

## Decreased cerebral oxygen extraction fraction (OEF) measured by MR qBOLD following stereotactic radiosurgery (SRS) in patients with metastatic brain tumors

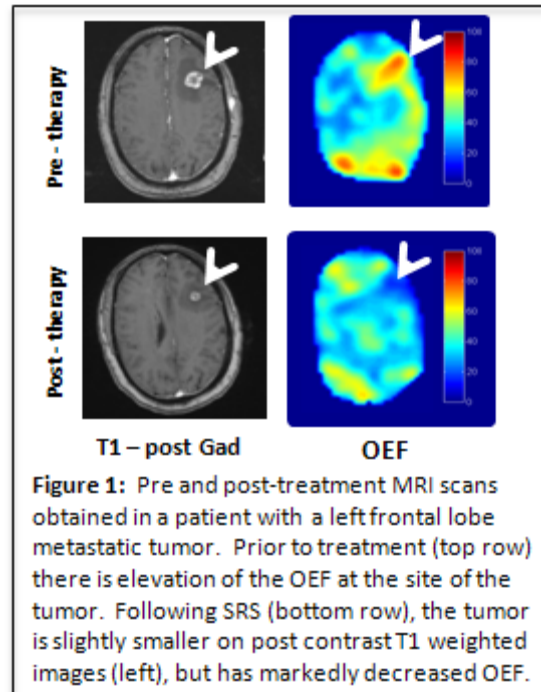
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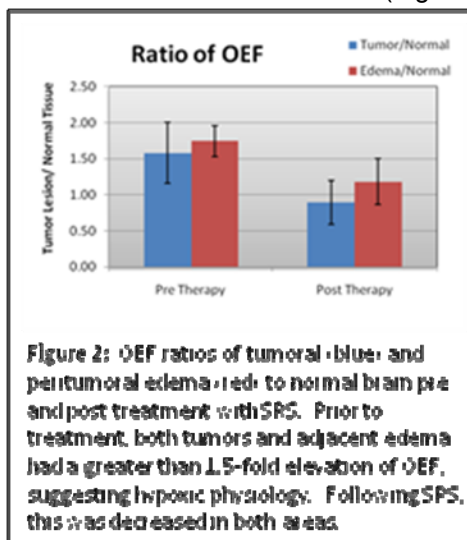
**Introduction:** In solid organ tumors, hypoxia is a critical factor in a tumor's response to a variety of treatment regimens. It is not clear whether this also plays a role when these tumors metastasize to the brain. Conventional estimation of cerebral oxygen extraction fraction (OEF) is performed using O<sup>15</sup>-PET; because of the short half life of this tracer and requirement for arterial blood sampling, there is only limited data for OEF measurements in patients with brain tumors. The recently developed MR qBOLD technique (1,2) allows for non-contrast MR quantification of cerebral OEF and may offer new insight into the underlying physiology of metastatic brain tumors and their response to therapy.

**Methods:** 10 patients (6 F) with metastatic brain tumors with planned treatment with SRS were prospectively recruited to the study. Primary tumors included lung (n=7), breast (n=2) and renal cell carcinoma (n=1). MRI was obtained prior to treatment, then at 2 month intervals with a mean follow up time of 114 days and a total of 24 imaging sessions. qBOLD imaging (3D version of gradient echo sampling of spin echo sequence (GESSE) was obtained at 1.5 T (Siemens Espree) and 3T (Siemens Trio). MR data was post-processed using Matlab scripts and were manually aligned and registered with the anatomic images (T1 pre and post contrast, FLAIR, and T2 weighted images). Regions of interest were drawn based upon contrast-enhancing tumor areas, non-enhancing T2-hyperintense areas of edema adjacent to tumor, and contralateral normal brain. Ratios of OEF were obtained for lesions compared to normal tissue.

**Results:** Prior to SRS, marked elevation of OEF compared to normal tissue was present for both metastatic tumors (1.58±0.42) and surrounding vasogenic edema (1.74±0.30). Following SRS, OEF ratios for tumor (0.90±0.31) and edema (1.18±0.32) both dropped, with a greater decrease found in tumoral areas (Figures 1 and 2).



**Figure 1:** Pre and post-treatment MRI scans obtained in a patient with a left frontal lobe metastatic tumor. Prior to treatment (top row) there is elevation of the OEF at the site of the tumor. Following SRS (bottom row), the tumor is slightly smaller on post contrast T1 weighted images (left), but has markedly decreased OEF.



**Figure 2:** OEF ratios of tumoral (blue) and peritumoral edema (red) to normal brain pre and post treatment with SRS. Prior to treatment, both tumors and adjacent edema had a greater than 1.5-fold elevation of OEF, suggesting hypoxic physiology. Following SRS, this was decreased in both areas.

**Conclusions:** Using MR qBOLD, we were able to quantify cerebral OEF in humans with metastatic brain tumors, thus providing information on tumor and peritumoral tissue physiology. Following SRS, OEF ratios decreased, suggesting qBOLD may provide a novel MR biomarker for tumor response. Longer term studies, with greater numbers of subjects will be needed to further evaluate the potential of this technique for evaluating brain tumors, tumor response, and complications, such as radiation necrosis or pseudoprogression.

**References:** 1. He and Yablonskiy (2007) *MRM*, 57:9868-9872.  
2. He et al. (2008) *MRM*, 60(4):882-8