A Simultaneous Measurement of Relative CMRO2 with MRI and FMISO Uptake with PET in Glioblastoma

H. Kim[1], C. Catana[1], G. Arabasz[1], D. Bolar[1], E. R. Gerstner[2], T. T. Batchelor[2], R. K. Jain[3], B. R. Rosen[1], and A. G. Sorensen[1]
[1]Radiology, A. A. Martinos Center, Charlestown, MA, United States, [2]Neurology, Massachusetts General Hospital, Boston, MA, United States, [3]Radiation Oncology, Massachusetts General Hospital, Boston, MA, United States

INTRODUCTION

Since hypoxia is a potent stimulator of tumor angiogenesis and an important factor that affects treatment efficacy, detection and modulation of tumor oxygenation could be used to enhance therapeutic effects. The uptake of FMISO assessed with positron emission tomography (PET) has been demonstrated to correlate well with tissue oxygenation. Functional MRI assessment of cerebral metabolic rate of oxygen ($CMRO_2$) has also been proposed to investigate oxygen metabolism. Simultaneous MR-PET data acquisition can provide these desirable measurements in tumors with excellent structural resolution. Our goal is to develop a novel method for combining the complementary information provided by BOLD-ASL MR [1] (i.e.relative $CMRO_2$ changes) and FMISO-PET (tumor hypoxia level) in newly diagnosed glioblastoma (nGBM).

METHODS

nGBM patients were scanned using the integrated MR-PET scanner (3T TimTrio&BrainPET, Siemens, Malvern, PA) at two specific time points (i.e. day -1 and 24) during the treatment (cediranib and chemo-radiation).

MRI Data Acquisition: The simultaneous BOLD-ASL sequence was developed based on pulsed ASL sequence by applying QUIPSS II technique and PICORE tagging followed by single-shot, gradient-echo EPI acquisition. Specific imaging parameters used were TI1/TI2 =700/1400ms, 13-slices, 6mm thickness, TR/TE=2000/19ms, FOV=220mm. The breathing paradigm consisted of baseline room air (1min), followed by two blocks of 100% O_2 (1.5min) and room air (1.5min) with 10L/min flow rate (the total scan time: 7min). T1-weighted images after injection of Gadolinium-DTPA were acquired to provide anatomical details.

PET Data Acquisition: 3.7 MBq/kg (0.1 mCi/kg) of FMISO was injected at the start of the data acquisition and then MR and PET data were collected simultaneously. The PET data were acquired in list-mode format. Corrections were applied to account for variable detector efficiency and dead time, random coincidences, photon attenuation and scatter and images were reconstructed with the standard 3D OP-OSEM algorithm. For these preliminary studies, volumes were reconstructed from the 20-minute frame acquired ~100 minutes after injection.

MRI-PET Data Analysis: The preprocessing of the raw data included motion correction, subtraction (CBF) and addition (BOLD) of the paired images, spatial smoothing using a 6mm kernel Gaussian filter, and general linear modeling (GLM) using Neurolens software. BOLD and CBF signal change maps in hyperoxia were analyzed using in house developed code to estimate relative $CMRO_2$ according to Davis' formula [2].

The reconstructed PET volumes co-registered to the high-resolution anatomical MR images where matched to the BOLD images. All data were anaylzed in ROIs defined on the tumor and the contralateral normal tissue.

RESULTS and DISCUSSION

The post-contrast T1-weighted image and the maps of BOLD and CBF changes in hyperoxia before the treatment in a representative subject are shown in **Figure 1a-c**. The relative $CMRO_2$ map evaluated from the above BOLD and CBF changes, and FMISO uptake from PET are shown **Figure 1d-e**. Significant increases of relative $CMRO_2$ (42%) and FMISO uptake (2.45 SUV) around enhancing tumor were observed. However, distinct patterns were reveled by MR and PET in different parts of the tumor (i.e. increased FMISO uptake with no $CMRO_2$ changes and vice versa). Furthermore, the increase of $CMRO_2$ was more widely distributed than that of FMISO uptake although there are also regions where they overlap. This might indicate that hyperoxia changes not only the oxygenation metabolism in hypoxic cancer cells but also in apparently normal tissue possibly affected by some of the infiltrating cancer cells. In **Figure 2a-e,** the corresponding images after 24 days of the treatment are shown. In addition to tumor regression, the relative $CMRO_2$ (19%) and FMISO uptake (1.55 SUV) largely decreased around the tumor compared to pre-treatment. This suggests that the treatment with an anti-angiogenic agent and chemo-radiation has a cytotoxic effect on hypoxic cells in nGBM.

CONCLUSION

Measurements of relative $CMRO_2$ changes with MRI and tumor hypoxia with FMISO-PET provide useful information in the assessment of tumor oxygenation metabolism. Since these methods offer complementary data, there is an opportunity for a novel way to integrate them. This could be relevant for studying the role of oxygen in tumor metabolism and angiogenesis, and could help us better understand the mechanism of action of the combined treatment in cancerous tissues.

REFERENCES [1] Wong EC et al. NMR Biomed 1997; [2] Davis TL et al. PNAS 1998;

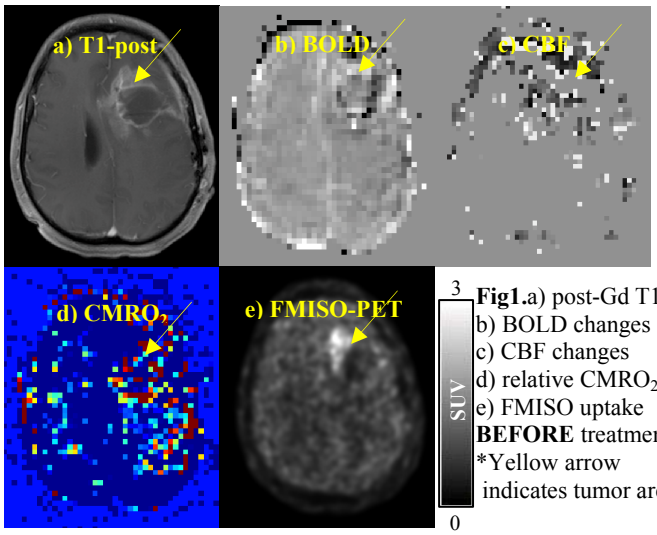

Fig1.a) post-Gd T1
b) BOLD changes
c) CBF changes
d) relative $CMRO_2$
e) FMISO uptake
BEFORE treatment
*Yellow arrow indicates tumor area

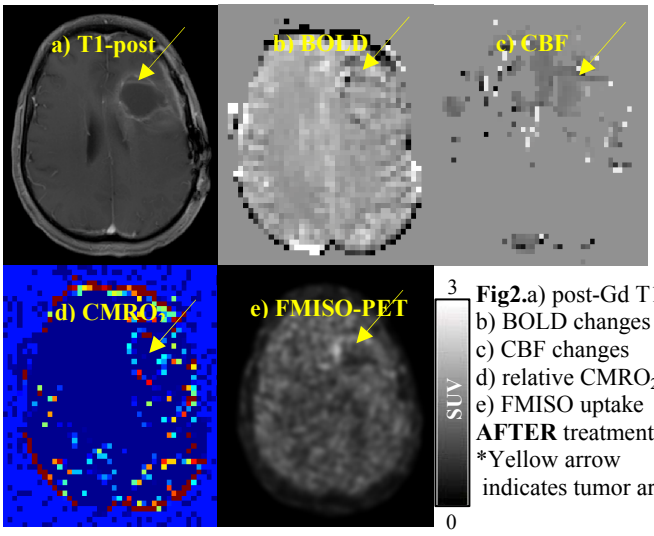

Fig2.a) post-Gd T1
b) BOLD changes
c) CBF changes
d) relative $CMRO_2$
e) FMISO uptake
AFTER treatment
*Yellow arrow indicates tumor area