impairment (MCI, n =16), and AD, (n = 16)] acquired by the Alzheimer's Disease Neuroimaging Initiative (ADNI) were analyzed with an automated segmentation software (HippUnfold) to compute thickness measurements. ADNI data such as Positron Emission Tomography (PET) biomarkers, Cerebrospinal Fluid biomarkers, and cognitive scores such as Mini-Mental State Exam (MMSE), Montreal Cognitive Assessment (MoCA), Alzheimer's Disease Assessment Scale (ADAS13), and Rey Auditory Verbal Learning Test (RAVLT), were correlated to thickness along the hippocampal long axis using linear regression models. Results: We found significant cluster correlations ($p < 0.05$) throughout the long axis between hippocampal subfield thickness to MoCA scores, ADAS13 scores, PET phosphorylated tau levels, and PET beta-amyloid levels. Conclusions: Subfield atrophy throughout the hippocampal long axis is associated with disease severity (as measured with existing biomarkers and cognitive testing) in patients with MCI and AD.

E.5

Large scale network changes immediately after Magnetic Resonance Imaging-Guided Laser Interstitial Thermal Therapy (MRgLITT) for hypothalamic hamartoma

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Background: Hypothalamic hamartomas (HH) are a challenging cause of seizure in children, partly because the neural circuitry involved in ictogenesis is incompletely understood. We review our institutions' use of magnetic resonance imaging-guided laser interstitial thermal therapy (MRgLITT) to treat hypothalamic hamartoma (HH) with resting-state fMRI performed immediately before and after ablation. Methods: Seed-based whole brain connectivity to thalamic regions of interest was performed immediately pre- and post- MRgLITT. Multivariable generalized linear models were used to correlate resting-state data with seizure outcomes. Results: Eight patients underwent MRgLITT treatments for HH, with a mean follow up of 29 months. Four patients (50%) were seizure free at 12 months and two (25%) had a significant improvement in seizure frequency. We identified reduced thalamocortical connectivity involving the anterior cingulate and posterior parietal regions, consistent with disconnection of the mammillothalamic tract and interruption of Papez circuit. Large-scale thalamocortical connectivity changes were driven by children who subsequently became seizure free. Conclusions: Disconnection of the mammillothalamic tract and interruption of thalamic circuitry in patients undergoing MRgLITT for HH appears to be associated with improved seizure outcomes. The ability to assess network changes immediately post- MRgLITT could enable operative adjustments to be made mid-procedure to optimize seizure outcome in real time.

Neurosurgery (CNSS)

F.1

DNA methylome profiling identifies stability of IDH mutations throughout glioma evolution

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Background: Isocitrate dehydrogenase (IDH) mutation status is a key diagnostic and prognostic feature of gliomas. There are conflicting reports regarding the stability of IDH mutations throughout glioma evolution and treatment. Here, we provide an institutional experience of patients with conflicting IDH mutation status longitudinally in order to determine if IDH mutation status changes over time. Methods: We retrospectively identified patients from 2009-2018 with immunohistochemistry (IHC)-recorded IDH mutation status discrepancies longitudinally. Archived frozen tissue samples were analyzed using methylation profiling, Sanger sequencing, and droplet digital PCR (ddPCR). Results were compared to the IHC-reported IDH mutation status. Results: We reviewed 1491 archived glioma samples including 91 patients with multiple tumour samples collected longitudinally. In all instances of IDH mutation discrepancy, we found reasonable explanations through multi-platform profiling that resolved the discrepancies. This included the presence of non-canonical IDH2 mutations identified through Sanger sequencing and perilesional tumour samples or reactive brain tissue identified through methylation profiling. Conclusions: Our findings support the hypothesis that IDH mutations occur early in gliomagenesis and are stable throughout glioma treatment and evolution. Our study highlights the importance of accurate surgical sampling and the role of DNA methylome profiling in diagnostically uncertain cases for integrated pathological and molecular diagnosis.

F.2

Multiplatform molecular analysis of vestibular schwannoma reveals two robust subgroups with distinct microenvironment

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Background: Vestibular schwannoma (VS) is the most common tumour of the cerebellopontine angle and poses a significant morbidity for patients. While many exhibit benign behaviour, others have a more aggressive nature. There is a need for a better understanding of the molecular landscape, and important subgroups therein, of this disease. Methods: We select all VS from our tumour bank with both methylation and RNA profiling.

Unsupervised clustering methods were used to define two distinct molecular subgroups of VS which were explored using computational techniques including bulk deconvolution analysis, gene pathway enrichment analysis, and drug repurposing analysis. Methylation data from two other cohorts were used to validate our findings. Results: A total of 75 tumours were analyzed. Consensus clustering and similarity network fusion defined two subgroups ("immunogenic" and "proliferative") with significant differences in immune, stroma, and tumour cell abundance. Gene network analysis and computational drug repurposing found critical differences in targets of immune checkpoint inhibition PD-1 and CTLA-4, the MEK pathway, and the epithelial-to-mesenchymal transition program with associated candidate drug targets, suggesting a need for subgroup-specific treatment/trial design in the future. Conclusions: We leverage computational tools with multi-omic molecular data to define two robust subgroups of vestibular schwannoma with differences in microenvironment and therapeutic vulnerabilities.

F.3

Comprehensive multiplatform analysis of CDKN2A alterations in meningiomas

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Background: In meningiomas, CDKN2A/B deletions are associated with poor outcomes but are rare in most cohorts (1-5%). Large molecular datasets are therefore required to explore these deletions and their relationship to other prognostic CDKN2A alterations. Methods: We utilized multidimensional molecular data of 560 meningiomas from 5 independent cohorts to comprehensively interrogate the spectrum of CDKN2A alterations through DNA methylation, copy number variation, transcriptomics, and proteomics using an integrated molecular approach. Results: Meningiomas with either CDKN2A/B deletions (partial or homozygous loss) or an intact CDKN2A gene locus but elevated mRNA expression ($CDKN2A^{high}$) both had poor clinical outcomes. Increased CDKN2A mRNA expression was a poor prognostic factor independent of CDKN2A deletion. CDKN2A expression and p16 protein increased with tumor grade and more aggressive molecular and methylation groups. $CDKN2A^{high}$ meningiomas and meningiomas with CDKN2A deletions were enriched for similar cell cycling pathways dysregulated at different checkpoints. p16 immunohistochemistry was unreliable in differentiating between meningiomas with and without CDKN2A deletions, but increased positivity was associated with increased mRNA expression. $CDKN2A^{high}$ meningiomas were associated with gene hypermethylation, Rb-deficiency, and lack of response to CDK inhibition. Conclusions: These findings support the role of CDKN2A mRNA expression as a biomarker of clinically aggressive meningiomas with potential therapeutic implications.

F.4

Relationship between poor postoperative pain control and surgical outcomes after elective spine surgery

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Background: Inadequate pain control after spine surgery is common, but its impact on long-term surgical outcomes has not been studied. Accordingly, this study aimed to investigate the relationship between poor postoperative pain control and surgical outcomes. Methods: Consecutive adult patients undergoing elective spine surgery were enrolled. Poor surgical outcome was defined as failure to achieve a minimal clinically important difference (MCID) of 30% improvement on the Oswestry Disability Index or Neck Disability Index at follow-up (3-months, 1-year, 2-years). Poor pain control was defined as a mean numeric rating scale score of >4 within 24-hours postoperatively. Univariable analyses followed by multivariable random-effects models were used, after adjusting for known risk factors that impact surgical outcomes. Results: 42.8% of 1305 patients failed to achieve MCID at follow-up. 56.9% had poor postoperative pain control. Poor pain control was independently associated with failure to achieve MCID (OR 2.15 [95%CI=1.42-3.25], $p<0.001$), after adjusting for age ($p=0.15$), sex ($p=0.59$), PHQ-9 score ($p=0.030$), ASA physical status >2 ($p<0.001$), ≥3 motion segment surgery ($p=0.003$), revision surgery ($p=0.032$), and follow-up time ($p<0.001$). Conclusions: Poor pain control 24-hours after elective spine surgery was an independent risk factor for poor surgical outcome. Perioperative strategies to improve pain control may lead to improved outcomes.

F.5

Spinal column and spinal cord injuries secondary to mountain biking accidents: a 15-year review at a provincial spine referral centre

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Background: Mountain biking (MTB) is an increasingly popular sport that has been associated with serious spinal injuries, which can have devastating effects on patients and significant impacts on healthcare resources. Herein, we characterized the occurrence of these MTB spinal injuries over a 15-year period and analyzed the affiliated acute-care hospital costs. Methods: Patients seen at Vancouver General Hospital for MTB spinal injuries between 2008-2022 were retrospectively reviewed. Demographics, injury details, treatments, outcomes, and resource requirements for acute hospitalization were collected. The Canadian Institute for Health Information was referenced for cost analysis. Results: Over the 15 years of analysis, 149 MTB spinal injuries occurred. The majority (87.2%) were male. 59 (39.6%) were associated with spinal cord injury; most of these were in the cervical spine (72.3%) and majority were AIS