Simultaneous BOLD and ASL for Characterizing Cerebrovascular Responses to Hyperoxia in Normal Brain and in Glioblastoma

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INTRODUCTION: Characterization of cerebral vascular responses to hyperoxia in normal brain is essential for investigating vascular regulation of cerebral hemodynamics. An understanding of its mechanisms can be also applied for predicting therapeutic responses in tumors. A very promising imaging tool that can be used for this purpose is combined Blood Oxygenation Level Dependent (BOLD) and Arterial Spin Labeling (ASL). Simultaneous BOLD-ASL measurements could provide a non-invasive quantification of physiologically relevant hemodynamic parameters, minimize the temporal and spatial variations, and they could potentially be used to obtain cerebral metabolic rate of oxygen consumption quantitatively [1]. This method was used to assess quantitatively the characteristic cerebral responses to 100% oxygen exposure in normal brain and in glioblastoma (GB).

METHODS:

Human Subjects: Eight healthy subjects and eight GB patients were scanned using a 3T Siemens MRI scanner with a 32-channel head coil.

Data Acquisition: The simultaneous BOLD and ASL sequence was developed based on pulsed ASL sequence by applying QUIPSS II technique for pre-saturation and PICORE tagging method followed by single-shot, gradient echo (GE) echo planar imaging (EPI) acquisition with a 64×64 matrix. Paired images were acquired alternately with and without tagging using TI1/TI2 =700/1400 ms. Eight-slice images with 8mm thickness were acquired using the optimized TE and TR for both BOLD and flow (TR/TE=2000/19ms, FOV = 220mm, 6/8 partial Fourier). The breathing paradigm consisted of baseline room air (2min), followed by 100% O_2 (4min) and then washout room air (4min) with 45L/min flow rate delivered via a custom-made respiratory mask. T2-weighted images for healthy volunteers and T1-weighted images after an injection of Gadolinium-DTPA for GB patients were acquired to provide anatomical details.

Data Analysis: Data processing consisted of motion correction, subtraction (Flow) and addition (BOLD) of paired images, and general linear modeling using Neurolens software. For healthy volunteers, two ROIs (i.e. gray matter (GM) and white matter (WM)) were defined on T2-weighted images. For GB patients, the data were analyzed in two ROIs - enhancing tumor (ET) and normal tissue on the contralateral side (cNT) – defined on the T1 post-contrast images. The output values having statistical significance by Student's t-test ($p < 0.05$) were analyzed.

RESULTS AND DISCUSSION:

Healthy Subjects: The images of T2, BOLD and Flow (CBF) responses overlaid on the anatomical T2-weighted images are shown in **Fig.1a** for a representative subject. BOLD and Flow effects were detected primarily in the cortex (increased BOLD and decreased CBF responses). The signal percentage changes (ΔS) are shown in **Fig.1b** for all eight subjects. BOLD signal change in GM was approximately twice than in WM (2% vs 0.9%). CBF signal change in GM was also larger than that in WM (34% vs 21%). These measurements agreed with previously published data[2].

GB Patients: The corresponding images for a representative GB patient and graphs for all patients are shown in **Fig.2a-c**. Heterogeneous BOLD signal (**Fig.2b**) was observed in the lesions (shadowed circle). The post-surgical cavity demonstrated decreased response, whereas the residual enhancing tumor and peritumoral regions around the cavity showed increased response. The ET region - defined by avoiding the cavity - showed an increase (1.4%) in BOLD and a decrease (12%) in CBF. In the cNT region, an increase (0.8%) in BOLD and a decrease (5%) in CBF were observed. The characteristic properties of the tumor vasculature (i.e. tortuous, large vessels), might explain the predominant vascular effects observed in the BOLD measurements. On the other hand, CBF responses in patients (in both ET and cNT) were less than those in healthy subjects, suggesting the cerebral blood circulation in tumor patients is not efficient.

CONCLUSION: Combining advanced MR imaging technique can help us better understand cerebral responses to hyperoxia in both normal and cancerous tissues. Ultimately, performing these measurements simultaneously will allow us to assess oxygenation metabolism in tumor, which could be beneficial for treatment response monitoring.

REFERENCES: **[1]** Wong EC et al., NMR Biomed 1997;10:237-249
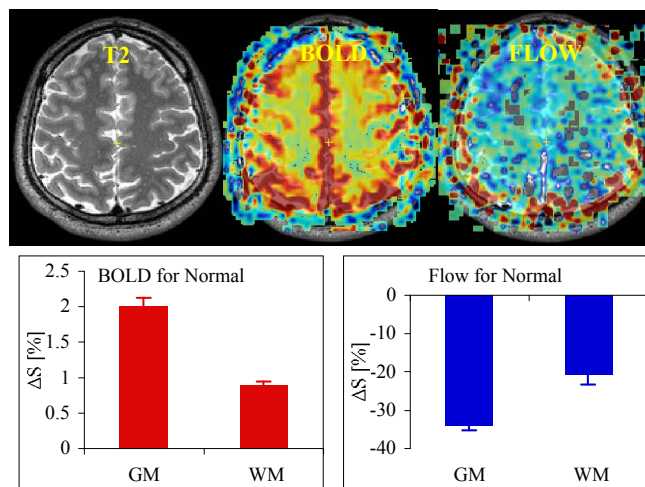[2] Floyd TH et al., J. Appl. Physiol. 2003;95:2453-2461

Fig.1. a) top: T2 and overlaid images of BOLD and Flow responses for healthy subjects
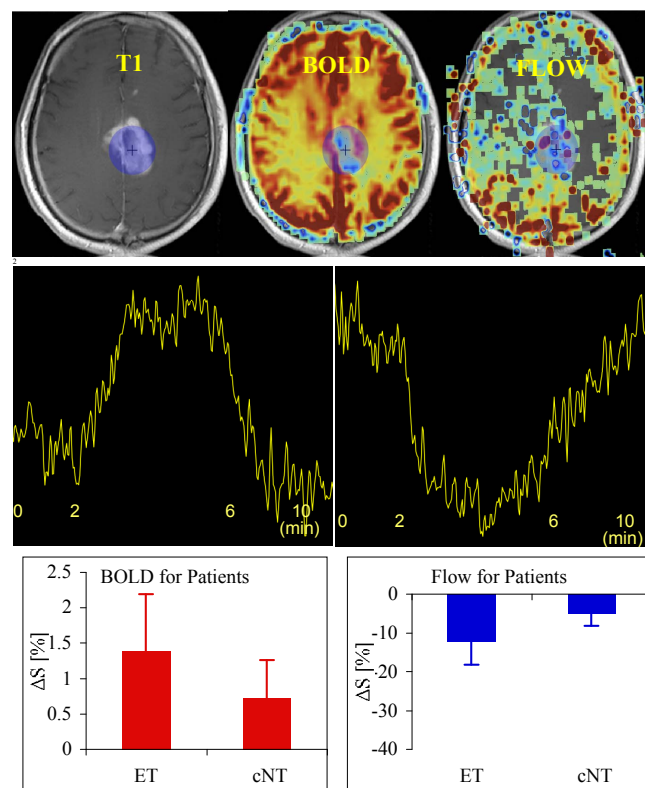**b) bottom:** graphs for signal changes in BOLD and in Flow

Fig2. a) top: T1 post-contrast and overlaid images of BOLD and Flow for GBM patients. Shadowed circle indicates tumor lesion.
b) middle: representative signals from one voxel in ET (Left) and from post-surgical cavity (Right)
c) bottom: graphs for signal changes in BOLD and in Flow