High-field ^{17}O Study of 3D $CMRO_2$ Imaging in Human Visual Cortex

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Introduction In the brain, oxygen is primarily utilized through oxidative phosphorylation in the mitochondrial respiratory chain according to the reaction of $4H^+ + 4e + O_2 \rightarrow 2H_2O$, and this process is tightly associated with the generation of high-energy phosphate compound ATP. Questions that involve the cerebral metabolic rate of oxygen consumption ($CMRO_2$) are encountered frequently in biomedical research for understanding either normal brain function or abnormalities induced by brain diseases. It is, therefore, important to develop neuroimaging methodology for imaging $CMRO_2$ in the human brain noninvasively. The simplest MR approach to determine $CMRO_2$ is to use *in vivo* ^{17}O MRS for directly measuring the metabolic $H_2{}^{17}O$ change during an inhalation of $^{17}O_2$ gas [1-4]. The weakness of low ^{17}O intrinsic sensitivity can be partially overcome by the dramatic sensitivity gain at high/ultrahigh fields[5]. The advantage of high-field ^{17}O has made it possible to obtain 3D $CMRO_2$ images in the anesthetized rat brain at 9.4T during a two-minute $^{17}O_2$ inhalation[4]. We have conducted a preliminary study to examine the feasibility of using *in vivo* ^{17}O MR spectroscopic imaging (MRSI) for directly obtaining 3D $CMRO_2$ images in the human visual cortex (V1) at 7T during a 2-3 minute inhalation of $^{17}O_2$ at resting condition and visual stimulation.

Method All MR experiments were conducted on a 90 cm bore 7T human magnet (Magnex Scientific, UK) interfaced with a Varian INOVA console (Varian Inc., CA). A multinuclear surface-coil probe consisting of a 7.5cm-diameter ^{17}O surface coil (40 MHz) and a larger quadrature ^1H coil (300 MHz) was used for detecting NMR signals of the human brain. The spatial localization of ^{17}O signal was achieved by using the 3D Fourier series window (FSW) MRSI technique[6]. The acquisition time for each 3D ^{17}O MRSI data set was 11 seconds (total scan number=322; FOV=10×10×8 cm^3, 9×9×7 phase encodes, 3.5 ml voxel size). The FIDs were zero-filled and a 100-Hz line broadening was used before Fourier transformation for SNR enhancement. During the ^{17}O MRSI study, the subject could breathe either normal air or mixed $N_2/{}^{17}O_2$ (~4:2 v:v ratio; ~80% ^{17}O enrichment) gas through mouth. The ^{17}O MRSI was acquired before, during and after a 2-2.5 minute inhalation of $^{17}O_2$ with a total data collection time of 18 minutes. For the functional study, a hemifield visual stimulus with reversal red-versus-black checkerboard at 8 Hz was used. The stimulus was started one minute prior to the $^{17}O_2$ inhalation and lasted a total of 10 minutes. The multiple slice GE EPIs were also acquired for generating BOLD-based fMRI maps using the block task design in the same study. The institutional review board at University of Minnesota approved all study procedures.

Results Figure 1 shows the stacked plots of the $H_2{}^{17}O$ signal measured by 3D ^{17}O MRSI (11-s temporal resolution) before (i.e., natural abundance $H_2{}^{17}O$ in brain tissue), during (i.e., metabolic $H_2{}^{17}O$ accumulation) and after (i.e., washout of $H_2{}^{17}O$) an $^{17}O_2$ inhalation (as indicated by a bar under stack plots in fig. 1) from two representative voxels located inside the human visual cortex. It indicates excellent ^{17}O detection sensitivity with relatively small fluctuations. The accumulation rate of the metabolic $H_2{}^{17}O$ measured during the inhalation was determined by the oxygen utilization rate (i.e., $CMRO_2$) [7]. A linear function was used to fit and approximate the accumulation rate of $H_2{}^{17}O$ during an inhalation for each ^{17}O MRSI voxels with sufficient SNR. The fitted values of linear coefficient were used to generate 3D $CMRO_2$ images *(relative $CMRO_2$ values)*. Fig. 2 illustrates one representative $CMRO_2$ image at resting condition showing relatively higher rates around the grey matter areas (e.g., near the center of image). The same subject shown in Fig. 2 participated another functional study at a different day. Two ^{17}O inhalation experiments were performed during the left-hemifield and right-hemifield visual stimulation, respectively. Because the hemifield stimulation only activates the contralateral hemisphere visual cortex, the ipsilateral hemisphere can be treated as control. Comparison between the 3D $CMRO_2$ images measured using two different stimuli reveals that each stimulus increases $CMRO_2$ significantly in the activated visual area in the contralateral hemisphere. The relative $CMRO_2$ increases were >10% in this subject.

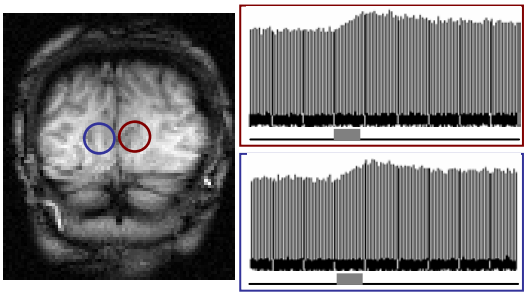

Fig.1 Stacked plots of $H_2{}^{17}O$ signal measured by 3D ^{17}O MRSI before (natural abundance), during and after an $^{17}O_2$ inhalation from two representative voxels (marked by colored circles) in the human visual cortex.

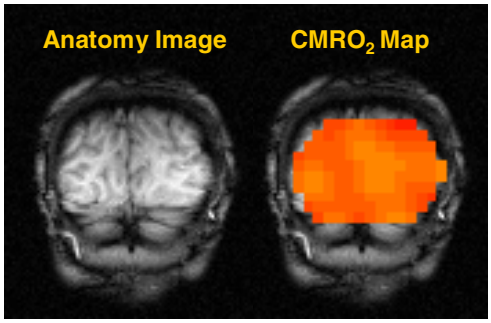

Figure 2. Anatomy and $CMRO_2$ images of human brain under resting condition.

Discussion and Conclusions Our preliminary results demonstrate great sensitivity of *in vivo* ^{17}O MRSI for imaging the production rates of the metabolic $H_2{}^{17}O$ concentration during a 2-3 minutes of $^{17}O_2$ inhalation in the human visual cortex at 7T. The achieved spatial resolution (3.5 ml) of 3D ^{17}O MRSI is comparable with the PET resolution of several ml [8]. Our initial results indicate a possibly significant increase in $CMRO_2$ by visual stimulation, though the relative $CMRO_2$ increase is likely smaller than the CBF change of 40-50% [8,9], which reveals the important role of oxidative metabolism in cerebral bioenergetics and brain function. In summary, the developed ^{17}O approach provides a new neuroimaging modality for studying normal brain activation and brain diseases. Currently, we are investigating the modeling aspects for quantifying the absolute $CMRO_2$ values in the human visual cortex and examining the reproducibility of $CMRO_2$ imaging at both resting and activated states.

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