wildtype), and 8 oligodendrogliomas (IDH mutated). The concentrations of glutamine and glycine were both significantly higher in enhancing tumors than in non-enhancing tumors (p=0.001 and 0.0001, respectively). The concentrations of glutamine and glycine were both positively correlated with MIB-1 (p=4E-5 and 1E-7, respectively). The sum of glutamine and glycine levels showed stronger association with MIB-1 (p=5E-10, r=0.89). In the Kaplan-Meier overall survival analysis, the survival was significantly shorter in patients with glutamine levels higher than 4.1 mM than those with concentrations less than 4.1 mM (p=0.02). For glycine, the patients with higher than 2.4 mM showed association with poor survival (p=0.03). The sum of glutamine and glycine levels showed stronger association with overall survival (p=0.008, cutoff 8.5mM). 2HG level greater than 0.5 mM was associated with long survival (p=0.01). We tested metabolic ratios to 2HG, in which 2HG estimates less than 1 mM were put as 1 mM (avoiding infinite ratios arising from null 2HG cases). The glutamine/2HG, glycine/2HG, and (glutamine+glycine)/2HG showed strong association with overall survival (p=2E-4, 2E-5 and 4.5E-7, respectively). Our data suggest that increased metabolism of glutamine and glycine is closely associated with rapid cell proliferation and poor survival, suggesting the metabolites are imaging biomarkers of glioma aggressiveness.

BIMG-10. IDH1 MUTATIONS INDUCE ORGANELLE DEFECTS VIA DYSREGULATED PHOSPHOLIPIDS

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BACKGROUND: Metabolic alterations of lipids have been identified as a hallmark of neoplasms, with the most prevalent being the balance between saturated fatty acid (SFA) and monosaturated fatty acid (MUFA). Stearoyl-CoA desaturase1 (SCD1), converting SFA to MUFA, is increased in many cancers, leading to worse prognosis. In glioma, the role of SCD1 remains unknown. Isocitrate dehydrogenase (IDH) mutations have been most commonly observed in glioma, but the involvement of mutant IDH in SCD1 expression also remains unknown. **METHODS:** We conducted metabolic analysis to examine the alteration of SCD1 expression in genetically engineered glioma cell lines and normal human astrocyte (NHA). Lipid metabolic analysis was conducted by using LC-MS, Raman Imaging Microscopy and SCD1 expression was examined by Western-blotting and RT-PCR method. Electron microscopy was employed for organelle structure and genetic knock-down of SCD1 gene was performed. **RESULT:** Herein, we uncovered increased MUFA and their phospholipids in Endoplasmic Reticulum (ER), generated by IDH1 mutation, that were responsible for Golgi and ER dilation. RNA seq data from The Cancer Genome Atlas, showed that SCD1 expression was significantly higher in IDH mutant gliomas compared with wild-type, and high SCD1 expression was associated with longer survival. Inhibition of IDH1 mutation or SCD1 silencing restored ER and Golgi morphology, while D-2HG and oleic acid induced morphological defects in these organelles. Moreover, addition of oleic acid, which tilts the balance towards elevated levels of MUFA, produced IDH1 mutant-specific cellular apoptosis. **CONCLUSION:** Collectively, our results suggest that IDH1 mutant-induced SCD overexpression can rearrange the distribution of lipids in the organelles of glioma cells, providing a new insight on the link between lipids metabolism and organelle morphology in these cells, with potential and unique therapeutic implications. The results of the present study may also provide novel insights into the discovery of metabolic biomarkers for IDH mutant gliomas.

BIMG-11. PHARMACODYNAMIC EVALUATION OF IDH AND EGFR INHIBITION IN HUMAN GLIOMAS USING MOLECULAR MRI

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Metabolic differences are inherent to specific glioma subtypes and can be altered using targeted treatments, including IDH and EGFR inhibition. Using a large cohort of patients scanned at UCLA and other centers over the last 5 years, we demonstrate that IDH, 1p19q, and EGFR alterations uniquely contribute to alterations in glycolysis and oxygen utilization using a clinically available molecular MRI technique termed amine chemical exchange saturation transfer spin-and-gradient-echo echoplanar imaging (CEST-SAGE-EPI). Our data shows that CEST-SAGE-EPI estimates of tumor acidity are strongly associated with the degree of glycolysis as evaluated with direct pH measurements, quantitative IHC, bioenergetics experiments, and correlations with 18F-FDG PET images. Data further reveals that IDH wild type gliomas have higher acidity and oxygen utilization compared with IDH mutant gliomas, 1p19q non-codeleted gliomas (astrocytomas) have higher tumor acidity compared to 1p19q codeleted gliomas (oligodendrogliomas), and EGFR amplified gliomas have higher oxygen utilization compared with non-amplified gliomas. Additionally, phase II clinical trial data suggests successful IDH inhibition results in an early and measurable increase in tumor acidity and further reduction in oxygen utilization, signifying suppression of oxidative phosphorylation and/or glutaminolysis in favor of glycolysis. Alternatively, phase II clinical trial data suggests successful EGFR inhibition with brain penetrant agents results in early reductions in tumor acidity and 18F-FDG PET uptake, consistent with a reduction in glycolysis. Data also indicates that continual increases in tumor acidity during routine follow-up after initial therapeutic changes results in uniformly worse outcomes in all tumor subtypes under all mentioned treatment scenarios.

BIMG-12. [18F]FLUCICLOVINE PET TO DISTINGUISH PSEUDOPROGRESSION FROM TUMOR PROGRESSION IN POST-TREATMENT GLIOBLASTOMA

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PURPOSE: Differentiation of true tumor progression from pseudoprogression (PsP) is a major unmet need in patients with glioblastoma (GBM). [^{18}F]Fluciclovine is a synthetic amino acid PET radiotracer that is FDA approved in the setting of biochemical recurrence in prostate cancer. The aim of this study was to assess the value of [^{18}F]Fluciclovine PET in differentiation of true tumor progression and PsP in post-treatment of glioblastoma. **METHODS:** 15 patients with GBM with new contrast-enhancing lesions or lesions showing increased enhancement (>25% increase) on standard MRI after completion of radiation underwent 60-minutes dynamic [^{18}F]Fluciclovine PET imaging. Patients subsequently (within 1 week) underwent resection of the enhancing lesion and the tumor percentage vs treatment-related changes were quantified on histopathology. Patients were considered true tumor progression if tumor represented ≥ 50% of the resected specimen and considered PsP if treatment-related changes represented ≥70% of the resected specimen. Summed 30- to 40-minute post-injection PET images were used to measure SUV_{peak}, SUV_{max}, and 50% threshold SUV_{mean}. **RESULTS:** 10 patients with true tumor progression and 5 patients with PsP were included. Patients who demonstrated true tumor progression had significantly higher SUV_{peak} compared to patients with PsP (5.3±1.4 vs 3.1± 0.9, p=0.002, AUC=0.92, p<0.0001). SUV_{peak} cut-off of 3.5 provided 100% sensitivity, 80% specificity and 93% accuracy for differentiation of true tumor progression from PsP. There was a moderate to strong correlation between SUV_{peak} and tumor percentage on histopathology (Rho= 0.68, p=0.004). Alternative SUV measures had similar performance. **DISCUSSION:** Our preliminary results indicated that [^{18}F]Fluciclovine PET imaging can accurately differentiate true tumor progression from PsP. Further studies are required to confirm these promising early results and determine the optimal criteria for interpreting [^{18}F]Fluciclovine PET to distinguish PsP from true tumor progression.

BIMG-13. A NOVEL RADIOPHARMACEUTICAL ([^{18}F]DASA-23) TO MONITOR PYRUVATE KINASE M2 INDUCED GLYCOLYTIC REPROGRAMMING IN GLIOBLASTOMA

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BACKGROUND: Pyruvate kinase M2 (PKM2) catalyzes the final step in glycolysis, a key process of cancer metabolism. PKM2 is preferentially expressed by glioblastoma (GBM) cells with minimal expression in healthy brain, making it an important biomarker of cancer glycolytic re-programming. We describe the bench-to-bedside development, validation, and translation of a novel positron emission tomography (PET) tracer to study PKM2 in GBM. Specifically, we evaluated 1-((2-fluoro-6-[^{18}F]fluorophenyl)sulfonyl)-4-((4-methoxyphenyl)sulfonyl)piperazine ([^{18}F]DASA-23) in cell culture, mouse models of GBM, healthy human volunteers, and GBM patients. **METHODS:** [^{18}F]DASA-23 was synthesized with a molar activity of 100.47 ± 29.58 GBq/μmol and radiochemical purity >95%. We performed initial testing of [^{18}F]DASA-23 in GBM cell culture and human GBM xenografts implanted orthotopically into mice. Next we produced [^{18}F]DASA-23 under current Good Manufacturing Practices United States Food and Drug Administration (FDA) oversight, and evaluated it in healthy volunteers and a pilot cohort of patients with gliomas. **RESULTS:** In mouse imaging studies, [^{18}F]DASA-23 clearly delineated the U87 GBM from the surrounding healthy brain tissue and had a tumor-to-brain ratio (TBR) of 3.6 ± 0.5. In human volunteers, [^{18}F]DASA-23 crossed the intact blood-brain barrier and was rapidly cleared. In GBM patients, [^{18}F]DASA-23 successfully