Neuroimaging based (PET and MR) measurements of cerebral oxygen extraction fraction (OEF) in patients with brain tumors

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Objective: To quantify and compare cerebral oxygen extraction fraction (OEF) measurements of human brain tumors, surrounding edema, and normal brain tissue using advanced MR and PET neuroimaging data in order to validate an alternative non-contrast oxygen sensitive MR technique[1] for studying brain tumor hypoxia. In general, tumor hypoxia is associated with sensitivity to radiation therapy, gene expression, and prognosis[2], but has not been widely studied in brain tumors. ^{15}O-PET and MR imaging can quantify OEF and provide insight into tumor pathology.

Introduction: The only in vivo noninvasive technique currently available to directly measure OEF is a combined ^{15}CO, $^{15}O_2$, and $H_2{}^{15}O$ positron emission tomography (^{15}O-PET)[3]; however, little data is available on brain tumor OEF in patient populations due to limited availability of this technique. The use of ^{15}O radiotracers, with 122-second half-life, requires close proximity of the imaging center, and the tracer-producing cyclotron to the PET scanner. Previously presented preliminary results of non-contrast MR and ^{15}O-PET indicated some discrepancies between the two methods in brain tumors OEF values[4]. In this study we further investigate the correlation and the discrepancies between the two methods using larger patient population.

Methods: MR protocol with standard clinical sequences and oxygen sensitive MR scans (a two-dimensional multi-echo gradient spin echo sequence)[1] was used on 30 participants (20 with brain tumors). Concurrent with the MR acquisition, subjects with brain tumors underwent PET scanning, which included 2 sets of 3 scans with serial inhalation of air with 40-75 mCi radiolabeled carbon monoxide ($C^{15}O$), 40-75 mCi radiolabeled oxygen ($^{15}O_2$), and injection of 25-50 mCi radiolabeled water ($H_2{}^{15}O$). MR and PET data were post-processed off line and registered to the anatomic T1 pre-and post-contrast images (Figure 1). Regions of interest were drawn based upon contrast-enhancing tumor areas, none-enhancing T2-hyper intensity (edema), contra-lateral normal white matter (NWM), and normal gray matter (NGM). Ratios of OEF (rOEF) were obtained for lesions compared to NGM. Pearson correlations coefficients and p values were calculated.

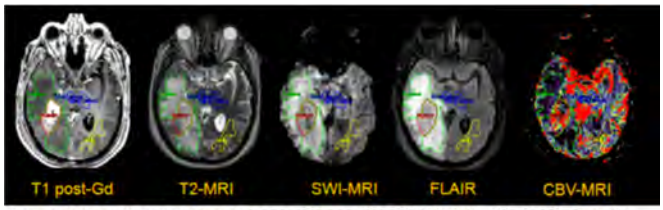

Figure 1: Sample of registered images (T1 post-Gd, T2-MR, SWI-MR, FLAIR, and CBV-MR) and ROI's (tumor in red, edema in green, NWM in yellow, and thalamus in blue) for a 57-year-old male with WHO grade IV glioblastoma.

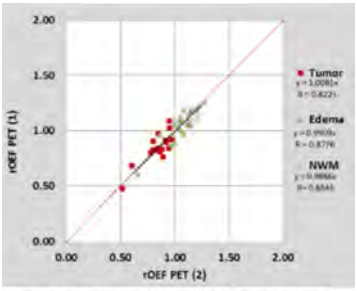

Figure 2: Relative OEF value of tumor (red square), edema (green triangle), and NWM (X marker) compared to thalamus for two sets of PET measurements. Slope (Y) and correlation (R) are given in the figure.

Results: As shown in Figure 2, high correlation were demonstrated between two rOEF-PET measurements for enhancing tumor (R=0.82 slope=1.01, p=0.00033), none-enhancing T2-hyperinternsity (R=0.88 slope=0.99, p<0.00001), and NWM (R=0.87 slope=0.99, p<0.00001). Figure 3 shows result of rOEF-MR and rOEF-PET data when subjects with SWI abnormalities (blood cloth, hemorrhage, and calcification) are excluded. The correlation, slope and P values are: R=0.39, slope=0.61, p=0.17 for enhancing tumor and R=0.3 slope =0.35, and P=0.04 for over all ROIs.

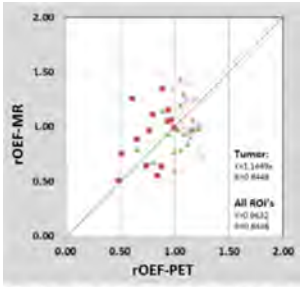

Figure 3: Relative OEF of tumor (red square), edema (green triangle), and NWM (X marker) compared to thalamus for MR and PET. By excluding lesions with SWI abnormalities (blood cloth, hemorrhage, calcification) overall correlation. Slope (Y) and correlation (R) are given in the figure.

Conclusions: Both MR and ^{15}O-PET can measure OEF in brain tumors and in peritumoral edema. Variable OEF measurements for tumor and edema may be implication for tumor grade and prognosis. BOLD MR fails in regions with signal loss on SWI or T2*. Both techniques have tremendous potential and may offer new insight into the underlying physiology of brain tumors and their response to therapy without requiring radiation or injected contrast.

References:

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