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 demonstrates 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 (1H-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 with 1H-MRS and LC-MS/MS in gliomas, and to detect IDH mutation with machine learning based on 1H-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. 1H-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). ICA-Model software was used for quantification of eighteen metabolites of 1H-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 metabolic concentrations measured with 1H-MRS and LC-MS/MS. Additionally, machine-learning algorithms were used to detect IDH mutation in gliomas based on metabolite concentrations obtained with 1H-MRS and LC-MS/MS. Consequently, there were statistically significant correlations between 1H-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 detection was determined by an accuracy of 92.42% (sensitivity=91.70%, specificity=93.46) and 82.94% (sensitivity=84.04, specificity=84.13) based on LC-MS/MS and 1H-MRS metabolic intensities, respectively. In conclusion, 1H-MRS and LC-MS/MS metabolic intensities were highly correlated across these metabolites, successful in the quantification of 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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Lactate and glutathione are cellular metabolites involved in tumor cell proliferation and metabolism. In glioblastomas, lactate is a marker of glycolysis, while glutathione is a marker of oxidative stress and detoxification. The current study aimed to evaluate the levels of lactate and glutathione in glioblastomas using 1H-MRS and LC-MS/MS. The patient cohort included 178 glioblastoma patients (100 IDH-mutant, 78 IDH-wildtype). 1H-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). ICA-Model software was used for quantification of eighteen metabolites of 1H-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 metabolic concentrations measured with 1H-MRS and LC-MS/MS. Additionally, machine-learning algorithms were used to detect IDH mutation in gliomas based on metabolite concentrations obtained with 1H-MRS and LC-MS/MS. Consequently, there were statistically significant correlations between 1H-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 detection was determined by an accuracy of 92.42% (sensitivity=91.70%, specificity=93.46) and 82.94% (sensitivity=84.04, specificity=84.13) based on LC-MS/MS and 1H-MRS metabolic intensities, respectively. In conclusion, 1H-MRS and LC-MS/MS metabolic intensities were highly correlated across these metabolites, successful in the quantification of IDH mutation in 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, radiotherapy, Western blot, and immunofluorescence microscopy, we identified pyruvate kinase (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 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. These findings 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 it 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.