Optimization of Oxygen Extraction Fraction Mapping using Joint Parametric Estimation

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TARGET AUDIENCE
The target audience is physicists and neuroscientists interested in oxygen extraction fraction mapping in the brain.

INTRODUCTION
Oxygen extraction fraction (OEF), the fraction of oxygen extracted from the blood that perfuses tissue, is an important indicator of the oxygen metabolism in the brain along with blood flow information. Currently there are two approaches to measure or map OEF in the brain using MRI - one approach measures the T_2 of venous blood and estimates the blood oxygenation using a T_2-oxygenation calibration curve[1,2]; the other uses the magnetic susceptibility difference between tissue and blood from multiple gradient and spin echo signals[3,4]. We introduce a novel OEF estimation method using the joint information of T2 and the magnetic susceptibility difference of blood signal obtained with a gradient echo sampling of spin echo (GESSE) sequence[3] and present voxel-wise cerebral metabolic rate for oxygen ($CMRO_2$) mapping in conjunction with CBF information obtained with an arterial spin labeling (ASL) method. In order to test the feasibility of our estimation algorithm, quantitative OEF, CBF, and $CMRO_2$ values were mapped under a breath-hold paradigm.

METHOD
OEF Estimation The procedures of OEF estimation are described in Fig.1. *Step1 (preprocessing)*: Phase and magnitude images obtained with GESSE acquisition were smoothed in temporal and spatial domains to reduce Gibbs ringing artifacts and improve image SNR. This smoothing also reduced the oscillations between odd and even echo signals due to the Eddy currents of interchanging gradient. *Step 2 (partial parameter fitting)*: The time course of the signal was characterized into three components: tissue, extracellular, and blood signals. This step extracts T_2 of tissue and CSF, signal coefficient (S_0), CSF signal fraction, and frequency and phase shift between the brain tissue and extracellular components with the initial assumption of hematocrit (Hct) and the magnetic susceptibility difference between completely oxygenated and completely deoxygenated red blood cells ($\Delta\chi$). *Step 3 (blood signal parameter fitting)*: The blood characteristic parameters, intravascular blood volume, characteristic frequency shift ($\delta\omega$), and T_2 blood were estimated by fitting the blood signals extracted from Step 2 into a theoretical model[5] using a non-least square fitting optimization. *Step 4 (OEF estimation using blood T2)*: OEF values per voxel were estimated using the relationship between OEF and the relaxation rate of the blood estimated in Step 3, which can be expressed in a quadratic equation[6]. *Step 5 (OEF estimation using frequency shift)*: A ratio of per-voxel-based $\delta\omega$ estimated in Step 3 and initially assumed global parameter $\Delta\chi$ in Step 2 provided an estimation of OEF. *Step 6 (joint parameter optimization)*: New Hct and $\Delta\chi$ values were calculated to minimize discrepancy in the per-voxel-based OEF values from Step 4 and 5. *Step 7 (constant update and iteration)*: The updated constants were used to repeat Step 3 through 6 and the iterative joint estimation process was terminated when the iterative coefficients converged and the difference between each iteration was within a given tolerance. The Bregman iterative (BI) optimization technique[7] was utilized to find the optimum solution which minimized the difference between the two OEF estimation approaches. **MRI Experiments** Three normal healthy volunteers participated in this study. All images were acquired on a 3T Siemens Skyra scanner with a 32-channel head coil. 2D GESSE sequence with three 5-mm slices and a sampling matrix of 104 x128 with 90 degrees flip angle was acquired. The GRE echo train spacing was 2 ms with a length of 41 echoes with 340 ms TR. The SE occurred during the 11th GRE, which was 48 ms after the center of the RF excitation pulse. The magnitude and phase data was obtained in a 21 second scan time. The participants were instructed to hold their breath for 30 seconds and another GESSE sequence started 10 seconds after onset of the breath-hold. We also collected pseudo-continuous arterial spin labeling (PCASL) data on all subjects with the following acquisition parameters: 2D EPI acquisition with 1600 ms bolus duration, 2800 ms TI, 3500 ms TR, 12 ms TE, 24 slices, 4 mm slice thickness, 3.4 x 3.4 mm in-plane resolution, 64 x 64 matrix size, 16 (with normal breathing) and 3 (with breath-hold) averages, total scan time of 2 min. (for normal breathing) and 24 sec (with breath-hold). Absolute $CMRO_2$ was calculated with obtained OEF and CBF maps as described in Xu el al.[8].

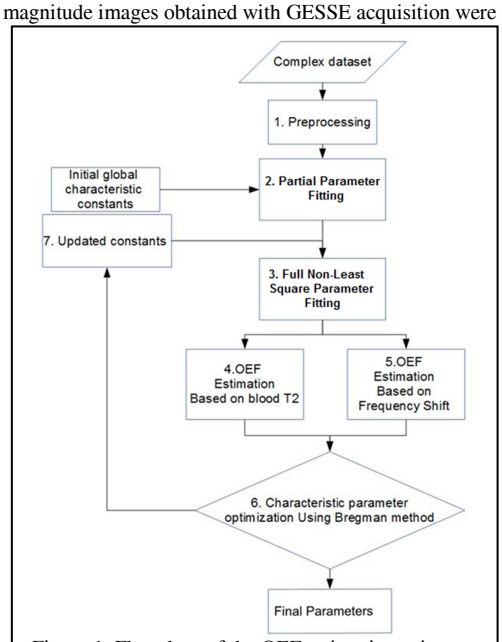

Figure 1. Flowchart of the OEF estimation using joint information of blood T2 and frequency shift.

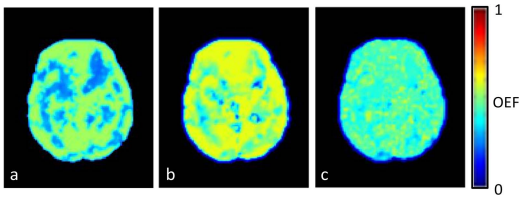

Figure 2. OEF maps from a representative subject using three different estimation methods: from the blood T2 (a), characterization frequency ($\delta\omega$) (b), and the proposed optimal minimization (c).

RESULTS AND DISCUSSION
Figure 2 shows OEF maps from three difference approaches. While the accuracy of the estimated OEF map is unknown, the map obtained with the proposed estimation algorithm (Fig. 2c) provided more uniform OEF values throughout the brain. In addition, the proposed method produced the least standard deviation in baseline OEF across three subjects (4.98% in GM) while the other two approaches showed higher values (5.93% in GM using blood T2, 8.98% in GM using blood $\delta\omega$). To test the feasibility of the proposed parametric estimation, we measured the values of deoxygenated blood volume (DBV), OEF, ASL, and $CMRO_2$ in the two different conditions of normal breathing and breath-hold. The summary of results is shown in Table 1; DBV, OEF, CBF, and $CMRO_2$ increased or decreased during a breath-hold challenge in agreement with previous studies, and all metrics (except DBV in WM) produced statistically significant responses in both gray and white matter during the challenge with three subjects.

Table 1. The mean and standard deviation of estimated DBV, OEF, CBF, and $CMRO_2$ parameters across all three subjects

Condition	DBV (%)		OEF		CBF (ml/100g/min)		CMRO2 (μmol/100g/min)	
	GM*	WM	GM*	WM*	GM*	WM*	GM*	WM*
Normal	1.90 ± 0.12	0.78 ± 0.14	0.52 ± 0.06	0.47 ± 0.05	53.0 ± 6.25	22.5 ± 2.81	226 ± 12.4	89.2 ± 19.7
Breath Hold	2.00 ± 0.10	0.80 ± 0.14	0.48 ± 0.05	0.46 ± 0.05	65.6 ± 6.61	34.7 ± 2.38	262 ± 23.9	134 ± 22.35
P-value (Paired T-Test)	0.034	0.101	0.044	0.034	0.032	0.003	0.017	0.004

*indicates statistical significance between the two conditions of normal and breath-hold ($p<0.05$).

CONCLUSION
In this study, we proposed a novel estimation approach for OEF extraction using GESSE acquisition and $CMRO_2$ measurement in conjunction with CBF measured with ASL. The expected modulation of the physiological parameters of DBV, OEF, ASL, and $CMRO_2$ in a respiratory challenge supports the feasibility of the proposed algorithm.

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