Quantitative Susceptibility Mapping (QSM) for High Resolution Quantitative Cerebral Metabolic Rate of Oxygen (CMRO2)

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TARGET AUDIENCE: $CMRO_2$, Stroke, Magnetic Susceptibility Contrast, Calibrated fMRI, Quantitative Susceptibility Mapping (QSM).

INTRODUCTION & PURPOSE: Accurate measurement of cerebral metabolic rate of oxygen ($CMRO_2$) is highly desired for the assessment of brain cell function in health and in stroke. MRI offers the potential to map $CMRO_2$ by estimating paragmagnetic deoxyhemoglobin concentration ([dHb]) from detected signal, which requires MRI signal modeling. Current models include 1) irreversible T2 effects due to water exchange and diffusion through the magnetic field of dHb[1-3], 2) theoretic model of T2' effects[4,5], 3) numerical model of T2* effects caused by dHb[6,7], and 4) phase model of dHb[8]. All these models are very complicated with multiple parameters that need to be calibrated from many measurements and may only be applicable in limited situations. Fundamentally, MRI signal is a convolution of [dHb], and models that do not deconvolve signal may be erroneous. Recently, a rigorous deconvolution technique called quantitative susceptibility mapping (QSM) has been developed to map tissue susceptibility. We propose to use QSM to map [dHb] and hence $CMRO_2$.

THEORY: The oxygen mass conservation leads to:

$$\mathbf{CMRO_2} = \mathbf{4CBF} * (\mathbf{[dHb]_v} - \mathbf{[dHb]_a}) \approx \mathbf{4CBF} * \mathbf{[dHb]_v} \quad (1),$$

where CBF is cerebral blood flow (ml/100g/min), $[dHb]_v$ and $[dHb]_a$ represent dHb concentrations (umol/ml) in the draining vein and supplying artery respectively, and 4 accounts for 4 hemes per Hb with one oxygen molecule per heme. Here we assume $[dHb]_a$~0. dHb molar susceptibility is $4*\chi_{heme}$, where χ_{heme}~ 144.23 ppb*ml/umol at 310K is the ferroheme molar susceptibility according to the average magnetic moment of the iron (II) ion in ferroheme 5.25 Bohr magnetons[9] and the Langevin formulae. Let Q_0 be susceptibility contribution from materials other than dHb. Let Q be the estimated total susceptibility value. Then we *have*

$$[\mathbf{dHb}] = \frac{(\mathbf{Q}-\mathbf{Q_0})}{(\lambda * \mathbf{4} * \chi_{\mathbf{heme}})} \quad (2).$$

λ is the cerebral blood volume fraction estimated from CBF[10]:

$$\boldsymbol{\lambda} = \frac{\mathbf{1}}{\mathbf{100}} * (\mathbf{0.27} * \mathbf{CBF} - \mathbf{7.27}) \quad (3).$$

Therefore,

$$\mathbf{CMRO_2} \approx \mathbf{CBF} * \frac{(\mathbf{Q}-\mathbf{Q_0})}{(\lambda * \chi_{\mathbf{heme}})} \quad (4).$$

If QSM and CBF are both measured for two brain states that have different CBFs but the same $CMRO_2$, $CMRO_2$ can be determined as:

$$\mathbf{CMRO_2} = \frac{\mathbf{1}}{\chi_{\mathbf{heme}}} * (\mathbf{Q_2} - \mathbf{Q_1}) * \frac{(\mathbf{CBF_1} * \mathbf{CBF_2})}{(\lambda_2 * \mathbf{CBF_1} - \lambda_1 * \mathbf{CBF_2})} \quad (5),$$

where the index denotes the brain state in which QSM and CBF are measured. Both Q_1 and Q_2 are global shift corrected according to ROI analysis in frontal ventricles.

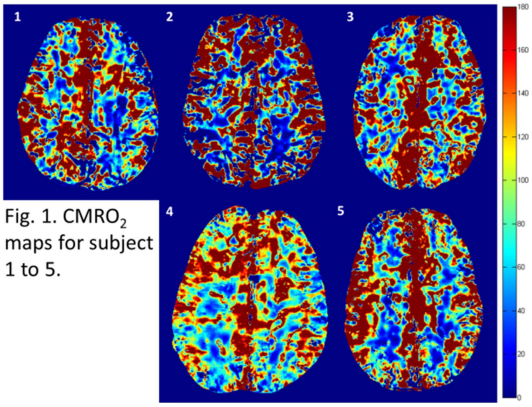

Fig. 1. $CMRO_2$ maps for subject 1 to 5.

Table 1. $CMRO_2$ ROI measurements on cerebral cortex, median±IQR

Subject #	$CMRO_2$ (umol/100g/min)
1	105 (49 – 190)
2	117 (33 – 231)
3	107 (54 – 191)
4	120 (83 – 167)
5	121 (64 – 208)

METHODS AND MATERIALS: Experiments were performed on healthy volunteers (N=5) on 3.0-T scanner (GE Healthcare). To achieve two brain states of the same $CMRO_2$ but different CBF, all volunteers drank 20 ounces of iced coffee containing 0.2g caffeine[11]. QSM was performed using a multi-echo 3D gradient echo (GRE) sequence (matrix size: 512×512×50, FOV: 240 ×240 mm^2, slice thickness: 3 mm, 11 echoes, TE range from 4.3ms to 52.4ms equally spaced), and CBF was acquired using an ASL sequence (matrix size: 512×512×50, FOV: 240 ×240mm2, slice thickness: 3.8mm). QSM images were obtained from GRE data using the Morphology Enabled Dipole Inversion (MEDI) algorithm[12]. CBF images were obtained from ASL data. QSM and CBF were measured before and 35 minutes after the consumption of the coffee, and all images were co-registered to their corresponding pre-coffee QSM image coordinates. $CMRO_2$maps were then generated using Eq.5 followed by Gaussian noise smoothing.

RESULTS: From pre-to post-coffee, CBF values decreased about 40% in cerebral cortex in all volunteers ($p<0.001$). Examples of $CMRO_2$ in color are shown in Fig.1. The cerebral cortex ROI measurements on $CMRO_2$ maps are listed in Table 1.The results are consistent with values reported in prior papers[7,10].

DISSCUSION and CONCLUSION: Our preliminary data show that QSM is a promising method for determining [dHb] and then CMRO2 mapping. Instead of the Grubb formulae[13], we used the Leenders formulae[9] (Eq.3) that is based on human data and modern and perhaps more accurate measurements. In the future study, cerebral blood volume fraction can be measured directly with dynamic susceptibility contrast MRI. Previous [dHb] estimations from T2, T2' and T2* effects are very complicated, involving estimates of many model parameters that may not be reliable. The phase model of [dHb] is based on the basic Maxwell equation, but fitting [dHb] from phase data only works for simple geometry such as a straight cylinder that usually does not exist in in vivo imaging. Deconvolution of the phase data to obtain susceptibility source is required, which is the QSM technology.

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