into PPIX. Our data suggest that different microenvironments within the tumour alter the activity of the heme biosynthetic pathway, resulting in differential fluorescence in glioblastoma. It paves the way for work to alter the glioblastoma microenvironment in order to further improve the use of FGS in guiding surgery across these devastating tumours.

BIMG-18. ELEVATED CYSTATHIONINE IN MEDULLOBLASTOMA DEMONSTRATES TUMOR-SPECIFIC METHIONINE METABOLISM

Andrey Tikunov, Elias Rosen, Ben Babcock, Seth Weir,
Stuart Parnham, Jeffrey Macdonald; Timothy Gershon UNC, Chapel Hill, NC, USA

We investigated tumor-specific metabolism medulloblastoma using a non-biased MS-imaging screen and identified a pattern of methionine flux that may present a therapeutic opportunity. We studied brain tumors that form in mice genetically engineered to develop Sonic Hedgehog (SHH)-driven medulloblastoma. We subjected sagittal sections including brain and medulloblastoma to MS-imaging, generating concentration maps for hundreds of metabolites MW 100–400. We then confirmed results by analyzing tumor, brain and blood by LC-MS/MS, high-resolution NMR and 2D NMR-TOCSY, and used immunohistochemistry to determine the cellular localization of implicated enzymes. MS imaging, accomplished by matrix-assisted laser desorption electrospray ionization (MALDESI), detected cystathionine at an order of magnitude higher concentration in medulloblastomas compared to adjacent brain. No other metabolite showed such a strong, tumor-specific localization. LC-MS/MS and NMR methods confirmed cystathionine elevation. As cystathionine is the product of homocysteine and serine, catalyzed by cystathionine beta-synthase (CBS), we investigated CBS expression by IHC. Consistent with prior studies, we found that only astrocytes expressed CBS, both in the normal brain and within the tumors. ScRNA-seq confirmed *Cbs* only in astrocytes, and showed tumor cells express methionine-metabolizing enzymes *Mat2a*, *Dnmt1*, *Ancy* and *Mtr*. Together, these findings show that tumor cells generate and export homocysteine, which astrocytes convert to cystathionine. Tumor cystathionine generation responded to changes in methionine- cycle metabolites. *In vivo*, systemic administration of homocysteine increased tumor cystathionine which decreased in response to systemic folate, the methyl donor for homocysteine methyltransferase. Cystathionine itself was inert in tumors as tumor cells cultured in up to 8 mM cystathionine showed no change in cell cycle progression. Our studies show that medulloblastomas utilize methionine and generate homocysteine, but avoid folate-dependent homocysteine-methionine recycling by exporting homocysteine for detoxification by local astrocytes. This model suggests that treatments that impose methionine scarcity, folate scarcity or CBS inhibition may produce anti-tumor effects in medulloblastoma.

BIMG-19. ^{18}F-FLUCICLOVINE PET/CT TO DISTINGUISH RADIATION NECROSIS FROM TUMOR PROGRESSION IN BRAIN METASTASES TREATED WITH STEREOTACTIC RADIOSURGERY: A PROSPECTIVE PILOT STUDY

Martin Tom; Miami Cancer Institute, Miami, FL, USA

PURPOSE: To estimate the accuracy of ^{18}F-Fluciclovine PET/CT in distinguishing radiation necrosis (RN) from tumor progression (TP) among patients with brain metastases (BM) having undergone prior stereotactic radiosurgery (SRS) who presented with a follow-up MRI brain (with DSC-MR perfusion) which was equivocal for RN versus TP. **METHODS:** Within 30 days of equivocal MRI brain, subjects underwent ^{18}F-Fluciclovine PET/CT on a Siemens Biograph mCT scanner with a 10 mCi bolus dose immediately prior to PET. Data were collected in list mode for 25 minutes post-injection and were reconstructed as a static image of data 10–25 minutes post-injection, and as a dynamic series of four 5-minute frames between 5–25 minutes post-injection. Quantitative metrics for each lesion were documented including SUVmax, SUVmean, SUVpeak, and normal brain SUVmean. Lesion to normal brain ratios were calculated. The reference standard was clinical follow-up with MRI brain (with DSC-MR perfusion) every 2–4 months until multidisciplinary consensus (or tissue confirmation) for diagnosis of RN versus TP. **RESULTS:** From 7/2019-11/2020, 16 of 16 planned subjects enrolled and underwent ^{18}F-Fluciclovine PET/CT for evaluation of 21 brain lesions. Primary histology included NSCLC (n=7), breast (n=5), melanoma (n=3), and endometrial (n=1). Ranges of quantitative metrics were: SUVmax, 2.18–12.1; SUVmean, 1.16–7.37; SUVpeak, 1.06–5.14; normal brain SUVmean, 0.19–0.50; SUVmax/normal ratio, 7.5–45.4; SUVmean/normal ratio, 4.2–26.3; and SUVpeak/normal ratio, 3.9–26.4. Among the patients 10 patients with 12 lesions who completed follow up, estimates of the area under the receiver operating characteristic curve for SUVmax, SUVmean, and SUVpeak were: 0.93, 0.93, and 0.82, respectively. **CONCLUSION:** In this population, ^{18}F-Fluciclovine PET/CT favorably produces a wide range of lesion quantitative metric values, low uptake in the normal brain, and promising accuracy to distinguish RN from TP. Completion of follow-up for all patients is required. Phase II and III studies are under development.

BIMG-20. METABOLIC BIOMARKERS IN MICRODIALYSATE OF IDH-1 MUTANT TUMORS

Karishma Rajani[1], Lucas Carlstrom[1], Joshua Jacobs[1], Mark Schroeder[1], Ian Olson[1], Matthew Hainy[1], Juhee Oh[2], William Elmquist[2], Jann Sarkaria[1], Terry Burns[1]; [1]Mayo Clinic, Rochester, MN, USA, [2]University of Minnesota, Minneapolis, MN, USA

Glioblastoma (GBM) is a common deadly malignant brain cancer of the central nervous system, with a median survival of 12–15 months. Scientific advancements are lacking in developing effective therapies for both primary GBM, as well as secondary GBMs, that typically originate as malignant transformation of lower-grade isocitrate dehydrogenase (IDH) 1-mutant tumors. The unique metabolomic profile of IDH1-mutant tumors presents opportunities to develop biomarker signatures of therapeutic efficacy. Microdialysis is an extracellular fluid sampling collection technique utilizing a perfused semipermeable catheter to permit diffusion of molecules between brain interstitium and the perfusate. We hypothesized that microdialysis may identify a metabolomics-based biomarker response to therapy in IDH1-mutant tumors. To test this hypothesis, orthotopic xenografts were generated from patient-derived xenografts (PDX) harboring mutant IDH-1 (R132H). Perfusates were collected from intra-cranial tumors in athymic nude mice sampled at baseline and 72h post treatment with temozolomide (TMZ), an oral alkylating agent used to treat IDH1-mutant gliomas, compared with vehicle treatment. Perfusates were analyzed via untargeted metabolomic profiling using liquid chromatography-mass spectrometry. Tumor specific metabolites such as (D)-2 hydroxyglutarate, were detected in microdialysate from IDH-1 mutant tumor bearing mice compared to non-tumor bearing mice. We also found high levels of metabolites such as 5-methylthioadenosine, and dimethylarginine and wide range of amino acids in microdialysate from IDH-1 mutant tumor bearing mice. TMZ treatment induced changes to metabolites in creatine and histidine metabolism. Our results indicate that microdialysis is a feasible technology to identify metabolomics-based biomarkers in IDH1-mutant gliomas and their response to therapy. We suggest that *in vivo* intratumoral microdialysis over several days could yield metabolic pharmacodynamic biomarkers of value to therapeutic translation for IDH-mutant gliomas.

BIMG-21. DEUTERIUM METABOLIC IMAGING (DMI), A NEW, MRI-BASED TECHNIQUE FOR MAPPING BRAIN TUMOR METABOLISM IN VIVO

Zachary Corbin, Robert Fulbright, Douglas Rothman, Robin de Graaf, Henk De Feyter; Yale University, New Haven, CT, USA

Deuterium Metabolic Imaging (DMI) combines 3D deuterium (^{2}H) magnetic resonance spectroscopic imaging (MRSI) with administration of a ^{2}H-labeled substrate to map uptake and metabolism of the substrate. DMI has been implemented on a 4 Tesla clinical research MRI scanner, and on an 11.7 Tesla preclinical MRI scanner, and has been used with ^{2}H-labeled glucose, acetate and choline. DMI data are presented as color maps of concentration of the ^{2}H-labeled substrate and its metabolites, overlaid on anatomical MR images. In rat and mouse models of glioblastoma, DMI data acquired at 5 to 8 uL resolution following intravenous ^{2}H-glucose infusion clearly showed the Warburg effect in the tumor lesions. The Warburg effect is indicated by the ratio of ^{2}H-labeled lactate/glutamate+glutamine (Glx). High levels of ^{2}H-labeled lactate and low levels of ^{2}H-labeled Glx are the result of a high rate of glycolysis and low rate of oxidative glucose metabolism. Because DMI detects both glucose and its downstream metabolism, the technique does not suffer from low image contrast with normal brain, as is the case with FDG-PET that detects glucose uptake only. For clinical research studies patients orally consumed 0.75g/kg of ^{2}H-glucose dissolved in water. The observations made in the animal models were confirmed in several patients with recurrent GBM, showing hotspots in the lac/Glx maps (8 mL resolution), coinciding with the area of the tumor lesion. In patients with meningioma, no Warburg effect was detected using DMI. Furthermore, DMI data acquired in a patient with GBM one week after finishing 30 days of radiation therapy, also showed no high levels of ^{2}H-labeled lactate in the lesion. These data indicate that the presence of the Warburg effect could correlate with tumor grade and/or aggressiveness, and that DMI of glucose metabolism could potentially be a biomarker of therapy effect.

BIMG-22. DEEP LEARNING SUPER-RESOLUTION MR SPECTROSCOPIC IMAGING TO MAP TUMOR METABOLISM IN MUTANT IDH GLIOMA PATIENTS

Xianqi Li[1], Ovidiu Andronesi[1], Bernhard Strasser[1], Kourosh Jafari-Khouzani[2], Daniel Cahill[1], Jorg Dietrich[1], Tracy Batchelor[3], Martin Bendszus[4], Ulf Neuberger[4], Philipp Vollmuth[4]; [1]Mass General Hospital, Boston, MA, USA, [2]IBM Watson Health, Boston, MA, USA, [3]Brigham and Women Hospital, Boston, MA, USA, [4]Heidelberg University Hospital, Heidelberg, Germany

Metabolic imaging can map spatially abnormal molecular pathways with higher specificity for cancer compared to anatomical imaging. However, ac-