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

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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

fMRIcorrelates of symptom-specific improvement in STN deep brain stimulation

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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

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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

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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

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contrast from hemorrhage. We sought to align the post EVT imaging practices with those after intravenous thrombolysis Methods: We reviewed the EMR records for all EVT patients from Jan 1, 2019 to Dec 31, 2021. We assessed quantity of CT within 24h of EVT, quantity of MRIs performed, and indications listed. We then undertook an educational program targeting stakeholders. The objective was to transition to MRI at 24h for imaging post EVT. Exceptions included neurologic change, need for antiplatelet infusion, or intraoperative complications. Results: Post intervention, a significant reduction in CT within 24h (-28%, P=0.01) and increase in MRIs (+42%, P<0.00). CT within 24h per patient dropped by 50% (1.12 pre vs 0.57 post). Radiation dose per patient dropped by 49%. Average imaging costs increased by 17%, and the number of transfers off unit for imaging increased by 11%. Good functional outcome dropped from 44% preintervention to 34% postintervention (P=0.06). Conclusions: This represents the first systematic evaluation of post EVT imaging in a single center. We demonstrate successful behavior changes for post EVT imaging.

NEUROSURGERY (CNSS)

F.1

Oscillatory network markers of subcallosal cingulate deep brain stimulation for depression

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Background: Identifying functional biomarkers related to treatment success can aid in optimizing therapy and provide a better understanding of the neural mechanisms of treatment-resistant depression (TRD) and subcallosal cingulate deep brain stimulation (SCC-DBS). Methods: Magnetoencephalography data were obtained from 16 individuals with SCC-DBS for TRD and 25 healthy subjects. We identified region-specific oscillatory modulations that both (i) discriminate individuals with TRD (SCC-DBS OFF) from healthy controls and (ii) discriminate responders from non-responders (SCC-DBS ON). The effects of stimulation intensity and frequency were also explored. Results: Discriminative regions that differentiated responders from non-responders based on modulations of increased alpha (8-12 Hz) and decreased gamma (32-116 Hz) power included nodes of the default mode, central executive, and somatomotor networks, Broca's area, and lingual gyrus. Furthermore, low stimulation frequency had stronger effects on oscillatory modulation. Conclusions: The identified functional biomarkers implicate modulations of TRD-related activity in brain regions involved in emotional control/processing, motor control, and interactions between speech, vision, and memory – all implicated in depression. These electrophysiological biomarkers have the potential to be used as functional proxies for therapy optimization. Additional stimulation parameter analyses revealed that oscillatory modulations are strengthened by increasing stimulation intensity or reducing frequency, which may benefit SCC-DBS non-responders.

F.2

Comprehensively mapping transcriptionally relevant histone modifications in aggressive meningioma leads to novel biologic insights and therapeutic vulnerabilities

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Background: We recently identified four molecular subgroups of meningioma with distinct biology and outcomes. While two (MG3/MG4) are associated with poor outcome, they display divergent transcriptional profiles (enriched in metabolic and cell cycling pathways, respectively) and therapeutic vulnerabilities (MG3 has no clear treatment target). We sought to understand drivers of these key differences at a chromatin level. Methods: We profiled MG3/MG4 meningiomas for common histone marks H3K27me3, H3K27Ac, H3K4me1, H3K4me3, H3K9me3, and H3K36me3. Multiple computational approaches were used to compare MG3 and MG4 tumours including superenhancer ranking, differential binding analysis, and unsupervised clustering. Results: Our cohort includes 11-20 meningiomas per histone mark. Clustering revealed striking separation of subgroups based on multiple histone marks, particularly H3K36me3. FOXC1, a known driver of the epithelial to mesenchymal transition, was identified as a recurrent superenhancer in both groups, whereas MG3-specific superenhancers mapped to immune regulatory networks. Integrated differential binding analysis confirmed an immune-rich microenvironment in MG3 tumours driven by multiple histone marks, suggesting a role for targeting novel immune checkpoint genes CD84 and CD48. Conclusions: This study is the first to apply integrated analysis of multiple histone modifications to aggressive meningioma. We further characterize MG3 tumours by identifying an epigenetically-driven immune phenotype and propose novel treatment targets.

F.3

Multicentre prospective validation of integrated molecular classification of meningiomas and prediction of recurrence risk using DNA methylation

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Background: Meningiomas have significant heterogeneity between patients, making prognostication challenging. For this

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