Effect of Abnormal Neovasculature and Metabolites on the BOLD fMRI Activation Volume for Brain Tumor Patients

B. L. Hou[1], S. B. Thakur[2], K. K. Peck[1], N. M. Petrovich[1], W. Huang[3], P. H. Gutin[4], A. I. Holodny[1]

[1]Functional MRI Laboratory, Radiology, Memorial Sloan-Kettering Cancer Center, New York, New York, United States, [2]Medical Physics, Memorial Sloan-Kettering Cancer Center, New York, New York, United States, [3]Medical Physics and Radiology, Memorial Sloan-Kettering Cancer Center, New York, New York, United States, [4]Surgery, Memorial Sloan-Kettering Cancer Center, New York, New York, United States

Introduction:

Blood oxygen level dependent (BOLD) functional MRI signal resulting from neural activity in normal brain can be described by a "Balloon model" (1). The signal is related to the changes in cerebral blood flow (CBF), cerebral blood volume (CBV), and cerebral metabolic rate of oxygen (CMR02). However, it is unclear if the model is still valid for a brain with a malignant tumor located near an eloquent cortex. Specifically, the tumor neovasculature may not respond normally to neural activity (2). The purpose for this study is to explore the influence of the abnormal neovasculature defined by perfusion MRI (rCBV) and the abnormal metabolite levels seen with proton MRS imaging on the BOLD fMRI activation volume for brain tumor patients.

Method and Materials:

13 brain tumors (7 GBMs, 3 metastases, 1 meningioma, 1 anaplastic astrocytoma, and 1 oligodendroglioma) located near or within the primary motor cortex (PMC) were scanned by using a 1.5T General Electric (GE) TwinSpeed MRI scanner with a standard quadrature head coil. The protocol included high resolution, anatomic, T2 or T1-weighted spin echo images (256 x 256 matrix, 21 axial slices, 4.5 mm slice thickness with 0 gap), BOLD fMRI with bilateral finger tapping (gradient echo EPI, TR/TE =4000/40 msec), perfusion MRI (gradient echo EPI, TR/TE =1000/40 msec, 0.1 mmol/kg Gd at 3cc/sec) and multi-voxel ^{1}H 3D MRSI PRESS sequence (TR/TE=1000/144 msec, 8x8x8 matrix). The slice thickness for the fMRI, perfusion, and MRSI scans was also 4.5 mm with no gap, and the axial slices were selected to match the locations of T2 or T1-weighted images. The fMRI data were analyzed using AFNI. Image processing was performed using correlation coefficients to threshold the activation volumes of the PMC. The significant threshold was set at $P<0.001$, typically for a correlation coefficient of 0.45-0.5. The rCBV values of both PMCs were calculated by integrating the areas under the curve of the gadolinium bolus. The ratios of fMRI activation and rCBV for the tumor sides to the non-tumor sides were calculated – fMRI(T/NT) and rCBV(T/NT). The Cho/NAA, Cho/Cr and Lac/Cr ratios for both PMCs were calculated by using GE's FuncTool software. The tumors were grouped as "the GBM in PMC (5 cases)", which means that the GBM was located directly in the PMC, and "the other tumors (8 cases)".

Results:

Figure 1 shows the BOLD fMRI, and rCBV maps for a GBM located in the right PMC. Figure 2 is the MRSI results: MRSI voxels labeled by number and MR spectrum in a voxel on the tumor side PMC (#9). The mean ratios and corresponding standard deviations (STD) of the BOLD and the rCBV, the ratios of Cho/NAA, Cho/Cr and Lac/Cr in the PMCs of both tumor and non-tumor sides for the two groups are listed in the Table 1.

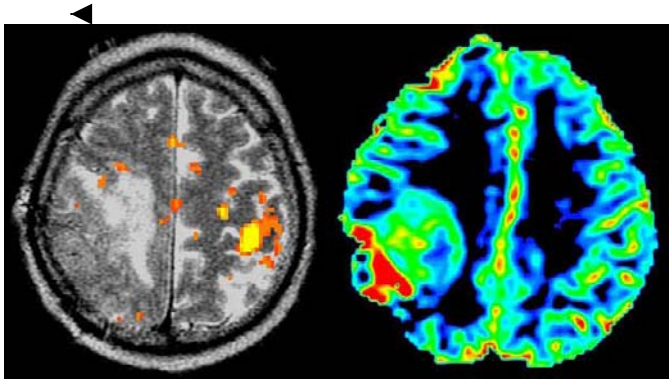

Figure 1. BOLD (the left) and rCBV (the right) for a case with the GBM located on the right side PMC. The inverse relationship between rCBV and BOLD response is demonstrated.

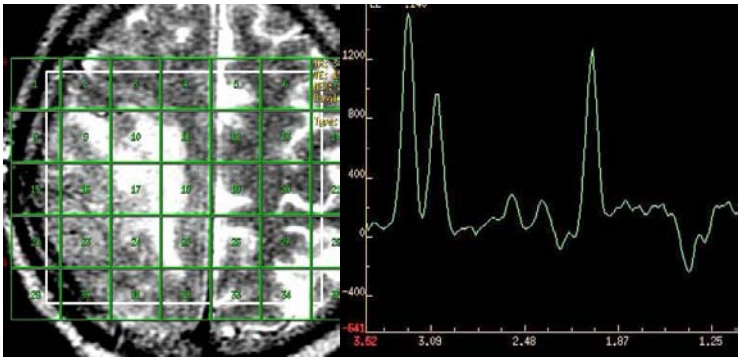

Figure 2. MRSI voxels (in green) and region of RF excitation (in white) shown in the left and the spectrum for the #9 voxel (i.e., the tumor side PMC) shown in the right of the figure. The lactate peak is the doublet at 1.3 ppm with an inverse phase.

	"the GBM in PMC" (mean (STD))		" the other tumors" (mean (STD))	
BOLD ratio	0.37 (0.13)		0.79 (0.24)	
rCBV ratio	3.08 (0.53)		1.23 (0.38)	
	Tumor side	Non-tumor side	Tumor side	Non-tumor side
Cho/NAA	2.22 (0.54)	0.63 (0.07)	0.83 (0.30)	0.57 (0.11)
Cho/Cr	2.3 (0.24)	1.09 (0.08)	1.41 (0.36)	1.13 (0.15)
Lac/Cr	0.43 (0.25)	non-detectable	non-detectable	non-detectable

Table 1: The ratios of the BOLD and the rCBV and the ratios of Cho/NAA, Cho/Cr and Lac/Cr in the PMCs of both sides for the groups of "the GBM in PMC" and "the other tumors".

Discussions:

The data in table 1 were analyzed by a paired t test, and demonstrated a significant difference between the BOLD fMRI and rCBV ratios in the two groups: fMRI, $p=0.03$ and rCBV, $p=0.01$. Lactate peaks were found only on the tumor side of "the GBM in PMC" group. There was also a significant difference in the mean ratios of Cho/NAA (2.22 vs 0.63, $p<0.01$) and Cho/Cr (2.3 vs 1.09, $p<0.02$) between the tumor side and the contralateral side for "the GBM in PMC" group. The differences for the Cho/NAA and Cho/Cr ratios in the two hemispheres were not significant in the "the other tumors" group.

The BOLD signal is due to increased neuronal activity leading to increased oxygen consumption and blood flow. Our results for "the GBM in PMC" group suggest that the presence of abnormal neovasculature (indicated by the high rCBV ratios) and the resultant decoupling of neuronal activity and blood flow lead to a muted BOLD response. Lactate peaks in tumor side PMCs suggest hypoxia which implies a) that the vessels may be nearly maximally dilated which further limits the BOLD response b) a corresponding decrease in oxygen consumption for resulting in even small BOLD response. If a tumor was not allocated in the PMC, the BOLD signal (i.e., the ratio) was much closer to the normal value probably due to less abnormal neovasculature and metabolites existence in the PMC.

References:

1. Buxton, R., NeuroImage, 2004, 23: S220-S233
2. Holodny, A. I., et al., AJNR Am J Neuroradiol, 1999, 20: 609-612