GR.4

Circadian rhythm influences ischemic core and penumbra volumes in pediatric and young adult populations

R Lun (Palo Alto) A Sreekrishnan (San francisco) S Lee (Palo Alto) G Albers (Palo Alto)*

doi: 10.1017/cjn.2024.71

Background: Circadian rhythms are implicated in timing of stroke onset and infarct progression in adults, but this has not been studied in pediatric/young adult populations. Methods: We queried the RAPID Insights database from centers in USA for unique patients <25 years with a CTP (10/05/2018-09/29/2023) and a minimum ischemic core volume (defined as relative cerebral blood flow (rCBF) reduction of <30%) of >0 cc and minimum mismatch of >0 cc. Imaging time was subdivided into three epochs: Nigh (23:00 h-06:59 h), Day (07:00 h-14:59 h), and Evening (15:00 h-22:59 h). We analyzed age by pre-defined strata: <2 years, 2-5, 6-11, 12-18 and 19-25. Perfusion parameters (core, perfusion volume, mismatch ratio) were analyzed using descriptive statistics. Results: 836 patients were included; 52.3% were in the 19-25 category. Median ischemic cores were larger during the Night (23.0cc [10.0 – 58.0]) compared to Day (19.0cc [8.0-42.0]) or Evening (15.0cc [7.0-33.0]), p=0.009. There was a trend towards larger perfusion volumes in the Night epoch. In the 19-25 group, perfusion volumes were significantly larger at Night (127.5cc [51.5 – 203.5]) compared to Day (74.0cc [33.0 – 139.0]) or Evening (76.0cc [38.0 – 157.5]), with larger mismatch volumes at Night. Conclusions: This is the first study to demonstrate diurnal fluctuations in perfusion parameters in a predominantly pediatric cohort.

GR.5

Establishing the utility of multi-platform liquid biopsy by integrating the CSF methylome and proteome in CNS malignancy

AP Landry (Toronto) JA Zuccato (Toronto) V Patil (Toronto) M Voisin (Toronto) JZ Wang (Toronto) Y Ellenbogen (Toronto) C Gui (Toronto) A Ajisebutu (Toronto) F Nassiri (Toronto) G Zadeh (Toronto)*

doi: 10.1017/cjn.2024.72

Background: Liquid biopsy represents a major development in cancer research, with significant translational potential. Similarly, the integration of multiple molecular platforms has yielded novel insights into disease biology and heterogeneity. We hypothesise that applying contemporary multi-omic approaches to liquid biopsies will improve the power of current models. Methods: We have compiled a cohort of 51 patients with glioblastoma, brain metastasis, and primary CNS lymphoma who underwent CSF sampling as part of clinical care. Cell free methylated DNA and shotgun proteomic profiling was obtained from the CSF of each patient and used to build tumour-specific classifiers. Integrated classifiers were compared with single platform classifiers using multiple approaches. Results: In this study, we show that the DNA methylation and protein profiles of cerebrospinal fluid can be combined to fully discriminate lymphomas from their major diagnostic counterparts with perfect AUCs of 1 (95% confidence interval 1-1) and 100% specificity. Each integrated lymphoma classifier significantly outperforms single-platform classifiers, suggesting synergistic biology is obtained using multiple molecular platforms. Conclusions: We present the most specific and accurate CNS lymphoma classifier to date by integrating the methylome and proteome of CSF. This has important implications for the future of cancer diagnostics and generates immediate utility for patients with CNS lymphoma.

GR.6

Meningioma molecular classification predicts response to surgery and adjuvant radiotherapy: an integrated clinicomolecular analysis & prospective validation

JZ Wang (Toronto) AP Landry (Toronto) V Patil (Toronto) J Liu (Toronto) A Ajisebutu (Toronto) A Cohen Gadol (Bloomington) C Wilson (Tulsa) DA Almiron Bonnin (Seattle) R Yakubov (Toronto) R Kaloti (Toronto) EC Holland (Seattle) G Tabatabai (Tübingen) M Tatagiba (Tübingen) J Barnholtz-Sloan (Bethesda) S Chotai (Nashville) LB Chambless (Nashville) C Horbinski (Chicago) S Yip (Vancouver) F Sahm (Heidelberg) K Aldape (Bethesda) F Nassiri (Toronto) G Zadeh (Toronto)*

doi: 10.1017/cjn.2024.73

Background: Meningiomas are the most common intracranial tumor with surgery, dural margin treatment, and radiotherapy as cornerstones of therapy. Response to treatment continues to be highly heterogeneous even across tumors of the same grade. Methods: Using a cohort of 2490 meningiomas in addition to 100 cases from the prospective RTOG-0539 phase II clinical trial, we define molecular biomarkers of response across multiple different, recently defined molecular classifications and use propensity score matching to mimic a randomized controlled trial to evaluate the role of extent of resection, dural marginal resection, and adjuvant radiotherapy on clinical outcome. Results: Gross tumor resection led to improved progression-free-survival (PFS) across all molecular groups (MG) and improved overall survival in proliferative meningiomas (HR 0.52, 95%CI 0.30-0.93). Dural margin treatment (Simpson grade 1/2) improved PFS versus complete tumor removal alone (Simpson 3). MG reliably predicted response to radiotherapy, including in the RTOG-0539 cohort. A molecular model developed using clinical trial cases discriminated response to radiotherapy better than standard of care grading in multiple cohorts (ΔAUC 0.12, 95%CI 0.10-0.14). Conclusions: We elucidate biological and molecular classifications of meningioma that influence response to surgery and radiotherapy in addition to introducing a novel molecular-based prediction model of response to radiation to guide treatment decisions.