Feasibility of quantitative measurements for regional cerebral metabolic rate of oxygen ($CMRO_2$) during functional change with visual stimulus using MRI

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Introduction: Functional MRI using BOLD (blood oxygenation level dependent) contrast is sensitive to local changes in cerebral hemodynamics during neural activity. The BOLD effect, however, is a complex function of cerebral physiology, including cerebral blood flow (CBF), venous oxygen saturation (Y_v), and cerebral metabolic rate of oxygen ($CMRO_2$). Absolute quantification of these parameters during rest and functional activity is an active area of research that may yield critical insight into cerebral physiology in health and disease [1]. Although whole-brain values for $CMRO_2$ have been reported using MRI [2], there is currently no established technique for local estimates of $CMRO_2$. Phase-based regional oxygen metabolism (PROM) is a method that combines independent measurements of Y_v from MR susceptometry and CBF from arterial spin labeling (ASL) to estimate local $CMRO_2$ [3]. Here we assess the feasibility of PROM to quantify regional $CMRO_2$ at rest and during visual stimulation.

Methods: Three healthy volunteers (ages 24-29, 2 males and 1 female) were scanned with a 32-channel head coil using a 3T Siemens Tim Trio. Functional EPI (TR/TE = 2500/25 ms, 2x2x2 mm^3) and PICORE-Q2TIPS pulsed ASL (TR/TE/TI = 2500/25/1800 ms, 2x2x4.5mm^3) were acquired with block presentation of a visual stimulus. The stimulus was a radial flashing checkerboard (8Hz contrast reversal), alternated with a blank screen in 20s on and 25s off epochs, throughout which the subject fixated a central target. Statistical analyses on the functional EPI data were done in SPM (Standard Parametric Mapping) with false positive threshold set at p=0.05 [4]. CBF maps were calculated separately for resting and active states by calibration with the fully relaxed longitudinal magnetization of arterial blood (M_{0B}), as estimated from the local tissue equilibrium magnetization [5].

For Y_v measurements, 3D flow-compensated FLASH was used to acquire axial magnitude and phase images (TA = 1:37 min, TE = 20ms, 0.5x0.5x1 mm^3) at baseline and during activation. The fixation task and presentation of either a blank screen or checkerboard stimulus began 30s before the acquisition and was maintained throughout the scan. Candidate vein segments approximately parallel to the main magnetic field were manually identified for Y_v estimation.

$$\Delta B = \frac{1}{3} 4\pi \, \Delta\chi_{do} \, Hct \cdot (1 - Y_v) \, B_0 \qquad (1)$$

$$CMRO_2 = (Y_a - Y_v) \cdot CBF \cdot C_a \qquad (2)$$

From the phase image, the field difference, ΔB, was measured between the inside of each vein segment and the surrounding tissue. Vessel Y_v was then estimated from ΔB as in Eq 1 [6], where $\Delta\chi_{do}$= 0.18*ppm* is the susceptibility difference between fully deoxygenated and fully oxygenated blood, and hematocrit values were assumed, *Hct* = 0.42 for males and *Hct* = 0.38 for females. Local CBF was estimated from an ROI spatially matched to the vessel proximity with mean volume of 210mm^3. From these measurements, regional $CMRO_2$ was determined using the Fick Principle (Eq 2) [2]. Here C_a = 793 μmol O_2/100ml blood is the carrying capacity of oxygen per gram of hemoglobin, and arterial oxygen saturation Y_a = 1.

Results: For each subject, BOLD statistical maps were used to select three candidate veins from activated areas in the visual cortex, which were compared to three control veins in unactivated frontal regions (Fig 1). Regional averages of absolute Y_v, CBF, and $CMRO_2$ were estimated for each subject, and means across subjects are presented in Table 1. Baseline values of these parameters are consistent with values reported by ^{15}O positron emission tomography [7]. Significant increases in Y_v (p<0.01), CBF (p<0.01), and $CMRO_2$ (p=0.02) during activation were detected in the visual cortex using a paired t-test, with no significant change observed in the frontal cortex. The measured absolute increase in oxygenation, ΔY_v = 10.8±3%, agrees with previously reported values of ΔY_v = 14±3% during activation in the motor cortex [6]. Similarly, $CMRO_2$ increased by 13.1±5% during activation, which is comparable to the 16±1% $CMRO_2$ increase measured in the visual cortex with calibrated BOLD techniques [8]. However, this method measured a 59±10% CBF increase during activation, which is higher than the 45±4% CBF increase previously reported in the visual cortex [8]. This may reflect contamination of ASL measurements from large arteries, and these potential bias sources deserve further investigation. Future work at 7T with higher spatial resolution will offer more accurate quantitative estimates of physiological parameters and determination of ASL drainage territories for candidate veins.

Conclusion: This work demonstrates feasibility of our MRI method to quantify regional $CMRO_2$ during visual stimulation. Baseline $CMRO_2$ in the visual cortex was estimated as 158±23 μmol/100g/min and increased by 13.1% to 178±18 μmol/100g/min with functional activation (p=0.02).

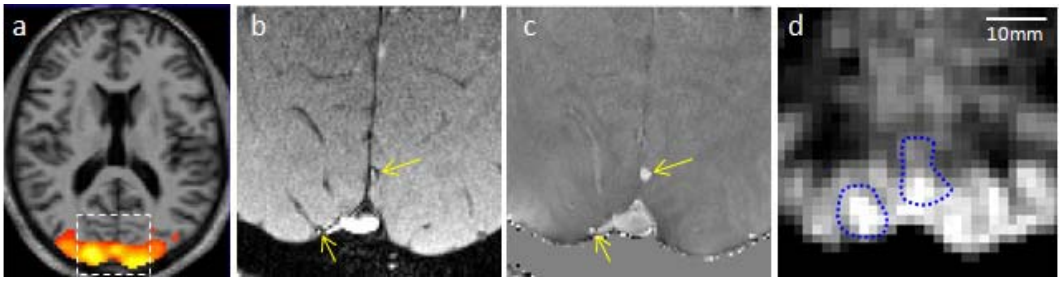

Figure 1. (a) BOLD t-statistic map indicating activated region in visual cortex. **(b)** FLASH magnitude and **(c)** phase where arrows indicate candidate veins in visual cortex. **(d)** CBF map during activation with ROIs spatially matched to veins in b,c.

References

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Acknowledgements: ROIEB007942, Siemens Healthcare, Siemens Medical Solutions, Siemens-MIT Alliance, NSF GRFP

	Y_v (%)			CBF (ml/100g/min)			$CMRO_2$ (μmol/100g/min)		
	Baseline	Activation	**ΔY_v**	Baseline	Activation	**ΔCBF**	Baseline	Activation	**$\Delta CMRO_2$**
Control	60.4 ± 5	60.2 ± 7	**0.2 ± 2**	42 ± 6	41 ± 5	**-0.8 ± 2**	125 ± 16	123 ± 26	**-2.7 ± 10**
Visual Cortex	61.7 ± 4	72.4 ± 4 *	**10.8 ± 2**	54 ± 8	86 ± 12 *	**32 ± 6**	158 ± 23	178 ± 18 *	**21 ± 5**

Table 1. Mean ± standard deviation across subjects (n=3) of absolute Y_v, CBF, and $CMRO_2$ at rest and during stimulation in visual cortex and control in frontal cortex