Abnormal Brain Tumor Neovasulature Affects BOLD fMRI Response

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Introduction:

It is hypothesized that the decrease in Blood Oxygenation Level Dependent (BOLD) fMRI activation seen adjacent to grade IV gliomas (glioblastoma multiforme-GBM) is due to the presence of abnormal neovasculature and the resultant decoupling of neuronal activity and blood flow[1]. This phenomenon is not seen in other tumors that lack abnormal neovasculature. The purpose is to test the hypothesis that the areas where the volume of fMRI activation is decreased correspond spatially to the presence of neovasculature defined by rCBV.

Method/Materials:

55 patients were investigated using a 1.5 T MR scanner. 20 cases were excluded due to prior surgery and the presence of susceptibility artefact which rendered inaccurate the comparison of the volumes of activation between the two brain hemispheres. Of the remaining cases, there were 12 GBM's, 10 grade II and III gliomas, 12 metastases and 3 meningiomas. The MR data were acquired by a T2* weighted gradient echo EPI (TR/ TE =4000/40 msec, 21 axial slices with a 4.5mm slice thickness and a 0 mm gap, a 128x128 matrix, and a 240 mm FOV) for BOLD fMRI using a bilateral finger tapping paradigm and for perfusion imaging (TR/ TE =1000/40 msec, 10 slices, a 128x128 matrix) following a Gd-DTPA contrast agent (0.1 mmol/kg, 3cc/sec) and a T1 weighted spin-echo (TR/TE =500/8 msec, a 256x256 matrix for the same slices of the EPI) for anatomical images. The fMRI data were analyzed using AFNI and co-registered to the T1-weighted images. The activation volumes of the Primarily Motor Cortex (PMC) were determined using cross-correlation-R values with a p value < 0.001 and a cluster size > 5. The rCBV values were calculated voxel by voxel from the integration of the peak in a time course of the first passage of the Gd-DTPA. Ratios of the activation volumes of the BOLD fMRI and the rCBV values in PMCs were calculated for the tumor side to the non-tumor side. We applied a linear regression for fitting the data of the rCBV and the BOLD fMRI activation volume ratios in the PMCs, and for the distances between tumors and the PMCs. The distance was measured as from the location of the maximum rCBV value of a tumor to the position of the BOLD signal with the highest r-value in the PMC.

Results:

Statistically significant correlation between Vol $(fMRI)_T$ /Vol $(fMRI)_{NT}$ and $rCBV_T$ /$rCBV_{NT}$ was only seen for the GBM group (the correlation coefficient R2 =0.6435, p-value=0.0017), where T=tumor side and NT=non-tumor side (Figure 1). The BOLD volume ratio linearly decreased as the distance of maximum rCBV (which defined the presence of the most malignant part of the GBM) to the PMC increased (R^2 =0.7). The ratio of $rCBV_T$ /$rCBV_{NT}$ linearly increased as the distance of maximum rCBV to the PMC decreased (R^2=0.9). For the GBM group, the average Vol $(fMRI)_T$ /Vol $(fMRI)_{NT}$ is 0.58 with a standard deviation 0.34, and the average $rCBV_T$ /$rCBV_{NT}$ is 1.98 with a standard deviation 1.07. For the low-grade gliomas, the BOLD ratio is 0.67 with a standard deviation 0.29, and the rCBV ratio is 1.18 with a standard deviation 0.25. For the metastases, both the BOLD ratio and the rCBV ratio are approximate 1.00 with a standard deviation 0.33 and 0.20, respectively. For the meningiomas, the BOLD ratio is 0.72 with a standard deviation 0.41, and the rCBV ratio is 1.50 with a standard deviation 0.72.

Discussion:

Our data demonstrate a statistically significant inverse correlation between the ratio of BOLD fMRI activation to the ratio of rCBV in malignant gliomas. In other words, and increase in rCBV, which is seen in GBM's (malignant gliomas), significantly correlates to a decrease in BOLD fMRI activation. rCBV is an indirect measurement of the presence of abnormal tumor neovasculature and correlates well with tumor histology[2]. Therefore, our data support the contention that a decrease in BOLD fMRI activation is due to the presence of abnormal neovasculature (as defined by rCBV). Our data failed to show a correlation between tumor histology and the ratio of BOLD fMRI activation. This may seem somewhat surprising in light of the statistically significant correlation between the ratio of BOLD fMRI activation to the ratio of rCBV. The explanation to this discrepancy is as follows: the most malignant part of the tumor defines its histology. Most brain tumors (especially GBM's) are heterogeneous with the histology becoming progressively less malignant as one moves further from the center of the tumor. For example, a biopsy of a brain tumor in the anterior aspect of the frontal lobe may reveal a GBM, whereas a biopsy of the same tumor in the pre-central gyrus (motor strip) may reveal a grade II/IV glioma. If such were the case, the rCBV would be increased in the anterior aspect of the frontal lobe and would be normal in the motor strip. In this case, the Vol $(fMRI)_T$ /Vol $(fMRI)_{NT}$ would be close to unity, notwithstanding the fact that the tumor is a GBM. This reasoning is supported by our data which shows an inverse relationship between the distance of the area of increased rCBV (which defines the location of the most malignant part of the tumor and the presence of abnormal neovasculature) to the motor cortex.

Conclusions:

The decrease in the activation volume of the BOLD fMRI adjacent to GBM's correlates spatially to an increase in an rCBV value. The ratio of BOLD fMRI activation of the tumor side to the non-tumor side is inversely proportional to the distance of the highest rCBV value to the PMC. This supports the hypothesis that the decease in fMRI activation adjacent to a GBM's is due to the presence of abnormal neovasculature and the decoupling of neuronal activity and blood supply.

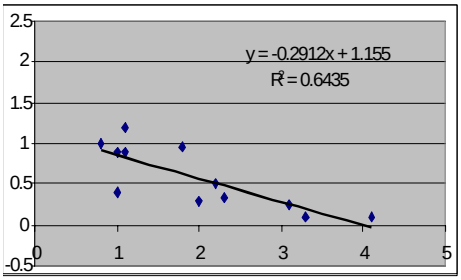

Fig 1. (Vol $(fMRI)_T$ /Vol $(fMRI)_{NT}$) vs. $rCBV_T$ /$rCBV_{NT}$ for GBM's without prior surgery.

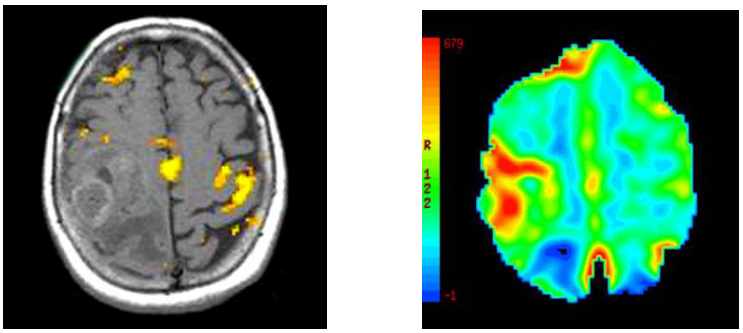

Fig 2. A patient with GBM involving the PMC with (Vol $(fMRI)_T$ /Vol $(fMRI)_{NT}$) = 0.1 (left) and the rCBV ratio = 4.1 (right).

References:

1. Holodny AI, et al., AJNR, 1999; 20:609-612.
2. Knopp EA, et al., Radiology, 1999; 3:791-798.