within three days. Data augmentation techniques were utilized to enhance the size of our data and increase generalizability. Data was split between training, validation, and testing sets using 65-15-20 percent ratios. Model inputs were 16x16x3 patches around biopsies on T1Gd and T2 MRIs for labeled data, and around randomly selected patches inside the T2 abnormal region for unlabeled data. The network was a 4-conv layered VGG-inspired architecture. Training objective was accurate prediction of Ki67 in labeled patches and consistency in predictions across repeat unlabeled patches. We measured final model accuracy on held-out test samples. Our promising preliminary results suggest potential for deep learning in deconvolving the spatial heterogeneity of proliferative GBM subpopulations. If successful, this model can provide a non-invasive readout of cell proliferation and reveal the effectiveness of a given cytotoxic therapy dynamically during the patient's routine follow up. Further, the spatial resolution of our approach provides insights into the intra-tumoral heterogeneity of response which can be related to heterogeneity in localization of therapies (e.g. radiation therapy, drug dose heterogeneity).

NIMG-41. PH-WEIGHTED MOLECULAR MRI AS AN EARLY BIOMARKER OF METABOLIC RESPONSE TO IDH INHIBITION IN IDH MUTANT GLIOMAS

Benjamin Ellingson[1], Yao Jingwen[1], Akifumi Hagiwara[1], David Nathanson[1], Talia Oughourlian[1], Chencai Wang[1], Catalina Raymond[1], Whitney Pope[2], Noriko Salamon[1], Albert Lai[1], Phioanh Nghiemphu[1], Richard Everson[1], Won Kim[1], Linda Liau[1], Susan Pandya[3], Lori Steelman[3], Islam Hassan[3], and Timothy Cloughesy[1]; [1]University of California Los Angeles, Los Angeles, CA, USA, [2]Department of Radiological Sciences, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA, [3]Servier Pharmaceuticals, Boston, USA

The current study tested the hypotheses that (1) pH-weighted MRI measurements of tumor acidity reflect glycolytic activity in human gliomas, (2) that tumor acidity, and thus glycolytic activity, differs between human IDH mutant (mIDH) and wild type gliomas, and (3) that an increase in tumor acidity, suggestive of increased glycolytic activity, occurs after inhibition of mutant IDH enzyme activity and reduction in 2HG, an oncometabolite. To test these hypotheses, we employed a custom pH-weighted amine chemical exchange saturation transfer echoplanar (CEST-EPI) technique in 152 patients with IDH mutant or wildtype glioma prior to surgery and 11 patients before and after treatment with AG120 or AG881 enrolled at our institution in a phase 1 perioperative study in patients with recurrent, non-enhancing, IDH mutant low-grade gliomas (NCT03343197). Results from image-guided biopsies in more than 100 patients demonstrated a significant correlation between MTR_{asym} at 3ppm, a measure of tumor acidity from pH-weighted amine CEST-EPI, and expression of key glycolytic proteins including GLUT3 (R^2=0.2188,P=0.0105), HK2 (R^2=0.1788,P=0.0314), LDHA (R^2=0.1111,P=0.0071), and MCT1 (R^2=0.1228,P=0.0039) as well as ex vivo extracellular flux analysis estimates of ATP consumption from glycolysis (R^2=0.6684,P=0.0021). Data suggests a significantly lower acidity (MTR_{asym}@3ppm) within non-enhancing tumor in IDH mutant gliomas when compared to IDH wild type gliomas (P< 0.0001). Patients in a phase 1 perioperative study showed a shift toward higher tumor acidity (i.e. higher glycolytic activity) following inhibition of IDH based on 2HG suppression in resected tumors, but at levels below that of IDH wild type gliomas. Levels of 2HG within the tumor after IDH inhibition were inversely correlated with post-treatment tumor acidity (R^2=0.6342, P=0.0180). Overall, results suggest mIDH gliomas have low levels of glycolytic activity, and successful inhibition of the mutant IDH enzyme results in reduction in 2HG and a measurable metabolic shift toward elevated glycolysis as evidenced using pH-weighted molecular MRI.

NIMG-42. MP-MRI-BASED TUMOR PROBABILITY MAPS TRAINED USING AUTOPSY TISSUE SAMPLES AS GROUND TRUTH NON-INVASIVELY PREDICT INFILTRATIVE TUMOR BEYOND THE CONTRAST ENHANCING REGION

Samuel Bobholz, Allison Lowman, Michael Brehler, John Sherman, Savannah Duenweg, Fitzgerald Kyereme, Jennifer Connelly, Elizabeth Cochran, Wade Mueller, Anjishnu Banerjee, and Peter LaViolette; Medical College of Wisconsin, Milwaukee, WI, USA

Infiltrative glioma beyond contrast enhancement on MRI is often difficult to identify with conventional imaging. In this study, we use large-format autopsy samples aligned to multi-parametric MRI to test the hypothesis that radio-pathomic machine learning models are able to accurately identify areas of infiltrative tumor beyond the contrast enhancing region. At autopsy, 140 tissue samples from 62 brain cancer patients were collected from brain slices sectioned to align with the patients' last clinical MRI prior to death. Cell, extra-cellular fluid (ECF), and cytoplasm densities were computed from digitized, hematoxylin and eosin-stained samples, and a subset of 20 slides from 9 patients were annotated for tumor presence by a pathologist-trained technician. In-house custom software was used to align the tissue samples to the patients' last clinical imaging, which included pre- and post-contrast T1, FLAIR, and ADC images. Bagging random forest models were then trained to predict cellularity, ECF, and cytoplasm density using 5-by-5 voxel tiles from each MRI as input. A 2/3-1/3 train-test split was used to validate model generalizability. A naïve Bayes classifier was trained to predict tumor class using cellularity, ECF, and cytoplasm segmentations within the annotation data set, again using a 2/3-1/3 train-test split to validate performance. The random forest models each accurately predicted cellularity, ECF, and cytoplasm density within the test data set, with root-mean-squared error values for each falling within one standard deviation of the ground truth. The histology-based tumor prediction model accurately predicted tumor, with a test set ROC AUC of 0.86. When using whole brain cellularity, ECF, and cytoplasm predictions from the random forest models as inputs for the naïve Bayes classifier, tumor probability maps identified regions of infiltrative tumor beyond contrast enhancement. Our results suggest that radio-pathomic maps of tumor probability accurately identify regions of infiltrative tumor beyond currently accepted MRI signatures.

NIMG-43. ADVANCED MULTI-PARAMETRIC HYPERPOLARIZED $^{13}C/^{1}H$ IMAGING OF GBM

Adam Autry, Sana Vaziri, Marisa LaFontaine, Jeremy Gordon, Hsin-Yu Chen, Javier Villanueva-Meyer, Susan Chang, Jennifer Clarke, Duan Xu, Janine Lupo, Peder Larson, Daniel Vigneron, and Yan Li; University of California San Francisco, San Francisco, CA, USA

INTRODUCTION: The goal of this study was to characterize progressive and pseudoprogressive GBM using multi-parametric hyperpolarized (HP)-^{13}C / ^{1}H MRI. METHODS: Dynamic HP-^{13}C MRI was acquired from 13 patients with progressive GBM [patients (scans): 2(3) IDH-mutant; 11(13) IDH-wildtype] and 2 IDH-wildtype patients (3 scans) demonstrating pseudo-progression following intravenous injection of HP [1-^{13}C]pyruvate. Frequency-selective echo-planar imaging (3s temporal resolution, 3.38 cm^3 spatial resolution) captured [1-^{13}C]pyruvate metabolism to [1-^{13}C]lactate and ^{13}C-bicarbonate in the brain. Dynamic ^{13}C data were kinetically modeled to obtain the pyruvate-to-lactate conversion rate constant k_{PL} and temporally summed to calculate ^{13}C-metabolite percentiles and ratios (linearly interpolated 2x in-plane). ^{1}H imaging included T2, post-Gd T1, perfusion (nCBV, %recovery), diffusion (ADC), and lactate-edited spectroscopy (CNI, choline-to-NAA index; ^{1}H-lactate). The normal-appearing white matter (NAWM), non-enhancing lesion (NEL), and contrast-enhancing lesion (CEL) were segmented from ^{1}H images. ^{13}C-resolution masks were iteratively applied on a voxel-wise basis to evaluate ^{1}H imaging parameters within each ROI and multi-parametric data were collectively evaluated using a mixed effects model in R. RESULTS: Progressive IDH-mutant GBM compared to wildtype counterparts displayed increased perfusion %recovery ($p < 0.001$) and k_{PL} ($p < 0.01$), together with reduced ^{1}H-lactate ($p < 0.001$) and pyruvate percentile ($p < 0.01$), in the T2 lesion. Among IDH-wildtype progressive GBM, the CEL was distinguished from NEL/NAWM by increased nCBV ($p < 0.05/0.001$), ^{1}H-lactate ($p < 0.05/0.001$); and decreased bicarbonate / lactate ($p < 0.05/0.001$). The CEL and NEL were collectively distinguished from NAWM by elevated CNI (p < 0.001/0.001), ADC ($p < 0.05/0.001$), pyruvate percentile ($p < 0.001/0.001$), lactate percentile ($p < 0.001/0.001$), and relative lactate / pyruvate ($p < 0.001/0.05$). Psuedo-progressive IDH-wildtype GBM displayed lower k_{PL} (T2 Lesion; $p < 0.01$) and nCBV (CEL; $p < 0.01$) compared to progressive GBM. CONCLUSION: HP-^{13}C parameters can potentially augment proton imaging and demonstrated Warburg-associated metabolic alterations.

NIMG-44. PROGNOSTIC VALUE OF PH- AND OXYGEN-SENSITIVE MRI IN GLIOMA PATIENTS

Yao Jingwen[1], Akifumi Hagiwara[1], Talia Oughourlian[1], Chencai Wang[1], Catalina Raymond[1], Whitney Pope[2], Noriko Salamon[1], Albert Lai[1], Phioanh Nghiemphu[1], Richard Everson[1], Won Kim[1], Robert Prins[1], Linda Liau[1], Timothy Cloughesy[1], David Nathanson[1], and Benjamin Ellingson[1]; [1]University of California Los Angeles, Los Angeles, CA, USA, [2]Department of Radiological Sciences, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA

Hypoxia and tissue acidosis are two key features of the glioma microenvironment, both associated with a more aggressive phenotype through promotion of invasion, angiogenesis, and resistance to a vast number of therapies. In the current study, we demonstrate that higher levels of acidity and hypoxia in glioma are associated with worse prognosis by using sim-