TUMOR INDUCED ALTERATIONS IN HEMODYNAMIC RESPONSES IN BOLD FMRI: IMPLICATIONS IN PRESURGICAL FUNCTIONAL BRAIN MAPPING

L. Wang[1,2], D. Chen[3], J. Olson[4], S. Ali[1], T. Fan[2], and H. Mao[1,2]

[1]Radiology, Emory University School of Medicine, Atlanta, GA, United States, [2]Center for Systems Imaging, Emory University, Atlanta, GA, United States, [3]Physics, Emory University School of Medicine, Atlanta, GA, United States, [4]Neurosurgery, Emory University School of Medicine, Atlanta, GA, United States

Introduction

The blood oxygenation level dependent (BOLD) fMRI has been widely applied in presurgical planning for brain tumor resection (1-2). Since BOLD fMRI detects brain activations inherently linked to an increase in blood flow that is disproportionate to the increase in oxygen consumption and metabolism, abnormal cerebral blood supplies associated with a disease may alter the hemodynamic response (HDR) of BOLD fMRI signals. Growth of brain tumor is commonly accompanied by the abnormal blood perfusion, therefore, may lead to an altered BOLD effect and inaccurate measurement of functional maps. In this study, we attempted to investigate the effect of the brain tumor to the HDR and BOLD signal time courses in brain tumor patients who underwent presurgical planning fMRI exams of motor cortices.
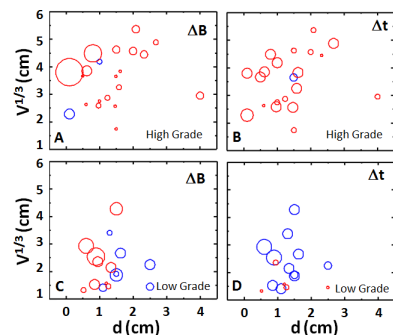
Materials and Methods

Brain tumor patients: 42 glioblastoma patients who underwent presurgical mapping of the primary motor cortex (PMC) were divided into the groups of high (WHO Grade IV-III, n = 24) and low (WHO Grade n = 18) grade glioblastoms based on pathology findings.

Group	Age	Pathology (WHO Grade)	Volume (mL)	Distance to PMC (mm)	BOLD (ΔB)	TTP (Δt)	rCBF
LG	48±10.1	GI-II	11±10.7	13±4.8	0.74±0.9	1.88±0.03	Low_5
HG	48±13.2	GIII-VI	53±39.7	14±8.9	2.26±3.0	2.11±0.02	High_10

MRI Data Collection: All MRI data were recorded on a 3T MRI scanner (Siemens Tim/Trio) using a standard head coil and clinical routine brain MRI protocol. Dynamic susceptibility enhanced perfusion MRI was performed on some patients (n=15) after fMRI exams to assess the relative cerebral blood flow (rCBF) in the brain. For mapping the sensory motor cortices, a block design paradigm with a time course of 70 points (3 ON and 4 OFF blocks) was used with patients performing sequential finger tapping (at a frequency of ~1 Hz) using either the left or right hand. Image acquisition parameters include: TR/TE=3000/35 ms, Field of View (FOV) = 240 mm, matrix = 64 x 64, 25 slices and slice thickness = 5 mm without gap. Susceptibility weighted contrast enhanced dynamic MRI was collected using parameters: TR/TE=1840/32 ms; FOV = 240 mm; slice thickness = 5 mm; slice gap = 0.5 mm; matrix = 128 x 128. A series of 50 multisection acquisitions with 25 slices was acquired.

Image Process and Data Analysis: The tumor volume was measured by the sum of the signal enhanced area manually traced from each slice and multiplied by the thickness of slice]. The distance between a tumor and activated foci was defined and measured as a closest distance between the boundary of a tumor and the point with the activated BOLD foci within or close to PMC. A simplified HRF based on Noll's model (3) was used in this study. Signal time courses from defined ROIs in the activated PMC in the tumor affected hemisphere and non-affected hemisphere of each patient were obtained at the selected thresholds to calculate the fMRI BOLD signal intensity ($\Delta B = B_{normal} - B_{affected}$) and TTP changes ($\Delta t = TTP_{affected} - TTP_{normal}$). The data were analyzed and compared in different groups using independent sample student t-tests from the Statistical Package for the Social Sciences (SPSS). A result with $P < 0.05$ was considered statistically significant. Perfusion MRI data were analyzed by the software package implemented on the scanner.

Results and Discussions

The demographic and functional data are summarized in the **Table**. **Fig. 1** shows the observed tumor affected BOLD signal time courses obtained from PMCs of the high grade tumor and low grade tumor patients. Reduction of BOLD signal levels in tumor affected PMCs were observed in 73.7% of patients with either Low or High Grade groups and in 90.9% of high grade tumor patients when compared to the non-affected PMC in the non-affected hemisphere. Averaged TTPs in the affected PMC was shorter than that of the non-affected hemisphere for the High Grade tumor group ($P < 0.0001$), however, longer in the affected hemisphere than non-affected hemisphere in the Low Grade tumor group ($P < 0.0001$). Degrees of alterations in time courses appear to relate to both the tumor volume and distance between the activated motor cortex and the tumor. **Figure 2** are 2D plots of changes of BOLD signal levels (ΔB) and delays of TTP

Fig. 1 Examples of fitted BOLD signal time courses from a high-grade (A) and a low-grade (B) patient. The tumor affected BOLD signal (blue) is from an ROI in activated PMC which can be compared with that from the normal PMC (red) in the contralateral hemisphere. High and low rCBF maps suggest the high and low grade tumors.

in the tumor affected PMC comparing that of normal hemisphere in both high grade tumor (A, B) and low grade tumor (C, D) groups. Cases with tumors closer to activated areas and with large tumor volumes exhibit relatively larger magnitudes of BOLD signal reduction since they appear mainly in the up left corner of the diagonal of the plot, suggesting that both tumor volume and distance affect the BOLD signal intensity. The plot of reduction of averaged intensity change as a function of tumor distance to activated foci shown in **Figure 2(A, C)** revealed that the effect of the tumor distance to activated foci on the BOLD signal level is evident when a tumor is within a distance less than 12 mm. In most instances, positive ΔB values (as shown as red colored cycle with the size of the cycle indicating the magnitude of changes) were observed. However, negative ΔB values were also found, suggesting that the tumor volume or the distance to activated foci may not alone, but coupled affect the BOLD signal. The effect of the tumor volume and the distance to activated foci were also observed in the TTP of BOLD signal time courses. The shifts of TTP (Δt) are positive in the most of high grade tumor cases (red circles in **Figure 2B**), indicating HDR delays were shortened in the tumor affected PMC. However, the effect of the tumor volume and the distance to activated foci on the TTPs of the BOLD signal time course is less obvious comparing BOLD signal intensity change. By taking into account of altered HDR delays in the fitting of BOLD time courses, improved activation maps can be obtained as shown in the examples in **Fig. 3**.
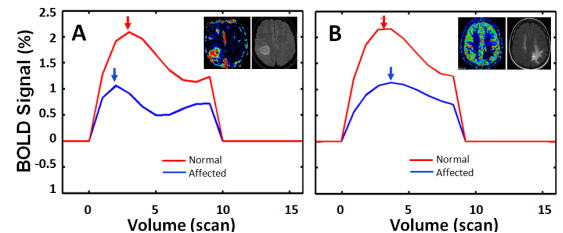

Fig. 2 2D plots of changes in BOLD signal intensity (ΔB) and TTP (Δt) in relationships to the tumor volume ($V^{1/3}$cm) and the distance to activated foci (d, cm) of the high grade (A,B) and low grade (C,D) groups.

Fig. 3 Activation maps of tumor affected PMC before (A) and after (B) making adjustments in HDR delays.
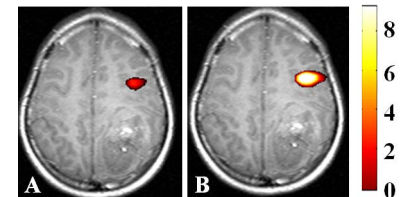
Conclusions

Hemodynamic responses associated to BOLD signal changes are affected by the presence of the glioblastoma which causes abnormal cerebral blood supplies in the area of the tumor. Observed alterations in BOLD signal time courses are strongly related to the tumor grade, tumor volume and the distance between the tumor boundary and activated foci. Such alterations may degrade accurate mapping of tumor affected functional areas when analyzing time courses of BOLD fMRI data using conventional fixed models.

References [1] Ahsan, H., M. Akbar, and A.U. Bhatti. *J Pak Med Assoc*,2009;59 **[2]** Feldman, S.C., et al. *AJNR*,2009;30 **[3]** Vazquez, A.L. and D.C. Noll. *Neuroimage,* 1998;**7**