High Resolution Cerebral Metabolic Rate of Oxygen (CMRO2) using Quantitative Susceptibility Mapping (QSM) and an Oxygen Extraction Fraction (OEF) Constraint

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Target Audience: Researchers and clinicians interested in quantitative cerebral metabolic rate of oxygen mapping.

Purpose: The cerebral metabolic rate of oxygen ($CMRO_2$) and the oxygen extraction fraction (OEF) are important markers for neuronal function and tissue viability. The R_2* blood oxygenation level-dependent (BOLD) signal has been used extensively to study neural oxygen metabolism. However, R_2* images are contaminated by blooming artifacts and are highly dependent on imaging parameters. Since blood oxygen saturation is linearly related to blood magnetic susceptibility, quantitative susceptibility mapping (QSM) provides an alternative method for quantitative $CMRO_2$ mapping[1]. However, the QSM-based $CMRO_2$ is sensitive to noise, which may cause the estimated OEF to exceed its physiological range. To overcome this limitation, we propose to obtain $CMRO_2$ indirectly by solving for OEF with physiological constraints ($0\% \le OEF \le 100\%$).

Methods: According to mass conservation, $CMRO_2 = 4CBF \cdot SaO_2[Hb] \cdot OEF$ (Eq 1), where CBF is volumetric flow rate; SaO_2 is arterial oxygen saturation; and [Hb] is hemoglobin concentration in blood. As shown in the literature, the effect of caffeine on $CMRO_2$ is minimal[2]. Therefore, OEF maps of pre and post caffeine brain states can be calculated by solving[1] $OEF = \frac{1}{SaO_2}\left(\frac{\chi - \chi_o}{CBV_v \cdot \Psi_{Hb}(X_{dHb} - X_{oHb})} - (1 - SaO_2)\right)$ (Eq.2). Here CBV_v is the volume fraction of venous blood in a voxel; Ψ_{Hb} is the volume fraction of Hemoglobin (Hb) within blood; X_{dHb} and X_{oHb} are the volume susceptibilities of pure deoxyHb (dHb) and oxyHb (oHb), respectively; χ is the voxel susceptibility measured by QSM; χ_o is susceptibility contributions from non-blood tissue sources (such as ferritin), pure oxygenated blood, and arterial dHb.

MRI was performed on healthy volunteers ($n = 13$) before and 25 min after the oral administration of 200mg caffeine challenge, using a 3T scanner and a protocol consisting of a 3D Fast Spin Echo Arterial Spin Labeling (3D FSE ASL) sequence and a 3D spoiled Gradient Echo (GRE) sequence. Total scan time was 60 minutes. The 3D FSE ASL sequence parameters were: 22cm FOV, 1500 ms labeling period, 1525 ms post-label delay, 3 mm isotropic resolution and 6 min scan time. CBF maps (ml/100g/min) were generated from the ASL data. The 3D spoiled GRE sequence parameters were: 11 echoes, $TE = 4.4$ ms $\Delta TE = 4.9\ ms$, $TR = 58.5\ ms$, 0.46 mm in-plane resolution, 3 mm slice thickness, 7 min scan time. QSM generated from magnitude and phase images using Morphology Enabled Dipole Inversion (MEDI)[3]. All images were co-registered to the first QSM acquisition.

Whole brain pre- and post- caffeine OEF maps were obtained by solving Eqs.1&2 using a gradient search method with searching steps constrained such that $OEF \in [0,1]$.

Grey matter (GM) masks were created on pre-caffeine CBF images covering the supratentorial brain parenchyma from the vertex to the superior aspect of the lateral ventricles. The GM mask was further segmented by a neuroradiologist into vascular territories for ROI analysis on the $CMRO_2$ maps. Paired t-test was performed to compare $CMRO_2$ and coefficient of variation (COV) between the two methods.

Results: Fig.1 compares $CMRO_2$ maps generated by direct estimation and by constrained OEF methods. Reduction in extreme values ($CMRO_2$ >500 µmol/100ml/min) and increase in anatomical details can be appreciated. Fig.2 shows the mean and standard deviation of COV at various VTs for GM $CMRO_2$ across all subjects. Mean $CMRO_2$ in GM was similar between the two methods (113 ± 15 vs 124 ± 33 with/without constraint (p>0.05)) while the constrained OEF method substantially decreased COV from 2.85 to 0.75 (P<0.01).

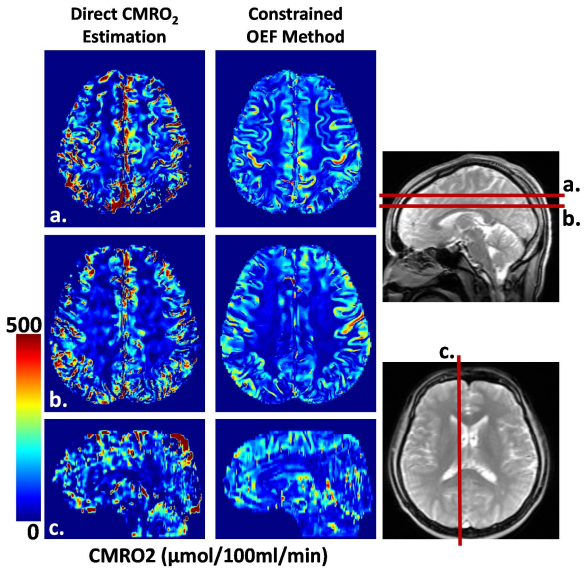

Fig.1. Comparison of CMRO2 maps between direct estimation and constrained OEF method.

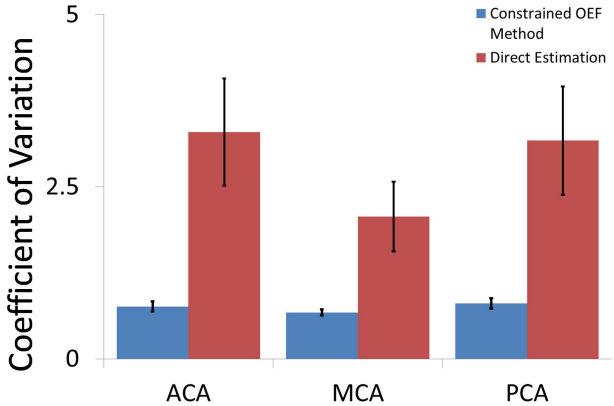

Fig.2. Coefficient of variation (COV) of $CMRO_2$ in vascular territories (VT =ACA, MCA, PCA) for both direct estimation and constrained OEF method. All differences are statistically significant.

Discussion: The constrained OEF method effectively reduces artifacts and unphysiological errors in $CMRO_2$ maps without significantly changing the mean value in GM across subjects. High resolution CBF maps may be desirable for high resolution $CMRO_2$ maps.

Conclusion: Constrained OEF method significantly improves $CMRO_2$ maps quality by reducing artifacts due to noise propagation.

Reference: 1). Zhang, J., et. al., MRM, 2014, doi: 10.1002/mrm.25463. 2) Perthen, JE et. al., Neuroimage 2008, 40(1):237-47. 3) Liu, T., et. al., MRM 2011;66(3):777-783.