Study of 17O NMR Sensitivity and Relaxation Times of Cerebral Water in Human at 7 Tesla

X. Zhu[1], X. Zhang[1], W. Chen[1]

[1]Center for Magnetic Resonance Research, University of Minnesota, Minneapolis, Minnesota, United States

Synopsis The cerebral metabolic rate of oxygen ($CMRO_2$) is an important physiological parameter for studying brain function and diseases. We demonstrated previously the possibility of using high-field ^{17}O MR approach for mapping metabolic $H_2{}^{17}O$ and imaging $CMRO_2$ in rat brain. Recently, we have studied ^{17}O relaxation times of the natural abundance $H_2{}^{17}O$ in human brain (T_1=5.46±0.09ms, T_2=4.32±0.24ms and T_2*=2.40±0.07ms), and sensitivity of 3D ^{17}O MRS image at 7 Tesla. Our results indicate that the excellent sensitivity of ^{17}O MRS image obtained at ultra-high field could be feasible for achieving 3D imaging of $CMRO_2$ in the human brain.

Introduction

In oxidative tissues such as the brain, oxygen is primarily utilized through oxidative phosphorylation in the mitochondrial respiratory chain according to the reaction:

$$4H^+ + 4e + O_2 \rightarrow 2H_2O, \quad [1]$$

and this process is tightly associated with the generation of high-energy phosphate compounds. Questions that involve the cerebral metabolic rate of oxygen consumption ($CMRO_2$) are encountered frequently in biomedical research when considering either normal tissue function or abnormalities induced by brain diseases. It is, therefore, important to have methods for measuring and imaging $CMRO_2$ accurately and noninvasively. The simplest NMR approach to determine $CMRO_2$ is to detect the metabolic $H_2{}^{17}O$ directly using ^{17}O NMR approach during inhalation of ^{17}O labeled oxygen gas (1-3). However, the spatial resolution of ^{17}O NMR is limited by the low gyromagnetic ratio of ^{17}O nucleus and consequently its relatively poor sensitivity, and the extremely low $H_2{}^{17}O$ concentration metabolized from inhaled $^{17}O_2$ gas. Therefore, the key factor for determining $CMRO_2$ using ^{17}O approach is the sensitivity of ^{17}O NMR signal acquired within a unit time, which is given by

$$SNR \propto B_o{}^{\beta}(T_2{}^*/T_1)^{1/2}, \quad [2]$$

where B_o is magnetic field strength, T_1 is longitudinal relaxation time and T_2* is apparent transverse relaxation time.

Recently, our results showed that the relaxation times of ^{17}O water are field *independent* presumably due to the dominance of quadrupolar relaxation, and the ^{17}O NMR sensitivity increased approximately *four-fold* at 9.4T compared to at 4.7T in the rat brain (4). With this significant sensitivity gain, we have successfully applied the 3D ^{17}O MRS imaging method to determine $CMRO_2$ in the anesthetized rat brain at 9.4 Tesla during a two-minute $^{17}O_2$ inhalation (5). In this study, we have extended our efforts toward the human brain study at 7 Tesla for determining the T_1, T_2 and T_2* relaxation times of the natural abundance water, as well as ^{17}O NMR sensitivity in the 3D ^{17}O MRS images with a voxel size of 6.6 ml.

Methods

All experiments were conducted on a 90 cm bore 7 Tesla Magnex magnet with a Varian INOVA console. A multinuclear surface-coil probe consisting of a 5cm-diameter ^{17}O surface coil (40 MHz) and a larger quadrature ^1H coil (300 MHz) was used for detecting NMR signals from the human visual cortex. Non-localized spin-echo (θ-TE/2-2θ-TE/2-acquisition) with phase cycling and inversion recovery (180°-TI-θ-acquisition) pulse sequences were applied to determine T_2 and T_1 values of natural abundance $H_2{}^{17}O$, respectively, where θ is the flip angle of a hard square pulse (200 μs). A total of 12 TE and 8 TI values were used to calculate T_2 and T_1 values. The T_2* values were calculated by $T_2{}^* = 1/(\pi \cdot \Delta\upsilon_{1/2})$, where $\Delta\upsilon_{1/2}$ is the line width of ^{17}O resonance peak. Other NMR parameters were: TR = 33 ms (> 5 T_1); scan number = 128-256; spectral width = 30 kHz. The spatial localization of ^{17}O MRS was achieved by using the 3D Fourier series window (FSW) MRS imaging technique (6). The acquisition time for each 3D ^{17}O-MRS image was 8.5 seconds (total scan number=254; spectral width=30 kHz; FOV=9.4×9.4×7.5 cm^3, 7×7×5 phase encodes). The image voxel size was 6.6 ml. The FIDs were zero-filled and a 100-Hz line broadening was used before Fourier transformation for SNR enhancement. The averaged RF power used in this study was below the FDA limit of SAR. Four human subjects participated this study. The institutional review board at University of Minnesota approved all study procedures.

Results

The ^{17}O relaxation times in the human visual cortex were found to be: T_1=5.46±0.09 ms, T_2=4.32±0.24 and T_2*=2.40±0.07 ms (n=4) at 7 Tesla. The averaged linewidth of ^{17}O resonance peak of cerebral water is 133±4 Hz (n=4). The 3D ^{17}O MRS imaging technique was applied to measure the natural abundance $H_2{}^{17}O$ distribution in the human brain with high temporal resolution of *8.5 seconds* and 6.6 ml voxel size. Figure 1a demonstrates results obtained from a representative subject showing one 2D coronal ^{17}O chemical shift image (CSI) of natural abundance $H_2{}^{17}O$ extracted from 3D ^{17}O image dataset acquired using the ^{17}O coil. The CSI slice was located in the visual cortex. The spatial distribution of ^{17}O NMR signal intensity is not uniform because of the inhomogeneous B_1 field of the ^{17}O surface coil used. Figure 1b displays a representative ^{17}O spectrum from one voxel showing the resonance peak of natural abundance $H_2{}^{17}O$ in the human visual cortex. Excellent SNR was achieved with a relatively short acquisition time at 7 Tesla, especially for the central voxels where SNR was optimized by the B_1 profile of the ^{17}O coil (SNR ≈ 60:1) as demonstrated in Fig. 1b.

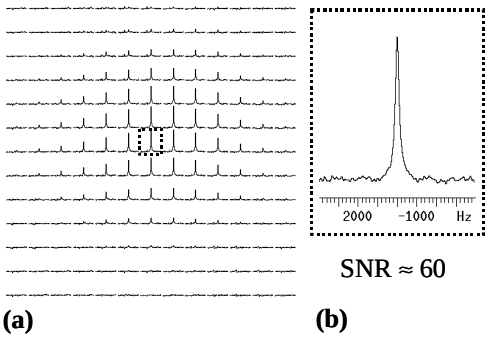

Fig. 1 (a) 3D ^{17}O CSI images (displayed in 2D) of natural abundance $H_2{}^{17}O$ in the human brain at 7T, and (b) central voxel ^{17}O spectrum.

Discussion and Conclusions

The ^{17}O relaxation times in the human brain at 7 Tesla are similar to that of rat brain at 9.4 Tesla (T_1 = 4.84±0.18 ms, T_2=3.03±0.09 ms, T_2* = 1.80±0.06 ms) (4), however, they are significantly higher than the values determined in the rat brain. These increases may reflect the differences between different species. The relatively large ratio of $(T_2{}^*/T_1)^{1/2}$ (=0.66) of human brain at 7 Tesla in comparison with the ratio (=0.61) in the rat brain at 9.4 Tesla will gain ~8% SNR according to Eq. [2]. Although ^{17}O nucleus has a relatively low gyromagnetic constant (only 14% versus that of the proton nucleus), excellent ^{17}O spectra of cerebral natural abundance water were obtained in the human brain by taking the advantage of ultra-high magnetic field and optimizations of NMR acquisition parameters (e.g., fast acquisition due to short T_1). This sensitivity made it possible to obtain a ^{17}O-MRS image of natural abundance cerebral $H_2{}^{17}O$ with a relatively high temporal resolution (8.5 s) in the human brain. Note that although the current voxel size used for the human brain is much larger than that of the rat brain, it is comparable to that provided by most conventional PET scanners for imaging $CMRO_2$ (7). The ^{17}O sensitivity and the temporal resolution of image acquisition in the human 3D ^{17}O MRS image is slightly better than that used in the rat brain study. Furthermore, the dynamic concentration change of metabolic $H_2{}^{17}O$ during $^{17}O_2$ inhalation is expected to be similar between the awaked human brain and the rat brain anesthetized with α-chloralose because of their similar values of both $CMRO_2$ (2.2 μmol/g/min in rat versus 1.7 μmol/g/min in human) and cerebral blood flow (0.53 ml/g/min in rat versus 0.54 ml/g/min in human) (5, 7). In summary, our results indicate the feasiblity for achieving 3D imaging of $CMRO_2$ in the human brain at 7 Tesla. Realization and utilization of this feasibility would have a great impact on studying the central role of oxidative metabolism in brain activation and pathological diseases.

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