Quantification of the Cerebral Metabolic Rate of Oxygen (CMRO₂) across the Cortex using Phase-Based Regional Oxygen Metabolism (PROM) MRI

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Introduction. Noninvasive quantification of venous oxygen saturation (Yᵥ) and the cerebral metabolic rate of oxygen (CMRO₂) can provide useful insight into cerebral physiology during normal function and in disease of the brain such as stroke and tumor [1]. Phase-based regional oxygen metabolism (PROM) is an MRI-based method that combines susceptibility-based estimates of Yᵥ with arterial spin labeling (ASL) measurements of cerebral blood flow (CBF) to quantify CMRO₂ on a local basis [2]. Here we demonstrate major developments to the PROM method, including (a) improved acquisition using high-resolution, isotropic 3D phase imaging with increased brain coverage; (b) more accurate removal of background fields for quantitative susceptibility mapping [3]; and (c) application of more sophisticated registration tools to generate maps of cortical CMRO₂ in vivo [4].

Methods. Acquisition. A healthy subject (male, age=24 yr) was scanned on a Siemens 3T MAGNETOM Trio a Tim System (Erlangen, Germany) with a 32-channel matrix coil. High resolution, 3D axial FLASH magnitude and phase were acquired (TR/TE=27/20ms; resolution=75x50x5mm³; matrix=576x504x64; BW=130Hz; flow-compensated). Dual-echo FLASH images (resolution=1.5x1.5x2.0mm, TR/TE=27/10/20ms) were also acquired with the same shim settings. For perfusion measurements, PICORE-Q2TIPS pulsed 2D ASL was acquired (TR/TE=3470/21ms, TI₁/TI₂=700/1800ms, resolution=2x2x4mm; averages=80). Phase processing. RF phase offset was estimated from the dual-echo scan with 3rd order polynomial fitting and subtracted from the unwrapped phase (FSL Prelude) [5,6]. Projection onto Dipole Fields (PDF) was performed on the normalized field map, δ₀=φ/(γ·B₀·TE), for 100 iterations to remove background field inhomogeneities [3].

Quantitative Susceptibility Mapping. L₁-regularized quantitative susceptibility mapping, with optimal TV-norm weighting λ=2·10⁻⁴ chosen using the L-curve method, was applied for 100 iterations to reconstruct magnetic susceptibility (χ) from the field distribution [7]. Vessel Yᵥ can be determined from susceptibility as Δχ_{ven-tissue}=Δχ_{tissue}·Hct·(1-Yᵥ), where Δχ_{tissue}=0.18ppm and hematocrit Hct=0.4 [8]. Estimates of Yᵥ in vessels were made from pixels above a threshold χ=0.28ppm and average χ_{tissue} in the parenchyma was assumed to be zero. The χ map was registered to an anatomical space (defined by a separate MPRAGE scan) using FreeSurfer, and Yᵥ was averaged in each of 31 cortical regions per hemisphere labeled by FreeSurfer. Quantification of CMRO₂. From the ASL scan, CBF maps were calibrated using the local tissue equilibrium magnetization (M₀) [9], and registered to the same space as Yᵥ. Finally, cortical CMRO₂ was computed using the Fick Principle as CMRO₂=(1-Yᵥ)·CBF·C₀, where C₀=793μmol/100mL is the carrying capacity of hemoglobin.

Results and Discussion. Numerical simulations revealed that PDF removal of background fields provided more accurate Yᵥ estimates in vessels perpendicular to B₀ than previously proposed Hanning filtering, with <5% error Yᵥ for most vessel tilt angles (Fig 1). For individual cortical regions, multiple colocalized vessel segments could be identified for oxygen saturation measurements, as illustrated in Fig 2. Across the cortex, mean±SD Yᵥ=62.3±4%, CBF=48.7±10mL/100g/min, and CMRO₂=134±32μmol/100g/min, which lie within the normal physiological range. We significantly improved PROM to quantify physiologically meaningful CMRO₂ across a large extent of the cortex (Fig 3), and 380% greater volumetric coverage than the previous implementation of the method [2]. With anatomical registration, the updated method is a potentially powerful tool to assess regional oxygen metabolism in broader subject populations.

Fig 1. Numerical brain simulation with realistic χ for tissue, air, and vein (diameter=2 pixels, true Yᵥ=60%). Removal of background fields with PDF and a Hanning filter (32x32) were compared for accuracy in Yᵥ after L₁-reconstruction.

Fig 2. Quantitative susceptibility with arrows highlighting cortical veins (left) and 1.5mm MIP illustrating spatial colocalization of vessels with Brodmann areas (right).

Fig 3. Quantitative measurements of Yᵥ (%), CBF (mL/100g/min), and CMRO₂ (μmol/100g/min) across the cortex of a healthy subject.