

**Stryker Neuro-Oncology Award**

154

**Genomic Landscape of Radiation-Induced Meningiomas**

Suganth Suppiah, MD; Sameer Aghinorti, PhD; Pete Tongs; Yasin Mamatjan; Kenneth D. Aldape, MD; Gelareh Zadeh, MD; PhD, FRCSC (C)

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

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

**RESULTS:** RIMs exhibited a five-fold increase in copy number alterations, commonly the loss of chromosome 1p (17/18 RIMs) and 22q (17/18 RIMs), which was significantly more than observed in sporadic meningiomas. Furthermore, RNA sequencing data revealed an NF2 gene fusion event in 35.3% of RIMs In all 6 cases, there was a complete NF2 exon spliced into a complete exon of a reciprocal gene, suggesting that the breakpoints of genomic rearrangement are intrinsic. All tumours with the NF2 fusion also possessed monosomy of chromosome 22q, rendering the cells with homozygous disruption of NF2. Clinically, RIMs with the NF2 fusion exhibited ill-defined borders and a tendency to develop in anatomic frontal location. The NF2 fusion RIMs, also, had a significantly faster growth rate compared to non-fusion RIMS (P < 0.05). Also, targeted sequencing panel confirmed that RIMs had fewer nonsynonymous NF2 mutations (6.5% vs. 30% in SM) and absence of mutations in TRAF7, SMO, KLF4, PIK3CA and AKT1, genes traditionally involved in SMs.

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

**American Brain Tumor Association Young Investigator Award**

155

**Topical Vancomycin Reduces Surgical-site Infections After Craniotomy: A Prospective, Controlled Study**

Kalil G. Abdullah, MD; Arka Mallela; Andrew Richardson; Timothy H. Lucas, MD, PhD

**INTRODUCTION:** Surgical site infections are an important cause of morbidity and mortality in neurosurgical patients. Topical antibiotics are one potential method to reduce the incidence of these infections. This study examined the efficacy of topical vancomycin applied within the wound during craniotomy in a large prospective cohort study at a major academic center.

METHODS: 355 patients were studied prospectively in this cohort study. 205 patients received 1 g of topical vancomycin powder in the subgaleal space while 150 matched control patients did not. Patients otherwise received identical care. The primary outcome variable was surgical-site infection rate factored by cohort. Secondary analysis examined cost-savings from vancomycin usage estimated from hospital costs associated with SSI in craniotomy patients.

**RESULTS:** The addition of topical vancomycin was associated with a significantly lower rate of surgical site infections than standard of care alone (0.49% (1/205) vs. 6% (9/150), P = 0.002). Based on the costs of revision surgery for infections, topical vancomycin usage was estimated to save $1367,446 per 1000 craniotomy patients. No adverse reactions occurred.

**CONCLUSION:** Topical vancomycin is a safe, effective, and cost-saving measure to prevent surgical-site infections following craniotomy. These results have broad implications for standard of care in craniotomy.

**Journal of Neuro-Oncology Award**

156

**Small Terminal Deletions/Duplications and Alternative Lengthening of Telomeres are Co-Occur in IDH Mutation Only Gliomas**

Desmond A. Brown, MD, PhD; Seiji Yamada, MD, PhD; Thomas Kollmeyer; Paul Decker; Matthew L. Kose, BS; Gobinda Sarkar, PhD; Alissa Caron, BS; Chandrasekhar Halder, BS; Vanessa Y. Ruiz, BS; Benjamin R. Kipp, PhD; Jesse S. Voss, CT, MB, (ASCP); Caterina Giannini; Robert Jenkins

**INTRODUCTION:** Genetic variability is central to gliomagenesis. We recently showed that gliomas fall principally into five molecular groups. Further characterization may refine diagnosis and provide the basis for novel molecular therapeutic targets.

**METHODS:** We performed comprehensive copy number OncoScan array analysis and a 50-gene glioma panel on 148 formalin-fixed paraffin-embedded gliomas. Data validation was performed on the TCGA glioma dataset. Telomere-specific FISH was performed on 87 cases to detect alternative lengthening of telomeres (ALT).

**RESULTS:** Small terminal deletions/duplications were found in 49 gliomas (33%) with 92% observed in IDH-only and TERT-only gliomas. There was increased prevalence of small terminal deletions/duplications in IDH-only relative to TERT-only gliomas (P < 0.0001). These terminal deletions/duplications were present in 20 of 28 (71%) ALT FISH positive cases, 7 of 24 (29%) ALT negative cases, and 4 of 11 (36%) equivocal cases (P = 0.006). ALT FISH positivity was seen in 86% IDH-only tumors versus 11% in TERT-only and triple-positive lesions (P < 0.001). Among IDH-only gliomas, ATRX mutations were detected in 23 of 24 (96%) ALT FISH positive cases versus, 2 of 3 (67%) equivocal cases and was wild type in one ALT FISH negative case (P = 0.023).

**CONCLUSION:** The co-occurrence of small terminal alterations and ATRX mutations in IDH-only tumors raises the probability that copy number variations are the direct result of the ALT phenotype. We found a statistically significant association between the ALT phenotype, ATRX loss and small terminal alterations all of which occur in IDH-only tumors with near exclusivity. Alternatively, more than 80% of tumors with small terminal deletions and duplications were both ATRX mutated and ALT.
FISH positive. Thus, we conclude that the ALT phenotype results in small terminal copy number abnormalities in tumors with a permissive genetic milieu.

Synthes Skull Base Surgery Award

157

Reinventing the Wheel: Intraoperative Continuous Flash Visual Evoked Potentials, a Novel Technique to Lessen Intraoperative Optic Nerves and Chiasmal Injury in Endoscopic Skull Base Surgery

Fahad A. Alkherayf, MD, MSc, CIP, FRCS; David Houlden, PhD; Chantal Turgeon; Charles B. Agbi, MD, FRCS; Andre Lamothe; Kristian Macdonald; Shaun Kilty

INTRODUCTION: Optic nerve/chiasmal injury is a devastating outcome that may happen during endoscopic surgery. A key goal of endoscopic skull-base surgery is visual improvement. Currently, however, there is limited intraoperative visual pathway monitoring. We examine a novel technique that uses continuous flash visual evoked potentials (FVEPs).

METHODS: Eyes were stimulated by light stimulators (3 LEDs on each side, 640 nm peak wavelength, 10 ms pulse width, 3000 mCd of luminous intensity). Uniform illumination was placed over eyelids. Recording electrodes were placed at Oz-Fz. The filter cuts were = 5 Hz and 100 Hz with amplifier gain 20,000 or 50,000. EEG was recorded. Recordings were correlated to pre and post operative VF and acuity. Dropping in the FVEP was examined in relation to intraoperative events. A drop of 20% from the baseline was considered positive.

RESULTS: 101 patients had FVEPs in addition to other neurophysiologic monitoring. Patients demographic data, co-morbidities, diagnosis, surgical approach, length of surgery, MAP, and blood loss during surgery were recorded. All patients’ visual acuity and field deficits were evaluated by neuro-ophthalmologist before their surgery and within 30 days after surgery. In our cohort, one patient had true positive pre-chiasmic while another patient had false negative test result. However, the latter patient’s deficit was post chiasmatic with no optic nerve or chiasmal injury. Another patient had false positive test (drop of 60%). Eight patients had transient changes related to traction of the chiasm or optic nerves. For predicting optic nerve or chiasmal injury, our study showed sensitivity of 100% (CI92.5-100), specificity of 99% (CI94.5-99.97) and negative predicting optic nerve or chiasmal injury, our study showed sensitivity of 99% (CI92.5-100), specificity of 99% (CI94.5-99.97) and negative predicting optic nerve or chiasmal injury. Eight patients had true negative test result. Our study showed that sensitivity of 99% (CI94.5-99.97) and negative predicting optic nerve or chiasmal injury. Eight patients had true negative test result. Our study showed that sensitivity of 99% (CI94.5-99.97) and negative predicting optic nerve or chiasmal injury.

CONCLUSION: FVEP is reproducible throughout surgery and can predict the post-surgical outcome. Additionally, we found that FVEP is transiently affected by different stages of surgery. Further validation is required given the small number of optic/chiasmal injuries in our study.

INTRODUCTION: Silent corticotroph staining pituitary adenoma (SCA), represents an uncommon more locally aggressive subset of Non-Functioning adenomas (NFAs). In this multicenter study, we investigate the safety and effectiveness of Stereotactic Radiosurgery (SRS) in patients with SCA compared with other non-SCA NFAs.

METHODS: Eight centers participating in the International Gamma-Knife Research Foundation (IGKRF) contributed to this study. Outcomes of 50 patients with confirmed SCAs and 307 patients with confirmed non-SCA NFAs treated with SRS were evaluated. Groups were matched. SCA was characterized by a lack of clinical evidence of Cushing disease, yet with positive immunostaining for corticotroph. Median age was 55.2 years (13.7-87). All patients underwent at least one trans-sphenoidal tumor resection prior to SRS. SRS parameters were comparable as well.

RESULTS: Median follow-up 40 months (6-163). Overall tumor control rate (TCR) 91.2% (n = 280). In the SCA group, TCR were 82% (n = 41) vs. 94.1% (n = 289) for the control-NFA (P = 0.0065). The SCA group showed a significantly higher incidence of new post-SRS visual deficit (P < 0.0001) assigned to tumor progression and growth, post-SRS weakness and fatigue (P < 0.0005), and post-SRS new pituitary deficit (P = 0.001). In univariate and multivariate analysis, only the status of silent corticotroph staining (P = 0.005, P = 0.009 respectively) and margin dose (P < 0.0005, P = 0.0037 respectively) significantly influenced progression rate. A margin dose of 17 Gy was noted to influence the adenoma progression rate in the entire cohort (P = 0.003).

CONCLUSION: Silent corticotroph staining represents an independent factor for adenoma progression and hypopituitarism after SRS. A higher margin dose may convey a greater chance of TCR.

159

Factors Associated with Postoperative Complications Following Transsphenoidal Surgery for Pituitary Tumor resection from the national Surgical Quality Improvement Program (NSQIP)

Andrew Karl Rock, MHS; Charles Frederic Opalak, MpH, MD; Kathryn Workman; Matthew Carr, BS; William C. Broadus, MD

INTRODUCTION: Pituitary tumors are the second most common brain tumor (15.9%) in the United States. Transsphenoidal surgery is commonly indicated for pituitary tumors and few studies have investigated postoperative complications following this procedure. Our objective was to utilize the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) to estimate the prevalence of and risk factors for complications following transsphenoidal pituitary surgery.

METHODS: Patients undergoing transsphenoidal surgery for pituitary tumor resection (CPT codes: 61 548, 62 165) from 2005 to 2015 were extracted from the ACS-NSQIP. The prevalence of postoperative complications was determined. Multivariable logistic regression was used to identify demographic, comorbid, and perioperative characteristics associated with any morbidity, severe (Clavien IV) complications, and mortality.

RESULTS: Within 1177 transsphenoidal surgeries, there were 105 (8.92%) cases with at least one non-fatal complication, 29 (2.46%) cases with a severe complication, and 11 (0.93%) cases of mortality. The three most common complications were: reoperation (3.40%), transfusion (2.04%), and unplanned intubation (2.70%). In multivariable