Baseline oxygenation in the brain: Correlation with BOLD and comparison between susceptibility and respiratory-calibration methods

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Purpose. New methods for noninvasive imaging of brain oxygenation show great promise. To date, these approaches have not been carefully compared to each other, or evaluated against known relationships with other physiological parameters such as the BOLD signal. Quantitative susceptibility mapping (QSM) allows mapping of baseline oxygen extraction fraction (OEF_0) along cerebral vessels based on the deoxyhemoblogin (dHb) susceptibility shift between veins and water [1]. Alternatively, quantitative O_2 imaging (QUO2) applies a biophysical model to measure OEF_0 in tissue from BOLD, cerebral blood flow (CBF), and end-tidal O_2 (EtO_2) signals acquired during two or more gas manipulations [2]. We propose to: ***Aim 1.*** Investigate whether BOLD signal changes during visual stimulus and gas depend on baseline OEF_0 (measured from susceptibility), as predicted by biophysical models [3,4]; and ***Aim 2.*** Compare absolute estimates of OEF_0 by QSM and by QUO2 in the visual cortex.

Methods. *Imaging.* Eight volunteers (seven female, 22-29 years) were scanned on a 7T Siemens MRI with a 24-channel head coil. Simultaneous BOLD-ASL scans were acquired continuously during hypercapnia (5% CO_2, 21% O_2, 74% N_2), hyperoxia (100% O_2), and carbogen (5% CO_2, 95% O_2). Each 3-min gas challenge was followed by 2-min of medical air. BOLD-ASL was acquired with TR=3s; TE=9.2/22.7ms; matrix=64x64x10; 3x3x3mm^3; FAIR-QUIPSS II; inversion times TI_1/TI_2=700/1400ms. Separate BOLD-ASL scans were acquired during a 30-s on-off checkerboard stimulus (8Hz, contrast-reversing) to identify the visual cortex. 3D flow-compensated gradient echo scans were also collected at rest for QSM reconstruction of OEF_0 along cerebral veins (TR=23s; TE=7.5ms; matrix=320x320x104; 0.6x0.6x0.6mm^3; GRAPPA R=3; time=4min).

Analysis. In each subject, the visual cortex was identified as the intersection of perfusion and BOLD visual activation maps in Neurolens. Background field was removed from the phase images by SHARP [5] and QSM images were reconstructed via a fast algorithm with total variation regularization [6]. $OEF_0=\Delta\chi_{vein}/(\Delta\chi_{do}\cdot 4\pi\cdot Hct)$ was calculated in individual veins draining the visual cortex (***Fig1***), where $\Delta\chi_{vein}$ is the measured susceptibility in each vein relative to cerebrospinal fluid, $\Delta\chi_{do}$=0.27ppm, and hematocrit Hct=40%. In subjects with sufficient signal-to-noise ratio (SNR) of gas data, the percent changes in BOLD and CBF in the visual cortex and the EtO_2 values were substituted into the generalized calibration model [6]. For these subjects, we solved the M-equations for the three gases to estimate M and baseline OEF_0 by QUO2 (***Fig4***).

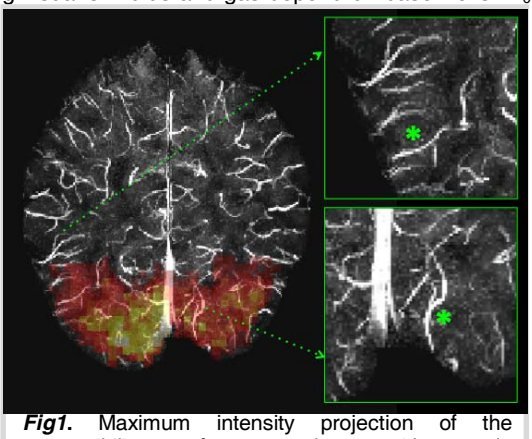

Fig1. Maximum intensity projection of the susceptibility map from one volunteer with example of veins (insets) draining the visual cortex (overlay). Mean OEF_0 from QSM in the veins was 31.2%.

Results and Discussion. Visually evoked changes in CBF depended strongly on baseline OEF_0 estimated from susceptibility (P<0.01) (***Fig2***), consistent with a previous study by Lu et al. [4]; although only a trend was observed for evoked BOLD changes. Strong correlations were also observed between percent changes in BOLD signal and OEF_0 from susceptibility during hypercapnia (P<0.01) and carbogen (P=0.02) (***Fig3***). These results are consistent with modeling work suggesting that relative changes in hemodynamic parameters are partly dependent on dHb content, and therefore on baseline metabolism. Absolute OEF_0 by both methods were available in four subjects, with comparable mean values of 30.6±2% by QSM and 31.9±12% by QUO2 (***Table1***). QUO2 fits were not available in the remaining subjects due to poor SNR of gas data.

Conclusion. Good fidelity was observed between BOLD-ASL signal changes and baseline OEF_0 by QSM during visual stimulus and gas breathing, as predicted by the dHb dilution model and work by Lu et al. [3,4]. This study also reveals encouraging concordance between absolute OEF_0 by QSM and by QUO2 that warrants examination in a larger cohort. ***References.*** [1] Haacke *Hum Brain Mapp* 5 (1997); [2] Gauthier *Neuroimage* 63 (2012); [3] Hoge *MRM* 42 (1999); [4] Lu *MRM* 60 (2008); [5] Schweser *Neuroimage* 54 (2011); [6] Bilgic *MRM* 72 (2014).

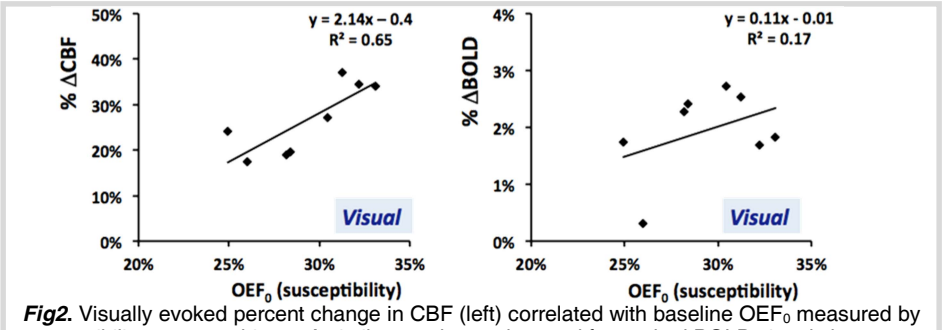

Fig2. Visually evoked percent change in CBF (left) correlated with baseline OEF_0 measured by susceptibility across subjects. A similar trend was observed for evoked BOLD signal changes.

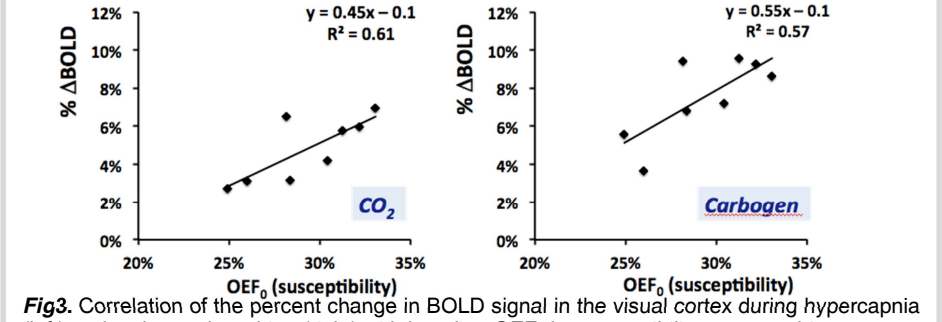

Fig3. Correlation of the percent change in BOLD signal in the visual cortex during hypercapnia (left) and carbogen breathing (right) with baseline OEF_0 by susceptibility across subjects.

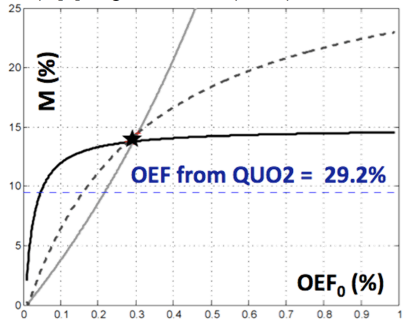

Fig4. M calibration parameter versus OEF_0 for each of three gases in the visual cortex of one volunteer. For QUO2, the intersection of the curves identifies baseline OEF_0 = 29.2%.

Subj	OEF_0 (%) from QSM	OEF_0 (%) from QUO2	M (%)
1	30.4	48.4	21
2	32.2	29.2	14
3	31.2	28.2	15
4	28.4	21.7	9
Mean	**30.6 ± 2**	**31.9 ± 12**	**15 ± 5**

Table1. Absolute OEF_0 from susceptibility and from QUO2 in visual cortex of four subjects.