are defined. Unique recommendations for DIPG response include an eight-week response duration, a twenty-five percent decrease for partial response, and the distinction of pontine and extra-pontine response for trials that use focal drug delivery. The recommendations presented here represent an initial effort to uniformly collect and evaluate response assessment criteria; these recommendations can now be incorporated into clinical trials to assess feasibility and corroboration with patient outcomes.

IMG-10. MRI-BASED RADIOMIC PROGNOSTIC MARKERS OF DIFFUSE MIDLINE GLIOMA

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BACKGROUND: Diffuse midline gliomas (DMG) are lethal pediatric brain tumors with dismal prognoses. Presently, MRI is the mainstay of disease diagnosis and surveillance. We aimed to identify prognostic image-based radiomics markers of DMG and compare its performance to clinical variables at presentation. METHODS: 104 treatment-naïve DMG MRIs from five centers were used (median age=6.5yrs; 18 males, median OS=11mos). We isolated tumor volumes of T1-post-contrast (T1gad) and T2-weighted (T2) MRI for PyRadiomics high-dimensional feature extraction. 900 features were extracted on each image, including first order statistics, 2D/3D Shape, Gray Level Co-occurrence Matrix, Gray Level Run Length Matrix, Gray Level Size Zone Matrix, Neighboring Gray tone Difference Matrix, and Gray Level Dependence Matrix, as defined by Imaging Biomarker Standardization Initiative. Overall survival (OS) served as outcome. 10-fold cross-validation of LASSO Cox regression was used to predict OS. We analyzed model performance using clinical variable (age at diagnosis and sex) only, radiomics only, and radiomics plus clinical variable. Concordance metric was used to assess the Cox model. RESULTS: Nine radiomic features were selected from T1gad (2 texture wavelet) and T2 (5 first-order features (1 original, 4 wavelet), 2 texture features (1 wavelet, 1 log-sigma). This model demonstrated significantly higher performance than a clinical model alone (C: 0.68 vs 0.59, p<0.001). Adding clinical features to radiomic features slightly improved prediction, but was not significant (C=0.70, p=0.06). CONCLUSION: Our pilot study shows a potential role for MRI-based radiomics and machine learning for DMG risk stratification and as image-based biomarkers for clinical therapy trials.

IMG-12. CHARACTERISATION OF MODELS OF *H3F3A*_G34R/V MUTANT PAEDIATRIC GLIOBLASTOMA *IN VIVO* USING MAGNETIC RESONANCE IMAGING

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Approximately 15% of paediatric/young adult cerebral hemispheric glioblastomas (pGBM) harbour G34R/V mutations in *H3F3A*, encoding the histone H3.3 variant. Development of novel therapeutic interventions demands models that accurately recapitulate this subset of disease and sensitive imaging methods with which to study tumours *in situ*. Three *H3F3A*_G34R primary-patient-derived cultures, alongside established cell-line KNS42 (*H3F3A*_G34V), were implanted orthotopically in immunocompromised mice. KNS42 (*TP53*_R342*) tumours were clearly detectable using T_2-weighted (T_2w)-MRI, enhanced following contrast agent administration, indicating impaired blood-brain barrier (BBB) integrity, and demonstrated minimal invasion. OPBG_GBM_001 cells (*TP53*_89-90X,*ATRX*_II2133-2144X) formed infiltrative tumours that were hyperintense on T_2w-MRI and demonstrated contrast-enhancement suggestive of heterogeneous BBB integrity. HSJD_GBM_002 cells (*TP53*_P278T,*ATRX*_R666*) spread diffusely throughout the brain with their full extent typically not discernible by T_2w-MRI, the BBB also remaining intact. No evidence of CHOP_GBM_001 tumour was detected by MRI 11months post-implantation. Immunocompetent syngeneic models using tumour cells induced by mutations modelling hemispheric pGBM (NRAS/shP53/shATRX±H3.3G34R) are being explored. Fast growing heterogeneous lesions with variable contrast-enhancement were identified; the H3.3G34R mutation conferred longer median survival (2 clones:25/28days, control:14days). These models have the advantage of an intact immune system and short latency for initial efficacy studies. Primary pGBM cells yield tumours that are more representative of the spectrum of clinical disease; variable hyperintensity on T_2w-MRI corresponding to cellular density, with diffusely infiltrative disease less clearly definable, a paucity of oedema and a range of contrast-enhancement. Pathological features including giant multinucleated cells, and mitotic figures were also evident.

IMG-13. MRI-BASED RADIOMICS PROGNOSTIC MARKERS OF POSTERIOR FOSSA EPENDYMOMA

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PURPOSE: Posterior fossa ependymomas (PFE) are common pediatric brain tumors often assessed with MRI before surgery. Advanced radiomic analysis show promise in stratifying risk and outcome in other pediatric brain tumors. Here, we extracted high-dimensional MRI features to identify prognostic, image-based, radiomics markers of PFE and compared its performance to clinical variables. METHODS: 93 children from five centers (median age=3.3yrs; 59 males; mean PFS=50mos) were included. Tumor volumes were manually contoured on T1-post contrast and T2-weighted MRI for PyRadiomics feature extraction. Features include first-order statistics, size, shape, and texture metrics calculated on the original, log-sigma, and wavelet transformed images. Progression free survival (PFS) served as outcome. 10-fold cross-validation of a LASSO Cox regression was used to predict PFS. Model performance was analyzed and concordance metric (C) was determined using clinical variable (age at diagnosis and sex) only, radiomics only, and radiomics plus clinical variable. RESULTS: Six radiomic features were selected (all T1): 1 first-order kurtosis (log-sigma) and 5 texture features (3 wavelet, 2 original). This model demonstrated significantly higher performance than a clinical model alone (C: 0.69 vs 0.58, p<0.001). Adding clinical features to the radiomic features didn't improve prediction (p=0.67). For patients with molecular subtyping (n=48), adding this feature to the clinical plus radiomics models significantly improved performance over clinical features alone (C = 0.79 vs. 0.66, p=0.02). Further validation and model refinement with additional datasets are ongoing. CONCLUSION: Our pilot study shows potential role for MRI-based radiomics and machine learning for PFE risk stratification and as radiographic biomarkers.

IMG-14. DEVELOPING A PREDICTIVE GRADING MODEL FOR CHILDREN WITH GLIOMAS BASED ON DIFFUSION KURTOSIS IMAGING METRICS: ACCURACY AND CLINICAL CORRELATIONS WITH SURVIVAL

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PURPOSE: To develop a predictive grading model based on diffusion kurtosis imaging (DKI) metrics in children affected by gliomas, and to investigate the clinical impact of the model via correlations with overall survival and progression-free survival. MATERIALS AND METHODS: We retrospectively studied 59 children (33M, 26F, median age 7.2 years) affected by gliomas on a 3T magnet. Patients with tumor locations other than infratentorial midline were included. Conventional and DKI sequences were obtained. Mean kurtosis (MK), axial kurtosis (AK), radial kurtosis (RK), fractional anisotropy (FA) and apparent diffusion coefficient (ADC) maps were obtained. Whole tumor volumes (VOIs) were segmented semiautomatically. Mean DKI values were calculated for each metric. The quantitative values from DKI-derived metrics were used to develop a predictive grading model with penalized logistic regression (glmnet package, R). Elasticnet regularization was used to avoid model overfitting. Fitted model coefficients from each metric were used to develop a probability prediction of a high-grade glioma (HGG). Grading accuracy of the resulting probabilities was tested with ROC analysis. Finally, model predictions were correlated to progression-free survival (PFS) with a Kaplan-Meier analysis. RESULTS: The cohort included 46 patients with low-grade gliomas (LGG) and 13 patients with HGG. The developed model predictions yielded an AUC of 0.946 (95%CI: 0.890–1). Model predictions were significantly correlated with PFS (23.1 months for HGG vs 34.7 months for LGG, p<0.004). CONCLUSION: In our cohort, a DKI-based predictive model was highly accurate for pediatric glioma

grading. DKI-based model predictions were significantly correlated with progression-free survival.

IMG-15. PEDIATRIC GLIOBLASTOMAS CONTRAST ENHANCEMENT PATTERN IS PREDICTIVE OF SURVIVAL

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BACKGROUND: Pediatric GBMs are rare, accounting for 3% of all pediatric CNS tumors. Despite advances in treatment, the outcomes for pediatric glioblastomas (GBM) have not significantly improved. Research suggests a link between enhancement patterns and survival in adult patients with glial tumors. We sought to study this relationship in a cohort of pediatric GBMs. METHODS: A radiology database was searched for cases < 22 years, pathology proven brain glioblastoma, and pre-surgical MR imaging available for review. Based on pre-treatment, T1-contrast enhanced MR images, size, and contrast enhancement patterns were characterized as focal, diffuse, or ring-like. The extent of resection was assessed by comparing pre- and post-surgery T2 hyperintensity and contrast enhancement. RESULTS: 64 eligible patients (age 2-21y, 14.6 + 5.4) were identified. The majority of lesions demonstrated enhancement on gadolinium-enhanced T1 imaging. (n=58/64; 90%). The lesions were categorized into six (9.4%) cases with focal enhancement, 37 (57.8%) cases with diffuse enhancement, and 15 (23.4%) with ring-like enhancement. Patients who received GTR/subtotal resection (STR) and had focal-enhanced GBMs had a significantly longer progression-free survival (PFS) – 14.1 months (p = 0.0308), comparing to diffuse and ring-like enhancing glioblastomas which had respectively 13.9 and 5.5 months of PFS. DISCUSSION: Our data suggests that the contrast enhancement pattern is a significant prognostic factor for survival in pediatric GBM. Patients with GTR/STR who had focal-enhancing GBMs had a significantly longer progression-free survival (p=0.03) comparing to other enhancement patterns.

IMG-16. WHOLE TUMOR DIFFUSION KURTOSIS IMAGING ANALYSIS FOR DISCRIMINATING PEDIATRIC POSTERIOR FOSSA TUMORS: ACCURACY AND REPEATABILITY

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PURPOSE: Diffusion kurtosis imaging (DKI) has not yet been tested for pediatric brain tumors. Estimating diffusion values from whole-tumor based (VOI) segmentations may improve diffusion measurement repeatability compared to conventional region-of-interest (ROI) approaches. Our purpose was to compare repeatability between ROI and VOI DKI-derived diffusion measurements and to assess VOI-based DKI accuracy in discriminating among pediatric posterior fossa tumors. MATERIALS AND METHODS: We retrospectively analyzed 34 children (19 M, 15F, mean age 7.48 years) with posterior fossa tumors who underwent preoperative 3T MRI including DKI. For each patient, two neuroradiologists independently segmented the whole solid tumor (VOI), the area of maximum tumor diameter and a smallROI.Inter-observer variability was assessed with coefficient of variation (COV) and Bland-Altman plots. VOI-based DKI metrics accuracy in discriminating among tumor histology and for tumor grading were assessed with MANOVA and ROC analyses respectively. Correlation between grading accuracy and inter-observer variability was assessed with Spearman's rho. RESULTS: Tumor histology included medulloblastoma (15), pilocytic astrocytoma (14) and ependymoma (5). VOI-based measurements presented lower variability than ROI-based measurements across all DKI metrics. DKI-derived metrics could accurately discriminate between tumor subtypes (Pillai's trace: p<0.001) and were accurate for tumor grading (AUCs of 0.919, 0.986, 0.996, 0.842 and 0.926 for RK, MK, AK, FA and MD respectively). VOI-based COV was significantly correlated to AUC values (R=-0.900, p<0.037). CONCLUSIONS: DKI-derived metrics are useful for pediatric posterior fossa tumor discrimination and grading. VOI-based diffusion measurements present improved repeatability compared to ROI-based measurements and are significantly correlated to diagnostic accuracy.

IMG-17. RADIOMICS CHARACTERIZATION OF FOUR PEDIATRIC BRAIN TUMOR SUBTYPES IN PDX MOUSE MODELS

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BACKGROUND: Previously, we have reported on the development of advanced magnetic resonance imaging (MRI) protocols for mouse brain tumors. The goal of this follow-up pre-clinical study was to develop a machine-learning MRI classifier (radiomics) for four subtypes of childhood brain tumor in patient-derived xenograft (PDX) mice. METHODS: MRI scans on orthotopic medulloblastoma, ependymoma, ATRT and DIPG PDX (each n=12 animals) were performed on the animal 9.4 Tesla scanner with an in-plane resolution of 47 microns. Image segmentation, as well as shape and texture based radiomics descriptors were modeled using a modified COLIAGE software for tumor classification and to characterize tumor habitat of each tumor subtype. RESULTS: The mean tumor volumes were 11.2 mm^3. Each MRI scan was segmented into three regions: (i) well defined tumor (including distant metastases); (ii) peritumoral edema; (iii) tumor necrosis. 360 radiomics features (capturing co-occurrence, grey-level dependence and directional gradients) were obtained for each region. The model classified four subtypes with high accuracy while achieving sufficient segmentation accuracy despite the small lesion size. A subset of fourteen tumoral, six peritumoral and five distant MRI radiomics features were found to be predictive of the tumor sub-type (p=0.0017) independently of tumor anatomical location. CONCLUSIONS: MRI protocols followed by radiomics feature analysis discriminated among specific radiological features for four distinct orthotopic PDX models: medulloblastomas exhibit low ADC values, high angiogenesis and cortical metastases as compared to ependymomas (high levels of edema and olfactory bulb metastases), ATRT (the highest level of necrosis) and DIPG (highest T2 signal intensities and spinal metastases).

IMG-18. ASSESSMENT OF SUSPECTED DISEASE PROGRESSION USING MULTIPARAMETRIC 18F-CHOLINE PET/MRI IN CHILDHOOD AND TEENAGE-YOUNG ADULT GLIOMAS

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OBJECTIVES: Evaluation of post-treatment glioma burden remains a significant challenge in children, teenagers and young adults (TYA). The aim of this study was to evaluate the utility of ChoPET/MRI for evaluation of suspected disease progression in childhood and TYA gliomas. METHODS: 27 patients (mean age 14 years, range 6–21 years) with suspected glioma disease progression were evaluated with ChoPET/MRI (n=59). Relative cerebral blood volume (rCBV), apparent diffusion coefficient (ADC) and maximum standardised uptake values (SUV_{max}) in enhancing (enh) and non-enhancing (ne) tumour and normal-appearing white matter (wm) were calculated ($rCBV_{enh}$, $rCBV_{ne}$, $rCBV_{wm}$, ADC_{enh}, ADC_{ne}, ADC_{wm}, SUV_{enh}, SUV_{ne}, SUV_{wm}). 2 blinded radiologists scored tumour probability (1 = unlikely; 5 = definitely). Sensitivity and specificity calculated with gold standard histopathology or clinical follow-up. RESULTS: Accuracy for the detection of residual/recurrent tumour on conventional MRI was 96.3% (91.7% ≤14 years, 100% ≥15 years) and ChoPET was 73.1% (66.7% ≤14 years, 80.0% ≥15 years). Lack of agreement was observed in 9/27 patients, with ChoPET superior to MRI in 1 case of a posterior fossa tumour. Tumour component analysis demonstrated significantly higher SUV_{enh} and SUV_{ne} than SUV_{wm} (SUV_{enh}: p<0.001; SUV_{ne}: p=0.004, equivalent to results were observed for ADV and rCBV (ADC_{enh}, ADC_{ne}: p<0.001 vs ADC_{wm}; $rCBV_{enh}$, $rCBV_{ne}$: p<0.001 vs $rCBV_{wm}$). CONCLUSIONS: MRI is more sensitive than ChoPET in the evaluation of suspected disease progression in TYA gliomas. However, quanititative ChoPET is able to detect enhancing and non-enhancing tumour and may be helpful in evaluating posterior fossa disease where MRI is equivocal.

IMG-19. RADIOMICS AND SUPERVISED DEEP LEARNING TO PREDICT MOLECULAR SUBGROUPS IN MEDULLOBLASTOMA BASED ON WHOLE TUMOR VOLUME LABELING: A SINGLE CENTER MULTIPARAMETRIC MR ANALYSIS

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PURPOSE: Medulloblastoma (MB) is a complex pathology. Four molecular subgroups have been unveiled (Wingless-WNT, Sonic Hedgehog-SHH, Group 3-G3 and Group 4-G4), characterized by significant differences in patient clinical outcome. We investigated the utility of a radiomic analysis to predict molecular subgroups in patients with MB. MATERIALS