Quantification of the Cerebral Metabolic Rate of Oxygen (CMRO$_2$) across the Cortex using Phase-Based Regional Oxygen Metabolism (PROM) MRI

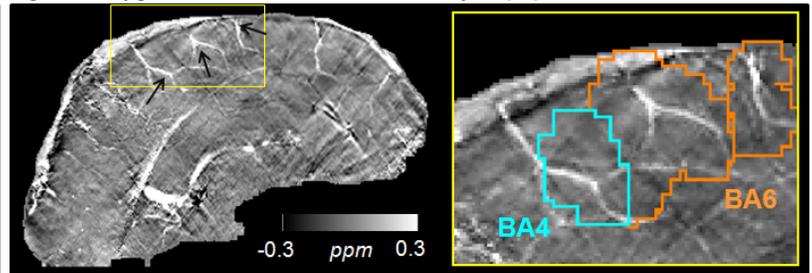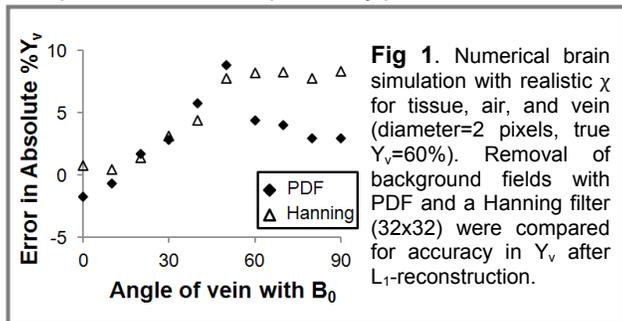Audrey P Fan[1,2], Berkin Bilgic[1,2], Keith A Heberlein[2], Bruce R Rosen[2,3], and Elfar Adalsteinsson[1,2]

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Introduction. Noninvasive quantification of venous oxygen saturation (Y_v) and the cerebral metabolic rate of oxygen (CMRO$_2$) 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 Y_v with arterial spin labeling (ASL) measurements of cerebral blood flow (CBF) to quantify CMRO$_2$ 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 CMRO$_2$ *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=0.5x0.5x0.5mm^3; matrix=576x504x64; BW=130Hz; flow-compensated). Dual-echo FLASH images (resolution= 1.5x1.5x2.0mm, TR/ TE$_1$/ TE$_2$=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, TI$_1$/TI$_2$=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, $\delta_n=\varphi/(\gamma \cdot B_0 \cdot TE)$, for 100 iterations to remove background field inhomogeneities [3].

Quantitative Susceptibility Mapping. L$_1$-regularized quantitative susceptibility mapping, with optimal TV-norm weighting $\lambda=2\cdot10^{-4}$ chosen using the L-curve method, was applied for 100 iterations to reconstruct magnetic susceptibility (χ) from the field distribution [7]. Vessel Y_v can be determined from susceptibility as $\Delta\chi_{vein-tissue}=\Delta\chi_{do}\cdot Hct\cdot(1-Y_v)$, where $\Delta\chi_{do}=0.18$ppm and hematocrit $Hct=0.4$ [8]. Estimates of χ_{vein} in vessels were made from pixels above a threshold $\chi=0.28$ppm 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 Y_v was averaged in each of 31 cortical regions per hemisphere labeled by FreeSurfer. *Quantification of CMRO$_2$.* From the ASL scan, CBF maps were calibrated using the local tissue equilibrium magnetization (M_{0t}) [9], and registered to the same space as Y_v. Finally, cortical CMRO$_2$ was computed using the Fick Principle as CMRO$_2=(1-Y_v)\cdot CBF\cdot C_a$, where $C_a=793\mu$mol/100mL is the carrying capacity of hemoglobin.

Results and Discussion. Numerical simulations revealed that PDF removal of background fields provided more accurate Y_v estimates in vessels perpendicular to B_0 than previously proposed Hanning filtering, with <5% error Y_v 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 Y_v=62.3±4%, CBF=48.7±10ml/100g/min, and CMRO$_2$=134±32μmol/100g/min, which lie within the normal physiological range. We significantly improved PROM to quantify physiologically meaningful CMRO$_2$ 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 Y_v=60%). Removal of background fields with PDF and a Hanning filter (32x32) were compared for accuracy in Y_v after L$_1$-reconstruction.

Fig 2. Quantitative susceptibility with arrows highlighting cortical veins (left) and 1.5mm MIP illustrating spatial colocalization of vessels with Brodmann areas (right).
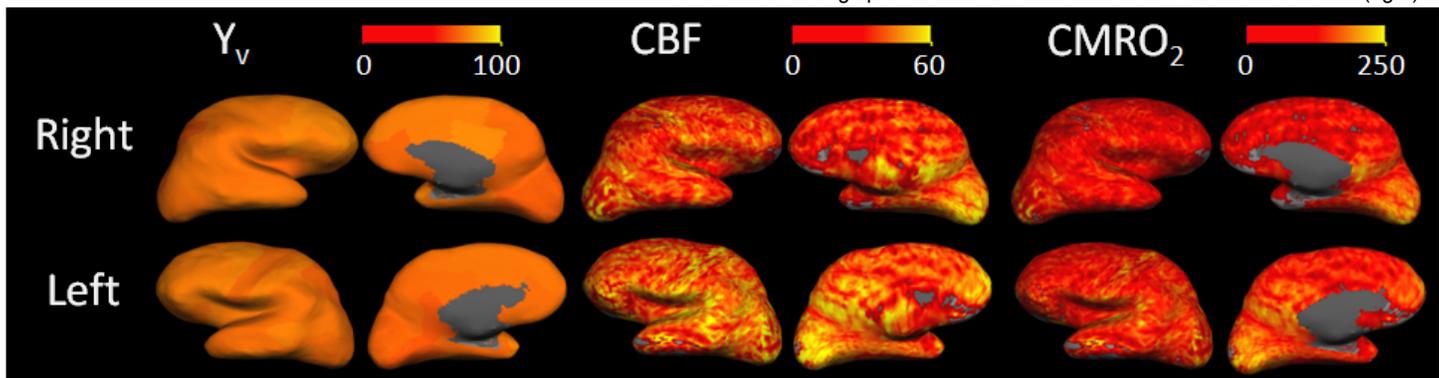
Fig 3. Quantitative measurements of Y_v (%), CBF (ml/100g/min), and CMRO$_2$ (μmol/100g/min) across the cortex of a healthy subject.

References. [1] Sobesky *Stroke* 2005. [2] Fan *MRM* 2011. [3] Liu *NMR Biomed* 2011. [4] Destrieux *Human Brain Mapp* 2009. [5] Schweser *ISMRM* 2011 #2657. [6] Jenkinson *MRM* 2003. [7] Bilgic *Neuroimage* 2011. [8] Haacke *Human Brain Mapp* 1997. [9] Cavusoglu *Magn Reson Imag* 2009.