outlined tumors visible on contrast-enhanced magnetic resonance imaging (MRI). The uptake of [^{18}F]DASA-23 was markedly elevated in GBMs compared to normal brain, and it was able to identify a metabolic non-responder within 1-week of treatment initiation. **CONCLUSION:** We developed and translated [^{18}F]DASA-23 as a promising new tracer that demonstrated the visualization of aberrantly expressed PKM2 for the first time in human subjects. These encouraging results warrant further clinical evaluation of [^{18}F]DASA-23 to assess its utility for imaging therapy-induced normalization of aberrant cancer metabolism.

BIMG-14. IDENTIFICATION OF IDH MUTATION STATUS USING PROTON MR SPECTROSCOPY AND MASS SPECTROMETRY: A STUDY OF 178 GLIOMAS

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IDH mutation, a key factor in predicting glioma prognosis, alters the levels of some metabolites in brain, including 2-hydroxyglutarate (2HG), glutamine (Gln), and glutathione (GSH). While proton MR spectroscopy (^{1}H-MRS) enables in-vivo detection of these metabolites, liquid chromatography-mass spectrometry (LC-MS/MS) is a sensitive in-vitro method to measure absolute metabolite concentrations. This study aims to examine the correlation of metabolic concentrations measured using ^{1}H-MRS and LC-MS/MS in gliomas, and to detect IDH mutation with machine learning based on ^{1}H-MRS and LC-MS/MS metabolic intensities. The patient cohort included 178 glioma patients (111M/67F, mean age:44.09±13.95 years, 100 IDH-mut, 78 IDH-wt). The patients were scanned pre-surgery by a 3T MR scanner with a 32-channel head coil. ^{1}H-MRS was obtained from a manually placed region of interest with no necrosis, edema, and hemorrhage, using a Point Resolved Spectroscopy (PRESS) sequence (TR/TE=2000/30ms). LCModel software was used for quantification of eighteen metabolites of ^{1}H-MRS data. Metabolite concentrations including creatine (Cr), choline (Cho), Gln, glutamate (Glu), gamma-aminobutyric acid (GABA), N-acetyl aspartate (NAA), myo-inositol (mIns), 2HG, and lactate (Lac) were also determined with LC-MS/MS for surgical specimen of the same patients. Spearman correlation coefficients were calculated between the metabolite concentrations measured with ^{1}H-MRS and LC-MS/MS. Additionally, machine-learning algorithms were used to detect IDH mutation in gliomas based on metabolite concentrations obtained with ^{1}H-MRS and LC-MS/MS. Consequently, there were statistically significant correlations between ^{1}H-MRS and LC-MS/MS results for 2HG (p=0.036), Cr (p=0.009), mIns (p<0.001), Lac (p=0.007) and NAA (p=0.004). IDH mutation was detected with an accuracy of 92.42% (sensitivity=91.70%, specificity=93.46) and 82.94% (sensitivity=84.04, specificity=81.43) based on LC-MS/MS and ^{1}H-MRS metabolic intensities, respectively. In conclusion, ^{1}H-MRS and LC-MS/MS metabolic intensities were highly correlated and these techniques were successful in identifying IDH mutation in gliomas. This study has been supported by TUBITAK 1003 grant 216S432.

BIMG-15. LACTATE AND GLUTATHIONE LEVELS DETECTED WITH PROTON MR SPECTROSCOPY ARE ASSOCIATED WITH POOR SURVIVAL IN IDH WILD TYPE TERTP MUTANT DIFFUSE GLIOMAS.

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Telomerase reverse transcriptase promoter (TERTp) mutations in the absence of IDH mutations (TERTp-only) are recently proposed as a characteristic of glioblastoma regardless of the morphological grade. This study aims to analyze metabolic profiles of TERTp-only gliomas using proton magnetic resonance spectroscopy (^{1}H-MRS) and evaluate the effect of metabolite concentrations on progression-free survival (PFS) and overall survival (OS). The patient cohort consisted of 56 TERTp-only gliomas (35M/21F, mean age: 58±10.37 years, 44 glioblastomas (GBM), and 12 lower-grade gliomas with TERTp-mutation but no IDH-mutations). All patients underwent preoperative diagnostic ^{1}H-MRS using a 3T MR scanner with a 32-channel head coil. ^{1}H-MRS was obtained from a manually placed region of interest with no necrosis, edema, and hemorrhage, using a Point Resolved Spectroscopy (PRESS) sequence (TR/TE=2000/30 ms, 1024 points). LCModel spectral fitting program was used for quantification of MR spectroscopic peak concentrations of 17 metabolites. The patients were divided into two groups using median values of the metabolite intensities, and Kaplan-Meier survival analysis followed by a log-rank test was used to determine the effects of metabolite concentrations on OS and PFS. Median PFS and OS of TERTp-only gliomas were 11 and 17 months, respectively. TERTp-only LGG patients had longer OS and PFS than TERTp-only GBM patients (p=0.022 for OS and p=0.018 for PFS). Significantly shorter OS and PFS were identified in TERTp-only gliomas, who had higher GSH/tCr (p=0.011 for OS and p=0.004 for PFS) and higher Lac/tCr (p=0.014 for OS and p=0.012 for PFS). Lactate is a marker of necrosis and a sign of malignancy. On the other hand, both tCr and GSH were lower, which resulted in higher GSH/tCr, in TERTp-only GBM. The results of this study indicate that high Lac/tCr and GSH/tCr might be indicators of poor prognosis in TERTp-only gliomas. This study has been supported by TUBITAK 1003 grant 216S432.

BIMG-16. TRACKING TTFIELDS-INDUCED ALTERATIONS IN GLIOBLASTOMA METABOLISM WITH [18F]DASA-23, A NON-INVASIVE PROBE OF PYRUVATE KINASE M2 (PKM2)

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Despite the anti-proliferative and survival benefits from tumor treating fields (TTFields) in human glioblastoma (hGBM), little is known about the effects of this form of alternating electric fields therapy on the aberrant glycolysis of hGBM. [18F]FDG is the most common radiotracer in cancer metabolic imaging, but its utility in hGBM is impaired due to high glucose uptake in normal brain tissue. With TTFields, radiochemistry, Western blot, and immunofluorescence microscopy, we identified pyruvate kinase M2 (PKM2) as a biomarker of hGBM response to therapeutic TTFields. We used [18F]DASA-23, a novel radiotracer that measures PKM2 expression and which has been shown to be safe in humans, to detect a shift away from hGBM aberrant glycolysis in response to TTFields. Compared to unexposed hGBM, [18F]DASA-23 uptake was reduced in hGBM exposed to TTFields (53%, P< 0.05) or temozolomide chemotherapy (33%, P > 0.05) for 3 d. A 6-d TTFields exposure resulted in a 31% reduction (P = 0.043) in 60-min uptake of [18F]DASA-23. [18F]DASA-23 was retained after a 10 but not 30-min wash-out period. Compared to [18F]FDG, [18F]DASA-23 demonstrated a 4- to 9-fold greater uptake, implying an improved tumor-to-background ratio. Furthermore, compared to no-TTFields exposure, a 6-d TTFields exposure caused a 35% reduction in [18F]DASA-23 30-min uptake compared to only an 8% reduction in [18F]FDG 30-min uptake. Quantitative Western blot analysis and qualitative immunofluorescence for PKM2 confirmed the TTFields-induced reduction in PKM2 expression. This is the first study to demonstrate that TTFields impairs hGBM aberrant glycolytic metabolism through reduced PKM2 expression, which can be non-invasively detected by the [18F]DASA-23 radiotracer.

BIMG-17. EFFECTS OF THE TUMOUR MICROENVIRONMENT ON PROTOPORPHYRIN IX ACCUMULATION IN GLIOBLASTOMA

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Glioblastoma is the most common primary brain tumour and has a poor prognosis. The median survival is less than two years despite clinical intervention that usually involves the resection of the tumour volume, chemotherapy and radiotherapy. Achieving gross-total resection is challenging due to poorly defined boundaries as a result of tumour infiltration. Fluorescence-guided surgery (FGS) utilises an apparently selective accumulation of protoporphyrin IX (PPIX) that occurs in areas of glioblastoma after administration of the metabolite, 5-aminolevulinic acid (5-ALA). 5-ALA and the fluorescent metabolite, PPIX, sit within the endogenous heme biosynthetic pathway, which suggests that FGS is not only an important clinical tool, but also highlights differing metabolic phenotypes naturally present throughout the tumour. Genetic and mechanistic studies into this phenomenon have shown that differential expression of metabolite transporters, altered activity of the heme pathway enzymes and variable nutrient availability are all factors in the accumulation of PPIX. However, little is known about the cellular driving force for the uptake of 5-ALA and subsequent conversion