

Correlations between PET and DTI data in newly diagnosed GBM patients receiving cediranib scanned on a hybrid PET/MR scanner

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INTRODUCTION Diffusion tensor imaging (DTI) is an advanced MRI technique that describes the molecular movement of bulk water. Due to the presence of cell membranes in tissues, diffusion of water molecules is not isotropic. This anisotropy can be described by the fractional anisotropy (FA), which is a measurement for the directionality of water, and the apparent diffusion coefficient (ADC), which describes the diffusion magnitude. It has been shown that abnormal DTI value changes in the area beyond the traditional contrast enhancing regions correlate with tumor cellularity and infiltration¹⁻⁴. However, distinguishing invading tumor cells from increasing water content in this peritumoral region continues to be a challenge for the treatment of brain tumors³. Positron emission tomography (PET) using 18-fluorodeoxyglucose (FDG) can provide additional insight into glucose metabolism in the peritumoral region⁴. DTI metrics can provide qualitative insight while PET on the other hand can provide quantitative information about the condition of the peritumoral region. The purpose of this study is to observe the response of DTI and PET metrics in glioblastoma patients receiving anti-angiogenic treatment and correlations are used to support their effectiveness.

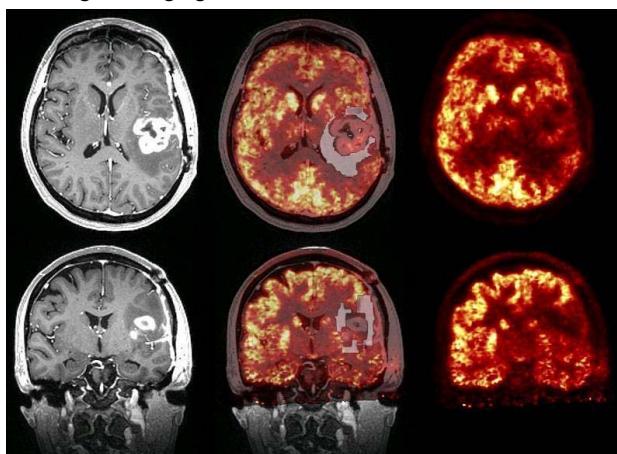


Figure 1. High resolution MPRAGE (left) and PET data (right) fused with NET region highlighted in white (middle) for the transverse (upper) and coronal (lower) plane

METHODS Ten patients (age range 22 to 74 years; mean 51.7 years) with newly diagnosed glioblastoma were scanned on the BrainPET, a prototype MRI-compatible PET scanner designed to fit inside the 3-T human MAGNETOM Trio MRI scanner (Siemens Healthcare Inc.) at two independent baselines (2-3 days apart) pretreatment onset and one day after treatment start. The patients were treated with cediranib, a VEGF signaling inhibitor, in combination with standard radiation therapy and temozolomide⁵. Immediately after the intravenous injection of ~5mCi F18-FDG, both PET data and diffusion weighted MR images were acquired. Diffusion weighted images were acquired (TE/TR = 84/7500 ms) with b-values of 0 and 700s/mm² in 42 directions. PET attenuation maps were generated from the CT volumes co-registered to the high resolution MPRAGE. Volumes were reconstructed for the forty to sixty minute time frame with the ordinary Poisson ordered-subset expectation maximization 3D algorithm from prompt and expected random coincidence, normalization, attenuation, and scatter coincidence sinograms using one subset and 64 iterations⁶. The non-enhancing tumor (NET) region was determined by subtracting the T1-weighted region of abnormality from the FLAIR region of abnormality as determined by a board-certified neuroradiologist. Regions of necrosis were excluded. The standardized uptake values (SUV) in the NET were normalized to the contralateral hemisphere (Fig. 1). These values were used to determine the mean SUV and the total glycolysis computed as $SUV_{mean} \cdot Tumorvolume$. FA and ADC means within the NET

region were calculated from the diffusion images (Fig. 2). The values of the two baselines were averaged. The relationship between changes in the mean SUV between the baseline average and day one, and FA and ADC changes in this period of time was investigated. For statistical analysis the Pearson coefficient was applied as measure of correlation.

RESULTS Mean SUV change between baseline and day one after treatment onset showed a significant negative correlation with mean FA change ($p = 0.032$). There was no significant correlation between the mean SUV change and the mean ADC change ($p = 0.107$). This suggests that lower glucose metabolism in the NET region is correlated with more anisotropic tracts. Also the total glycolysis change showed a significant negative correlation with the mean FA change ($p = 0.031$), but no significant correlation with mean ADC change ($p = 0.142$).

DISCUSSION Correlation between PET SUV data and the DTI metric FA in the peritumoral region of glioblastoma implies that changes in metabolism are related to directional changes in diffusion of the white matter tracts. A decrease in glucose metabolism is indicative of a decrease in the number of tumor cells or in the tumor cell activity, and an increase in values of FA reflect more anisotropic tracts. Both of these changes occur in apparently “healthy” white matter and their quantitative correlation might be clinically relevant. Since the tumor is not expected to change significantly between the two time points, our observations likely reflect changes in edema⁵. Changes in water content in the NET region or tumor cell migration might explain this. It is known that cediranib alleviates edema and has a rapid onset (within one day), so changes in edema content are likely caused by administration of the drug. A metric derived from combined MR and PET measurements could be a potentially useful biomarker of treatment response in brain tumor patients.

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