Title

NIMG-50. INITIAL EXPERIENCE: DETECTION OF ABERRANT HYPERPOLARIZED [1-13C]PYRUVATE METABOLISM IN PATIENTS WITH GBM PRIOR TO RESECTION

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cerebral blood volume (nrCBV); a novel metric that characterizes glycolytic status (aerobic glycolytic index, AGI) was calculated by dividing amine CEST contrast by rOEF. Patients in Study I were additionally scanned by ^{18}F-fluorodeoxyglucose (FDG)-PET. Stereotactic image-guided biopsies were performed on patients in Study II and III, and samples were analyzed by immunohistochemistry (IHC) and extracellular flux bioenergetic analysis, respectively. Pairwise correlation between MR metrics and standardized uptake value of ^{18}F-FDG, IHC metrics, or indices of cellular metabolism was calculated using Spearman's correlation analysis. In Study I, AGI showed very strong significant correlation with ^{18}F-FDG uptake in glioma (correlation coefficient $\rho = 0.86$, $P = .014$). In Study II, AGI was significantly correlated with glucose transporter 3 ($\rho = 0.71$; $P = 0.0041$) and hexokinase 2 ($\rho = 0.73$; $P = 0.0029$) in IDH wild-type glioma, while it was significantly correlated with monocarboxylate transporter 1 ($\rho = 0.59$; $P = 0.0094$) in IDH mutant glioma. This result may reflect the different glycolytic statuses of these gliomas; specifically, the rate-limiting steps in glycolysis. In Study III, a strong significant correlation with cellular AGI derived from the bioenergetic analysis was found for AGI derived from MRI ($\rho = 0.79$, $P = .036$). In conclusion, AGI derived from MRI was correlated with FDG, IHC measurements, and cellular AGI. Future studies investigating the clinical utility of AGI in prediction and evaluation of treatment effects are warranted.

NIMG-50. INITIAL EXPERIENCE: DETECTION OF ABERRANT HYPERPOLARIZED [1-^{13}C]PYRUVATE METABOLISM IN PATIENTS WITH GBM PRIOR TO RESECTION

Adam Autry[1], Jeremy Gordon[1], Marisa LaFontaine[1], Hsin-Yu Chen[1], Javier Villanueva-Meyer[1], Susan Chang[1], Jennifer Clarke[2], Duan Xu[1], Janine Lupo[1], Peder Larson[1], Daniel Vigneron[1], and Yan Li[1]; [1]University of California, San Francisco, San Francisco, CA, USA, [2]Department of Neurological Surgery, University of California (UCSF), San Francisco, San Francisco, CA, USA, San Francisco, CA, USA

INTRODUCTION: Detecting radiological response or resistance to treatment in patients with GBM is difficult with conventional MRI. In response to this challenge, hyperpolarized carbon-13 (HP-^{13}C) MRI techniques were developed to probe real-time [1-^{13}C]pyruvate metabolism. METHODS: Dynamic HP-^{13}C MRI was acquired pre-operatively from 6 patientswith recurrent GBM following intravenous injection of HP [1-^{13}C]pyruvate. Five were confirmed with tumor progression and one had treatment effects without progression. Frequency-selective echo-planar imaging (8 slices, 3s temporal resolution, 3.38 cm^3 spatial resolution, 60s acquisition) captured [1-^{13}C]pyruvate metabolism to [1-^{13}C]lactate and [1-^{13}C]bicarbonate in the brain. Proton imaging included 3-D FLAIR, T1-weighted post-Gd IRSPGR, and spectroscopy. Carbon-13 voxels with non-enhancing lesion (NEL) or contrast-enhancing lesion (CEL) were identified for subsequent analysis. Temporally-summed HP-^{13}C metabolite data within the CEL and NEL were evaluated using the pyruvate-to-lactate ratio; a modified ratio that takes into account vascular contributions of pyruvate; and parameter percentile ranks over the entire brain. Proton spectroscopy data were processed to obtain choline-to-NAA index (CNI) maps, which provide z-scores of relative tissue abnormality. RESULTS: All of the anatomic lesions displayed abnormal CNI with maximum values of 3.22-6.35. The 5 patients with CEL lesions demonstrated 87th– 98thpercentile levels of pyruvate in the brain; and 95th-100thpercentile levels of lactate in 4 progressed patients and 60thpercentile in the patient presenting with treatment effects. For the patient with an exclusively non-enhancing lesion, percentile levels of pyruvate and lactate were 66thand 88thin the brain, respectively. The mean+/-SD percentile of the lactate-to-pyruvate and modified ratios were 75+/-22, 86+/-23 and 60+/-3, 71+/-12 in the progressed and non-progressed patients, respectively. CONCLUSION: These data importantly demonstrate aberrant [1-^{13}C]pyruvate metabolism in patients with GBM in both contrast-enhancing and non-enhancing lesions. Ongoing studies will further characterize the utility of HP imaging markers.

NIMG-51. CONVENTIONAL MRI RADIOMIC FEATURES IMPROVE PROGNOSTICATION AND ARE PREDICTIVE OF H3 K27M STATUS IN DIPG

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BACKGROUND: Genomic profiling of DIPG suggests distinct and clinically relevant molecular subgroups based on the presence and isoform of histone H3 K27M mutation. We evaluated the impact of radiomic features on the classification and prognostication of 81 histologically confirmed and centrally reviewed DIPG. METHODS: We utilized a combination of manual and automatic segmentation (DeepMedic) to define tumor volume and Pyradiomics for computation of radiomic features. Imaging feature stability was assessed by calculating concordance correlation coefficient (CCC) for each radiomic parameter from two separate pretreatment MRIs. Bootstrapped least absolute shrinkage and selection operator (LASSO) was used for feature selection. Classification and prognostication models, incorporating H3 status and clinical variables, were developed using random forest, Cox proportional hazards, and deep learning algorithms and assessed for goodness of fit using the c-index. RESULTS: Eighty of 386 imaging features demonstrated stability (CCC, $p< 0.001$) between pretreatment scans. LASSO identified 26 prognostic imaging features and 38 and 57 imaging features predictive of the presence of H3 K27M mutation and H3 K27M isoforms, respectively. Using five-fold cross validation, the accuracy of distinguishing H3 K27M mutant and WT tumors was 85% and 77% for H3.3 K27M, H3.1 K27M, and WT tumors. C-index for prognostication was 0.77 for Cox, 0.55 for random forest, and 0.72 for deep learning. All models were more predictive than the Jansen survival prediction model. CONCLUSIONS: Stable, predictive radiomic features may be a surrogate for H3 status and enhance current prognostication of DIPG. Model validation in cohorts of prospectively treated patients with DIPG is ongoing.

NIMG-52. CHARACTERIZATION OF COGNITIVE FUNCTION IN SURVIVORS OF DIFFUSE GLIOMAS USING MORPHOMETRIC CORRELATION NETWORKS (MCN)

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Advanced multimodality treatments have led to improved survival and quality of life for patients with diffuse gliomas, and widespread functional reorganization has been reported to be associated with improved cognitive function. However, investigation of morphological alterations in patients with diffuse gliomas has been problematic, largely due to the tumor resection cavities. This pilot study has overcome these challenges and aims to characterize the relationship between structural plasticity and cognitive function in survivors of diffuse gliomas. High-resolution T1 weighted images were collected from 24 patients with diffuse gliomas (mean age 44.5 ± 11.5) who had completed their treatment within the previous ten years. Interregional correlations of cortical thickness were computed to establish morphometric correlation networks (MCN) for twelve cognitively impaired and twelve non-impaired glioma patients, as well as correlated with self-reported cognitive impairment. Our findings demonstrated that both cognitively impaired (σ=1.5979) and non-impaired (σ=1.3683) glioma patients have a small world architecture in disrupted morphological networks. Although the left fusiform (p=0.0409), left inferior (p=0.0209), and temporal (p=0.0173) gyri were observed to be thicker in non-impaired patients, the robustness of their morphological network was weak and easily vulnerable to pathological attacks and neurological deterioration. Furthermore, regions such as the superior temporal gyrus (p=0.0126) and rostral middle frontal gyrus (p=0.0148) were not only identified as predominant nodes in the MCN of patients but were also found to have greater gray matter thickness, which is associated with better FACT-cognitive function. Together, these results support our hypothesis that a widespread morphological network is altered in survivors of diffuse gliomas. Predominant regions obtained by topological analysis may lead to reliable imaging biomarkers that help evaluate patients' cognition and ability to function.

NIMG-53. GLUTAMATE/GABA RATIO ON MRS IS ELEVATED IN PATIENTS WITH LOWER GRADE GLIOMAS AND SEIZURES

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BACKGROUND: There is lack of information on the role of excitatory and inhibitory neurotransmitters in the development of seizures in patients with lower grade gliomas. Increase of glutamate and downregulation of GABA have been suggested in preclinical models and human surgical samples to be associated with brain tumor-related epilepsy. MATERIAL AND METHODS: We prospectively investigated with the use of magnetic resonance spectroscopy (MRS) the differences in the ratio of metabolites (glutamate/GABA, glutamate/creatine and GABA/creatine) in the peritumoral areas between patients with or without seizures in a series of lower grade gliomas. Tumors were classified according to WHO Classification of 2016 as follows:11 grade II IDH mutated and 1p/19q codeleted; 3 grade III IDH mutated and 1p/19q codeleted; 6 grade II IDH mutated and 1p/19q intact; 1 grade III IDH mutated and 1p/19q intact; 1 grade II IDH wild-type. Pa-