated by the oncometabolite, 2-HG. These defects render IDH1/2-mutated cells exquisitely sensitive to PARP inhibitors (PARPi's), suggesting a novel therapeutic strategy. Here, we studied the potential in vitro and in vivo efficacy of a CNS-penetrant PARPi, BGB290, in combination with radiation therapy (RT) and temozolomide (TMZ) against IDH1/2-mutated gliomas. Our central hypothesis is that multi-modality therapy using agents that are active against 2HG-producing cells will increase efficacy, while allowing lower doses of RT and TMZ as a means to mitigate normal tissue toxicity.

Methods: We performed a comprehensive series of DNA repair functional studies, short- and long-term viability assays, and in vivo studies, using engineered and patient-derived IDH1/2-mutant glioma models. We tested unique combinations of BGB290, TMZ and RT in these experiments.

Results: In vitro short-term viability assays in model IDH1-wild-type (WT) and -R132H mutated glioma cells demonstrated that the mutation confers enhanced TMZ sensitivity (IC50 602 vs. 9.5 uM, respectively). A similar differential sensitivity was observed with RT. We also demonstrated significant, mutant IDH1-selective BGB290 sensitivity in vitro (IC50 0.67 vs. 141 uM). Western blot analysis of PARylation, a functional readout of PARPi activity, confirmed PARylation inhibition by BGB290 in a dose-dependent manner. We also demonstrated synergistic interactions between TMZ and RT combined with BGB290, particularly at low doses of both DNA damaging agents. Finally, we demonstrated the activity of PARPi's against IDH1-mutant tumors in vivo.

Conclusion: BGB290 is a promising, CNS-penetrant PARPi that may selectively target IDH1/2-mutated gliomas, based on intrinsic HR defects associated with these tumors. BGB290 appears to act synergistically with TMZ and RT, which are the backbone of GBM therapies. These data lay the groundwork for a future trial testing trimodality therapy (i.e., BGB290, RT and TMZ) against IDH1/2-mutant gliomas.

567: Differentiating Recurrent Tumor and Treatment Effect in Post-Treatment Recurrent High-Grade Glioma using a Convolutional Neural Network

Deborah Boyett (New York, NY); Jack Grinband, PhD; Kai Canoll; Michael Argenziano, BA; Zachary Englander, MD, MS; Akshay Save, BS; Angela Lignelli, MD; Andrew Lassman, MD; Guy McKhann, MD; Peter Canoll, MD, PhD; Jeffrey Bruce, MD

Introduction: Accurately diagnosing tumor recurrence in post-treatment glioma is difficult because contrast-enhancing (CE) lesions are a mixture of tumor cells, uninvaded brain, and treatment effect. This study characterizes intratumoral heterogeneity using quantitative digital pathology to correlate intraoperative MRI-localized biopsies with histopathology in the post-treatment setting. Findings were used to inform a convolutional neural network (CNN) capable of differentiating recurrent tumor from treatment effect.

Methods: 162 MRI-localized samples obtained during resection of recurrent high-grade glioma in 66 patients were analyzed (median 2 samples/patient). Immunohistochemistry (IHC) with SOX2, CD68, KI67 and NeuN was used to characterize biopsies. Slides were digitized and quantified using an automated cell-counting algorithm. K-means clustering analysis was used to classify biopsies. Clustering designations, quantitative IHC, and radiographic data from 6 MRI sequences were used to train a CNN and generate voxel-wise predictive maps that correlate MRI features with histologic features.

Results: Clustering analysis revealed 3 groups of biopsies: 1) recurrent tumor defined by high SOX2/KI67/H&E; 2) reactive tissue defined by high CD68/low SOX2; and 3) less involved brain defined by high NeuN/low SOX2. Of 48 patients with multiple biopsies, 30 (63%) demonstrated heterogeneity, and 17 (35%) yielded samples demonstrating tumor and treatment effect. The CNN had high accuracy for distinguishing recurrent tumor from treatment effect and normal brain. Model predictions across the entire brain volume revealed heterogeneity of histologic features within both CE and non-enhancing radiographic regions.

Conclusion: Most patients demonstrated intratumoral heterogeneity, highlighting the potential for misdiagnosis from inadequate tumor sampling in post-treatment glioma. Quantitative IHC allowed for clustering of biopsies into 3 distinct groups. The CNN was capable of significantly differentiating between tumor and treatment effect in the post-treatment setting. Future validation with additional biopsies would establish the CNN as a reliable non-invasive methodology for accurately diagnosing tumor recurrence.

568: Longitudinal Analysis of Serum-derived Extracellular RNA for Monitoring of Treatment Response to Dacomitinib in Adult Patients with EGFR Amplified Recurrent Glioblastoma

Anudeep Yekula, MD (Boston, MA); Sudipto Chakraborty; Robert Kitchen; Bob Carter, MD, PhD; Xandra Breakefield, PhD; Johan Skog, PhD; Balaj Leonora, PhD

Introduction: Dacomitinib is a second-generation irreversible tyrosine kinase inhibitor, recently used in a clinical trial (NCT01112527) for recurrent, Epidermal Growth Factor Receptor (EGFR) amplified glioblastomas (GBM). Serum samples were collected prior to the first drug administration and serially thereafter. The goal of the study was to determine whether circulating extracellular RNA (exRNA) are a source of mRNA gene signature that can distinguish (i) a patient with a GBM from a healthy control, (ii) a responder from a non-responder, as defined by the 6 month progression free survival.

Methods: We performed whole-transcriptome sequencing profiling of serum exRNA extracted from 2 ml of sera from 7 responders and 7 non responders.

Results: We compared exRNA profiles of pre-treatment GBM patients and healthy controls, and observed differential expression profiles in several genes implicated in gliogenesis, apoptosis, cell proliferation, cell death and immunomodulation. Individually, exRNA CREBBP, CXCR2 and S100A9 could distinguish GBM patients from healthy controls with > 92.9 % sensitivity and 100% positive predictive value (PPV). We also compared pre-treatment (t=0) and one month post-treatment (t=1) exRNA profiles of responders (n=7) and non-responders (n=7) and determined that exRNAs such as LAMTOR2, ZNF35 and DNMT3A can distinguish responders from non-responders with > 71.4% sensitivity and > 71.4% PPV.

Conclusion: This is a unique study representing the first longitudinal profiling of the extracellular RNA transcriptome in a cohort of EGFR amplified GBM patients. These findings are a tantalizing step toward liquid biopsy-based biomarkers for the detection of GBM, as well as patient stratification and monitoring response to therapy.

569: Reprogrammed TCA Cycle Maintains a Stem-Like Epitranscriptome and Therapeutic Persistence in Glioblastoma Stem Cells

Leo J.Y. Kim, AB (Cleveland, OH); Esther W. Lim, MS; Jason W. Locasale, PhD; Andrew E. Sloan, MD; Christian M. Metallo, PhD; Jeremy N. Rich MD, MHS, MBA

Introduction: Glioblastomas are lethal cancers driven by cancer stem cell (CSC) hierarchies. IDH mutations establish DNA hypermethylation to promote tumorigenesis. Yet how IDH-wildtype glioblastoma stem cells (GSC) metabolically support their epigenetic plasticity remains unclear.

Methods: Whole metabolomes of patient-derived GSCs and their paired differentiated progeny cells (DGCs) were profiled via ¹³C-labeled glucose and glutamine tracing experiments resolved by gas chromatography-coupled mass spectrometry (GC/MS). Metabolic profiles were integrated with matched RNA-seq and enhancer landscapes from H3K27ac ChIP-seq, cross-referenced with bulk tumor single cell RNA-seq. Gene expression was modulated through CRISPR/Cas9 system.

Results: GSCs compared to matched DGCs and neural stem cells depend on the malate-aspartate shuttle (MAS) to fuel proliferation and maintain a stem-like N6-methyladenine (m6A) RNA methylome. High malate dehydrogenase 2 (MDH2) expression was closely associated with TCA cycle intermediate flux into nucleotide synthesis. CRISPR-Cas9-mediated MDH2 disruption reduced GSC stemness and accumulated α-ketoglutarate, an important co-factor for RNA demethylases. MDH2 upregulation by the transcription factor MYC promoted RNA m6A methylation and transcript stability of stem factors, including OLIG1/2. MDH2 upregulation was associated with poor response to dasatinib, a wide-spectrum receptor tyrosine kinase inhibitor. Dasatinib and MDH2 inhibition treatment of GSCs achieved combinatorial therapeutic efficacy in vitro and in vivo.

Conclusions: Stemness in GSC hierarchy requires the MAS system to stabilize stem transcription factor stability through m6A RNA methylation. Exploiting critical metabolic nodes permits simultaneous disruption of GSC epitranscriptome and therapeutic persistence.

570: Identification of 48 Novel Long Noncoding RNAs (lncRNAs) Modulating Glioblastoma Invasion via CRISPR-Interference Functional Screen

Frank Joseph Attenello III, MD (Los Angeles, CA); Kathleen Tsung, MS; Yong-Hwee Loh, PhD; Isaac Bishara, MD; Frank Attenello, MD, MS

Introduction: Glioblastoma (GBM) invasion studies traditionally target coding genes and noncoding microRNAs. Long noncoding RNAs (lncRNAs), are transcripts > 200 nucleotides without coding potential, comprising up to 80% of the genome, but with limited data regarding function. We leveraged CRISPR-interference, repressing lncRNA transcription via Cas9-KRAB, to evaluate invasive function of GBM-associated lncRNAs in a CRISPRi functional screen. We further evaluated pharmacologic lncRNA targeting via antisense oligonucleotide (ASO) aptamers.

Methods: 2,307 candidate lncRNAs were assembled from GBM differential gene expression. Guide RNAs (sgRNAs) targeting candidates were lentivirally incorporated into GBM screening populations (23 million U87 cells, 10 sgRNA/lncRNA, 1000-fold coverage, 247 control scrambled sgRNAs). Cell populations were evaluated via Matrigel invasion, comparing sgRNA populations before/after a 24-hour invasion period. Duplicate screens identified lncRNA sgRNAs associated with reduced GBM invasion relative to control sgRNAs. Individual knockdown of 5 lncRNA "hits" assessed accuracy of screen phenotypes, with invasion assessed via crystal violet stain and lncRNA expression via quantitative PCR. ASO treatment evaluated pharmacologic targeting of candidate lncRNAs in vitro, with in vivo phenotype evaluated via mouse cortical xenografts

Results: Forty-eight lncRNAs were significantly associated with GBM invasion, with lncRNA repression associated with decreased invasion of 31-87% over 24 hours ($p < 0.01$). Individual knockdown validation of candidate lncRNA "hits" confirmed phenotypic invasion effect equal to screening data. Notably, lncRNA LH02236 (non-annotated) repression decreased in vitro growth in addition to decreasing invasion ($p < 0.005$). Furthermore, LH09763 repression was associated with 16-fold decrease in GBM-proliferation in vivo ($p < 0.005$). ASO aptamers decreased lncRNA expression up to 96%

Conclusion: Multiple uncharacterized and non-annotated lncRNAs are associated with in vitro invasion, as well as in vitro and in vivo GBM growth. ASO aptamers offer potential for pharmacologic knockdown of novel lncRNA targets.