E.2

Proof of concept for liquid biopsy: positive correlation between extracellular vesicles shed by high grade gliomas and volume of hypervascular tumour tissue on MRI

*E Gaudette (Halifax) M Willms (St. John's) J Han (Halifax) J Roy (Moncton) A Weeks (Halifax) M Schmidt (Halifax)**

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Background: High grade gliomas (HGGs) shed extracellular vesicles (EVs) into the bloodstream. EV-derived RNA (EV-RNA) can be detected in plasma, making it a potential biomarker for HGG recurrence after treatment. We sought to establish a baseline relationship between EV-RNA in plasma and hypervascular HGG tissue on MRI. Methods: Eight patients with a new diagnosis of HGG had measurements of plasma EV-RNA and contemporaneous dynamic susceptibility contrast (DSC) MRI. Patient-specific median signal intensity of corpus callosum (mSI-CC) was determined from 10 measurements on the relative cerebral blood volume (rCBV) map. Tumour tissue with signal intensity > mSI-CC and > 2x, > 3x, > 4x and > 5x mSI-CC was segmented on the rCBV map. EV-RNA plasma concentration was correlated with tissue volumes. Results: Pearson correlation showed a significant positive relationship between EV-RNA plasma concentration and tissue volume with signal intensity > mSI-CC ($r(6) = 0.899$, $p = 0.002$). No significant relationship could be detected for progressively smaller tissue volumes with signal intensity > 2x, > 3x, > 4x and > 5x mSI-CC. Conclusions: EV-RNA plasma concentration correlates strongly with the total volume of hypervascular HGG tissue on DSC MRI at baseline and merits further evaluation as a biomarker of tumour behaviour in longitudinal imaging studies.

E.3

fMRI correlates of symptom-specific improvement in STN deep brain stimulation

B Santyr (Toronto) A Loh (Toronto) J Germann (Toronto) A Boutet (Toronto) A Ajala (Niskayuna) J Qiu (Niskayuna) M Abbass (London) A Fasano (Toronto) A Lozano (Toronto)*

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Background: Subthalamic nucleus (STN) deep brain stimulation (DBS) improves the cardinal symptoms of Parkinson's disease (PD). However, the therapeutic mechanisms are incompletely understood. By leveraging patient-specific brain responses to DBS using functional magnetic resonance imaging (fMRI) acquired during stimulation, we identify and validate symptom-specific networks associated with clinical improvement. Methods: Forty PD patients with STN-DBS were enrolled for fMRI using a 30-sec DBS-ON/OFF cycling paradigm. The four cardinal motor outcomes of PD were chosen *a priori* and measured using the Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale, part III (MDS-UPDRSIII): axial instability, tremor, rigidity, bradykinesia. Stimulation-dependent changes in blood oxygen level-dependent (BOLD) signal were correlated with each symptom. Results: The relationship between BOLD response and outcomes revealed significant networks of clinical response ($p<0.001$). Using BOLD responses from the network hubs, each symptom-specific model was significantly predictive of actual improvement: axial instability ($R^2=0.38$, $p=0.000026$), bradykinesia ($R^2=0.29$, $p=0.00033$), rigidity ($R^2=0.40$, $p=0.000013$), tremor ($R^2=0.26$, $p=0.00073$). Conclusions: Using patient-specific imaging, we provide evidence of an association between DBS-evoked fMRI response and individual symptom improvement. Brain networks associated with clinical improvement were different depending on the PD symptom examined, suggesting the presence of symptom-specific networks of efficacy which may allow personalization of DBS therapy.

E.4

Machine learning based patient classification to predict neurological deterioration in mild Degenerative Cervical Myelopathy

A Al-Shawwa (Calgary) M Craig (Calgary) K Ost (Calgary) D Anderson (Calgary) B Jacobs (Calgary) N Evaniew (Calgary) D Cadotte (Calgary)*

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Background: Degenerative Cervical Myelopathy (DCM) is the functional derangement of the spinal cord because of compression from degenerate tissues. Typical neurological symptoms of DCM include gait imbalance and upper extremity paresthesia. While it is thought that greater spinal cord compression leads to increased neurological deterioration, our clinical experience suggests a more complex mechanism involving spinal canal diameter (SCD). Methods: 124 MRI scans from 59 non-operative DCM patients underwent manual scoring of cord compression and SCD measurements. Unsupervised machine learning dimensionality reduction techniques and k-means clustering were used to establish patient groups. These patient groups underwent manual inspection of common compression patterns and SCD similarities to define their unique risk criteria. Results: We found that compression pattern is unimportant at SCD extremes (≤14.5 mm or >15.75 mm). Otherwise, stenosis with clear signs of cord compression at two disc levels and stenosis without clear signs of cord compression at two disc levels result in a relatively higher and lower likelihood of deterioration, respectively. We elucidated five patient groups with unique associated risks for neurological deterioration, according to both SCD range and their cord compression pattern. Conclusions: The specific combination of narrow SCD with focal cord compression increases the likelihood of neurological deterioration in non-operative patients with DCM.

E.5

Designing a paradigm for post endovascular therapy imaging

*C Gargan (Rochester) C Jay (Rochester) L Thompson (Rochester) DE Roberts (Rochester) T Bhalla (Rochester) MT Bender (Rochester) DA Schartz (Rochester) TK Mattingly (Rochester)**

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Background: There is no guideline for imaging post endovascular therapy (EVT). MRI is considered superior to noncontrast CT for assessment of final infarct volume and to distinguish