Proton MRI Detection of Metabolically Generated $H_2{}^{17}O$ from Inhaled $^{17}O_2$

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INTRODUCTION

Cellular aerobic metabolism results in the conversion of oxygen to water. A technique that can detect the relatively small amount of water produced by cellular respiration and distinguish it from the large pool of water already present in biological tissue can hence serve as a tool for quantifying metabolic activity. ^{17}O-nuclear magnetic resonance (NMR) is well suited for this purpose. Since inspired $^{17}O_2$ is visible to ^{17}O-NMR only after conversation to $H_2{}^{17}O$, it can be used as a tracer for NMR-based quantification of metabolism. Two studies reported to date have performed ^{17}O-NMR spectroscopy and imaging of rats [1] and cats [2] while the animals were subject to enriched $^{17}O_2$ inhalation. However, due to the low natural abundance (0.037%) and relatively small gyromagnetic ratio of ^{17}O, direct ^{17}O-NMR suffers from poor signal/noise (SNR) and spatial resolution. To overcome this problem, indirect $H_2{}^{17}O$ imaging methods have been proposed [3, 4]. Here we report the first *in vivo* demonstration of indirect (proton) magnetic resonance imaging (MRI) of $H_2{}^{17}O$ metabolically generated from inspired $^{17}O_2$.

METHODS AND MATERIALS

A female Sprague-Dawley rat (200 g) was used for this demonstration. The animal was anesthetized with Nembutol®(50 mg/kg) via IP injection, and its trachea was cannulated surgically. The cannula was attached to a Y-piece which connected the animal to a closed ventilation circuit (see Figure 1.), and the animal was allowed to breath spontaneously. The circuit prepped to maintain 100% oxygen inspiration for the rat throughout the experiment. The animal was wrapped with an insulating pad to help maintain body temperature and placed in a specially designed head coil optimized for proton imaging on a 4T GE-Signa Scanner. The coil was mounted on a motion-resistant platform and oriented along the x direction (B_o along z). The $T_{1\rho}$-dispersion sequence used was similar to the one employed in [3] except that, instead of spin-echo imaging, a fast spin-echo readout was used here. A spin-locking length (TSL) of 120 ms and high and low spin-locking frequencies of 1500 (ω_h) and 125Hz (ω_l), respectively, were determined to be optimal (maximum $H_2{}^{17}O$ sensitivity and SNR=50) and used as sequence parameters. All images were acquired using a single brain slice taken in the y-z plane (axial with respect to the rat) and a FOV, matrix size, slice thickness, scan time, and interscan delay, of 5 x 5 cm, 256 x 128, 3 mm, 10 s, 3 s, respectively. Prior to the time denoted by the arrow in the plot in Figure 2, only the $^{16}O_2$ bag was open to the circuit. At the time indicated by the arrow, the circuit was switched to the $^{17}O_2$ bag (containing 100 mL of 100% oxygen with $^{17}O_2$ enrichment of 40 a%). The switch allowed $^{17}O_2$ to enter the circuit (volume of ~700 mL) at a rate equal to the ratís rate of oxygen uptake (~5mL/min). From the images collected, the concentration of $H_2{}^{17}O$ was computed for a region of interest (bilateral cerebral cortex) based on the method described in [3].

RESULTS AND DISCUSSION

The bottom panel of Figure 2 shows the time course of $H_2{}^{17}O$ accumulation in the region of interest, and the top panel provides the images at points A and B as labeled on the plot. The sensitivity of our technique is ~2% change in $T_{1\rho}$image intensity per 2mM increase in $[H_2{}^{17}O]$. As evident from the data, we were able to measure metabolically produced $H_2{}^{17}O$ in the rat brain with high spatial resolution. In order to use this technique for mapping cerebral metabolic rate of oxygen ($CMRO_2$), the wash in and wash out of $H_2{}^{17}O$, to and from the cerebrum need to be considered. As described in [2], a measurement of the brain arterial input function of $H_2{}^{17}O$ is needed to account for this wash in and wash out. We are presently conducting studies towards obtaining this function and mapping $CMRO_2$.

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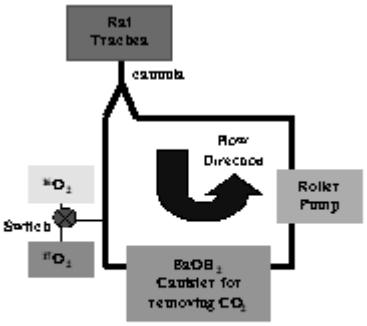

Figure 1. The ventilation circuit.

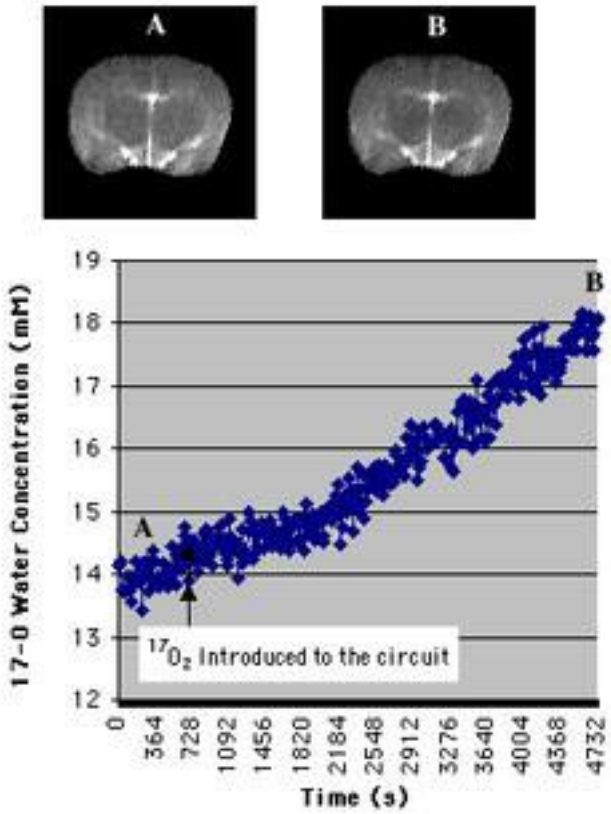

Figure 2. The top panel shows the images corresponding to points A and B on the plot below it. The bottom panels plots the time course of $H_2{}^{17}O$ accumulation in the brain due to metabolism of inspired ^{17}O gas.