In Vivo $^{17}$O Measurements of Water Rotational Correlation Time and Hydrodynamic Radius in Rat Brain

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Introduction

Water content is extremely high in a biological system. It plays essential roles in maintaining normal cellular functionalities, and is sensitive to the microscopic environment of intra- and extra-cellular spaces. This study exploits new MR approaches for noninvasively assessing the rotational correlation time ($\tau_c$) and hydrodynamic radius ($R_h$) of the brain tissue water. In vivo $^{17}$O MRS was used to measure the longitudinal relaxation time ($T_1$) of the quadrupolar $^{17}$O spin of water, and the $T_1$ value can be used to calculate water $\tau_c$ according to a simple, field-independent relation. $^1$H MRI was applied to image the brain translational diffusion coefficient ($D_t$), and the $D_t/T_1$ ratio can be used to determine $R_h$. These approaches were tested and evaluated at 9.4T using the rat brain model with varied brain temperature.

Theory

$^{17}$O spin has a quantum number of $I = 5/2$ and possesses an electric quadrupolar moment that can interact with local electric field gradients. The temporal fluctuation in this interaction induced by molecular motion dominates the $^{17}$O relaxation process. For the water molecule with the extreme narrowing limit (i.e., $\tau_c \omega << 1$, $\omega$ is the $^{17}$O Larmor frequency), there is a simple relation between water $T_1$ (unit: ms) and $\tau_c$ (unit: picosecond) according to Eqs. [1] and [2]:

$$\frac{1}{T_1} = 3\pi \left( \frac{2I+3}{9} \right) \left( \frac{\eta \hbar}{3} \right) \tau_c$$ \hspace{0.5cm} [1]; \hspace{0.5cm} \tau_c = \frac{13.8}{T_1} \text{(ps)} \hspace{0.5cm} [2]; \hspace{0.5cm} \tau_cD_t = 2R_h^2/9 \hspace{0.5cm} [3]; \hspace{0.5cm} R_h = 78.8\sqrt{\frac{D_t}{T_1}} \hspace{0.5cm} [4],$$

where $\eta \hbar/3$ is the $^{17}$O quadrupolar coupling constant, $\eta$ is an asymmetry parameter and they are constant and field independent.$^{12}$

The relation between the translational diffusion coefficient ($D_t$; mm$^2$s$^{-1}$ unit), $\tau_c$ and $R_h$ (unit: Å) can be derived using the Stokes-Einstein and the Debye–Stokes–Einstein equations$^{3}$, leading to Eq. [3] indicating that $\tau_cD_t$ should be a constant. Solving Eqs. [2] and [3] gives Eq. [4], in which $D_t$ can be imaged using conventional DTI with two b factors, thus, $R_h$ can be calculated according to Eq. [4].

Methods

All NMR experiments were conducted using Male Sprague–Dawley rats on a 9.4 T animal magnet interfaced to a Varian INOVA console. A dual surface-coil probe consisting of a butterfly-shape $^1$H coil (400 MHz) and an oval-shape $^{17}$O coil (~1cmx2 cm, 54.25 MHz) was used for acquiring $^1$H and $^{17}$O data, respectively. Non-localized $^{17}$O MR spectroscopy with inversion recovery pulse sequences and 8 inversion recovery times were applied for measuring $T_1$ values of natural abundance $^2$H/$^17$O in the rat brains (6 animals) with varied body temperature ($T$: 27-37°C, or 300-310 K). $^1$H MR images were acquired using adiabatic spin-echo sequence with two b-values (0 and 668 s/mm$^2$) to measure $D_t$ in the ROI covering a large brain region and its temperature dependence (2 animals).

Results

Figure 1A shows the relation between the $^{17}$O $T_1$ of brain tissue water and the inverse of temperature ($1/T$) from different rat measurements. It indicates that the increasing temperature resulted in a longer $T_1$. The relation obeys a linear function ($R^2=0.983$). Figure 1B shows the relation between the rotational correlation time, $\tau_c$, and the inverse of temperature ($1/T$), indicating a reversed linear relation ($R^2=0.976$), i.e., the increasing temperature shortened $\tau_c$. Figure 2 displays the results of $R_h$ measurements across the temperature range of 27-37°C, indicating an independent relation of $R_h$ on temperature. Both rats had a similar trend though one animal (Rat A) showed a slightly higher $R_h$ value compared to the other. The average $R_h$ from two animals was 1.00±0.01 Å.

Discussion and Conclusion

In this study, we tested novel MR-based approaches for in vivo measurements of two important parameters of rotational correlation time and hydrodynamic radius that reflect the brain tissue water dynamics at the molecular scale. It was found that the brain water $\tau_c$ was in a range of several picoseconds and is sensitive to the brain temperature change; the measured $\tau_c$ values were longer than the bulk water $\tau_c$. For instance, based on the linear relation shown in Fig. 1B, we predicted the tissue water $\tau_c$ value of 3.5 ps at 25°C in the rat brain, which was significantly longer than that of bulk water (=2.7 ps) at the same temperature.$^4$ This result reveals that $\tau_c$ is sensitive to microscopic environment in the biological system as one would expect. The measured $R_h$ values were stable across a large range of brain temperature (see Fig. 2). This result provides convincing evidence in supporting the validity of Eq. [3] and the methods proposed herein for in vivo measurements of brain water $\tau_c$ and $R_h$. The measured $R_h$ value of ~1 Å was in line with the size of water molecular radius (~1.3 Å). This work indicates excellent utilities of in vivo $^{17}$O MRS methods for potentially imaging the microscopic dynamics and cellular environment of brain tissue water in vivo.

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References