

**GP.4****The epilepsy surgery experience in children with infantile spasms at a tertiary care centre in Canada**

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**Background:** Infantile spasms (IS) is an epileptic encephalopathy, characterized by spasms, hypsarrhythmia, and developmental regression. This is a retrospective case series of children with IS who underwent epilepsy surgery at The Hospital for Sick Children (HSC) in Toronto, Canada. **Methods:** The records of 223 patients seen in the IS clinic were reviewed. **Results:** Nineteen patients met inclusion criteria. The etiology of IS was encephalomalacia in six patients (32%), malformations of cortical development in 11 patients (58%), atypical hypoglycaemic injury in one patient (5%), and partial hemimegalencephaly in one patient (5%). Nine patients (47%) underwent hemispherectomy and 10 patients (53%) underwent lobectomy/lesionectomy. Three patients (16%) underwent a second epilepsy surgery. Fifteen patients (79%) were considered ILAE Seizure Outcome Class 1 (completely seizure free; no auras). The percentage of patients who were ILAE Class 1 at most recent follow-up decreased with increasing duration of epilepsy prior to surgery. Developmental outcome was improved in 14/19 (74%) and stable in 5/19 (26%) patients. **Conclusions:** Our study found excellent seizure freedom rates and improved developmental outcomes following epilepsy surgery in patients with a history of IS with a structural lesion detected on MRI brain.

**GP.5****Identifying clinically relevant prognostic epigenetic subtypes of chordoma and their non-invasive detection in plasma**

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**Background:** Chordomas are rare malignant skull-base/spine cancers with devastating neurological morbidities and mortality. Unfortunately, no reliable prognostic factors exist to guide treatment decisions. This work identifies DNA methylation-based prognostic chordoma subtypes that are detectable non-invasively in plasma. **Methods:** Sixty-eight tissue samples underwent DNA methylation profiling and plasma methylomes were obtained for

available paired samples. Immunohistochemical staining and publicly available methylation and gene expression data were utilized for validation. **Results:** Unsupervised clustering identified two prognostic tissue clusters (log-rank  $p=0.0062$ ) predicting disease-specific survival independent of clinical factors (Multivariable Cox: HR=16.5, 95%CI: 2.8-96,  $p=0.0018$ ). The poorer-performing cluster showed immune-related pathway promoter hypermethylation and higher immune cell abundance within tumours, which was validated with external RNA-seq data and immunohistochemical staining. The better-performing cluster showed higher tumour cellularity. Similar clusters were seen in external DNA methylation data. Plasma methylome-based models distinguished chordomas from differential diagnoses in independent testing sets (AUROC=0.84, 95%CI: 0.52-1.00). Plasma methylomes were highly correlated with tissue-based signals for both clusters ( $r=0.69$  &  $0.67$ ) and leave-one-out models identified the correct cluster in all plasma cases. **Conclusions:** Prognostic molecular chordoma subgroups are for the first time identified, characterized, and validated. Plasma methylomes can detect and subtype chordomas which may transform chordoma treatment with personalized approaches tailored to prognosis.

**GP.6****The Impact of Brain Invasion on Intracranial Meningioma Grading**

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**Background:** In 2016, the WHO Classification of Brain Tumors included brain invasion as a standalone diagnostic criterion for grade 2 meningioma diagnosis. In this study we explored the impact of this change on the incidence and distribution of meningioma grades. **Methods:** All cases of meningiomas diagnosed from 2007-2020 at a tertiary care hospital were identified. The distribution of meningioma grades before (WHO 2007) and after (WHO 2016) the introduction of the 2016 WHO criteria were compared. Each case in the 2007 cohort was re-graded according to the 2016 criteria to determine the intra-class correlation (ICC) between grading criteria. **Results:** Of 814 cases, 532 (65.4%) were in the 2007 WHO cohort and 282 (34.6%) were in the 2016 WHO cohort. There were no differences in the distribution of meningioma grades between cohorts ( $p=0.11$ ). Upon re-grading, 21 cases (3.9%) were changed. ICC between original and revised grade was 0.92 (95% CIs: 0.91-0.93). Amongst Grade 2 meningiomas with brain invasion, 75.8% had three or more atypical histologic features or an elevated mitotic index. **Conclusions:** Brain invasion alone has minimal impact on the incidence or distribution of specific meningioma grade tumors, likely due to cosegregation of grade elevating features.