reveals reduced ADCs in responding tumors, with the percent change in ADC from baseline correlating with deeper RANO responses. CONCLUSION: DWI analysis reveals reductions in ADC values that correlates with treatment response and a shift toward more normal cellularity in tumors treated with DAY101. Changes in ADC may represent a novel imaging biomarker, reflecting biological response to DAY101 treatment.

IMG-06. PREDICTING SURVIVAL FROM PERFUSION AND DIFFUSION MRI BY MACHINE LEARNING

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INTRODUCTION: Magnetic Resonance Imaging (MRI) is routinely used in the assessment of children's brain tumours. Reduced diffusion and increased perfusion on MRI are commonly associated with higher grade but there is a lack of quantitative data linking these parameters to survival. Machine learning is increasingly being used to develop diagnostic tools but its use in survival analysis is rare. In this study we combine quantitative parameters from diffusion and perfusion MRI with machine learning to develop a model of survival for paediatric brain tumours. METHOD: 69 children from 4 centres (Birmingham, Liverpool, Nottingham, Newcastle) underwent MRI with diffusion and perfusion (dynamic susceptibility contrast) at diagnosis. Images were processed to form ADC, cerebral blood volume (CBV) and vessel leakage correction (K2) parameter maps. Parameter mean, standard deviation and heterogeneity measures (skewness and kurtosis) were calculated from tumour and whole brain and used in iterative Bayesian survival analysis. The features selected were used for k-means clustering and differences in survival between clusters assessed by Kaplan-Meier and Cox-regression. RESULTS: Bayesian analysis revealed the 5 top features determining survival to be tumour volume, ADC kurtosis, CBV mean, K2 mean and whole brain CBV mean. K-means clustering using these features showed two distinct clusters (high- and low-risk) which bore significantly different survival characteristics (Hazard Ratio = 5.6). DISCUSSION AND CONCLUSION: Diffusion and perfusion MRI can be used to aid the prediction of survival in children's brain tumours. Tumour perfusion played a particularly important role in predicting survival despite being less routinely measured than diffusion.

IMG-07. GADOLINIUM IS NOT NECESSARY FOR SURVEILLANCE MR IMAGING IN CHILDREN WITH CHIASMATIC-HYPOTHALAMIC LOW GRADE GLIOMA

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BACKGROUND: Patients with chiasmatic-hypothalamic low grade glioma (CHLGG) have frequent MRIs with gadolinium based contrast agents (GBCA) for disease monitoring. Cumulative gadolinium deposition in children is a potential concern. The purpose of this research is to establish whether MRI with GBCA is necessary for determining tumor progression in children with CHLGG. METHODS: Children with progressive CHLGG were identified from Texas Children's Cancer Center between 2005–2019. Pre- and post-contrast MRI sequences were separately reviewed by one neuroradiologist who was blinded to the clinical course. Three dimensional measurements and tumor characteristics were collected. Radiographic progression was defined as a 25% increase in size (product of two largest dimensions) compared to baseline or best response after initiation of therapy. RESULTS: A total of 28 patients with progressive CHLGG including 683 MRIs with GBCA (mean 24 MRIs/patient; range: 10–43 MRIs) were reviewed. No patients had a diagnosis of NF1. Progression was observed 92 times, 91 (98.9%) on noncontrast and 90 (97.8%) on contrast imaging. Sixty-seven radiographic and/or clinical progressions *necessitating management changes* were identified in all (100%) noncontrast sequences and 66 (98.5%) contrast sequences. Tumor growth >2 mm in any dimension was identified in 184/187(98.4%) on noncontrast and 181/187(96.8%) with contrast imaging. Non primary metastatic disease was seen in seven patients (25%), which were better visualized on contrast imaging in 4 (57%). CONCLUSION: MRI without GBCA effectively identifies patients with progressive disease. One should consider eliminating contrast in imaging of children with CHLGG with GBCA reserved for monitoring those with metastatic disease.

IMG-08. UNUSUAL IMAGING FINDINGS IN TWO CASES OF PAEDIATRIC LOW GRADE GLIOMA

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Low grade gliomas (LGG), including pilocytic astrocytoma (PCA), are the commonest paediatric brain tumours and their behaviour is well understood, typically following a benign course. BRAF fusion is common, particularly in PCA of the cerebellum and optic pathway. Here we present two patients whose LGG behaved in an unusual fashion. The first patient who was treated 6 years previously on LGG2 with vincristine and carboplatin for a tectal plate lesion was identified on routine imaging to have local tumour progression and underwent completion staging. This showed a new enhancing soft tissue abnormality within the spinal cord at the level of L2. Due to radiological dubiety both lesions were biopsied for histological and molecular analysis, confirming LGG of the tectal plate and finding the spinal lesion to be a myxopapillary ependymoma. The second patient presented with acute hydrocephalus following a 2 year history of neurocognitive impairments. He was found to have a large, complex tumour centred in and expanding the bodies of both lateral ventricles with significant mass effect. Radiologically this was most in keeping with a central neurocytoma but histological analysis confirmed it to be a PCA with KIAA1549-BRAF fusion. The first case demonstrates the utility of molecular analysis in confirming two distinct tumour types in one patient, in a situation where metastasis would not be expected and would significantly alter treatment and prognosis. The second is an example of how imaging can be misleading in a KIAA1549-BRAF fused PCA presenting as an intraventricular mass.

IMG-09. RESPONSE ASSESSMENT IN DIFFUSE INTRINSIC PONTINE GLIOMA (DIPG): RECOMMENDATIONS FROM THE RESPONSE ASSESSMENT IN PEDIATRIC NEURO-ONCOLOGY COMMITTEE

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Optimizing the conduct of clinical trials for diffuse intrinsic pontine glioma (DIPG) involves use of consistent, objective disease assessments and standardized response criteria. The Response Assessment in Pediatric Neuro-Oncology (RAPNO) committee, an international panel of pediatric and adult neuro-oncologists, clinicians, radiologists, radiation oncologists, and neurosurgeons, was established to address unique challenges in assessing response in children with CNS tumors. A subcommittee of RAPNO was formed to specifically address response assessment in children and young adults with DIPG and to develop a consensus on recommendations for response assessment. Distinct issues related to the response assessment of DIPG include its definition and recent molecular classifications, dearth of imaging response data, the phenomena of pseudoprogression, and measuring response in the era of focal drug delivery. The committee has recommended response be assessed using magnetic resonance imaging (MRI) of brain and spine, neurologic examination, and use of supportive medication, i.e. steroids and anti-angiogenic agents. Clinical imaging standards and imaging quality control

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