Measuring $T_{1\rho}$ Changes Related to Acidosis and Alkalosis

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Introduction

While the brain maintains a constant pH level globally, local variations in pH may play a significant role in brain function. The ability to image pH dynamics could offer a novel, more direct approach to map brain function as well as detect disease and assess treatment response. In this study, we evaluated the utility of an MR imaging technique known as $T_1\rho$, T_1 relaxation in the rotating frame, to measures pH dynamics. The sensitivity of $T_1\rho$ to changes in pH was evaluated in both phantoms and an in vivo mouse model using a set of pharmacological challenges. Real-time fiber optic monitoring of pH was employed throughout the in vivo imaging experiment.

Methods

Six agar phantoms were prepared by dissolving 3.5% agar powder in 0.1-M phosphate buffer. pH was adjusted with HCl and NaOH to create phantoms that varied from pH 6.0 to 8.0, a range extending beyond values likely to occur in vivo. pH levels in the agar phantom were assessed before and after solidification and after scanning. All images were acquired on a 4.7T Varian small-bore MRI scanner (Varian, Palo Alto, CA), using a volume transmit and receive Litz-cage RF coil (Doty, USA). $T_1\rho$ weighted images were acquired using a spin-echo sequence with a spin-locking preparation pulse which created a B_1 field of 1000Hz. A 1mm slice was acquired through the center of the phantoms, (field of view=60x30mm, imaging matrix size=512x128, TR=2000ms, and TE=12ms), at spin-locking times of 10, 20, 40, and 60ms. To evaluate the capability of $T_1\rho$ to detect changes in mouse brain pH, $T_1\rho$ images were obtained in four mice under three conditions: 1) while breathing 20% CO_2, 2) while breathing room air, and 3) following HCO_3^- injection (5mmol/kg, ip). A fiber optic sensor, which was previously implanted into the amygdala, was used to continuously measure brain pH during the entire experiment. Axial $T_1\rho$ mouse images were acquired using the same parameters used in the phantom experiment. A least squares fitting algorithm was used to generate $T_1\rho$ maps on a per voxel basis. The signal intensity (S) from the spin-lock sequence can be approximated by: $S=S_0e^{-TSL/T1\rho}$, where S_0 is the signal intensity produced when no spin-lock pulse is applied and TSL is the duration of spin-lock encoding. The average pH measurement obtained from the fiber optic sensor during the MR image acquisition was compared against the computed $T_1\rho$ decay times.

Results

Fig. 1 shows $T_1\rho$ maps for the agar phantoms with different pH values. $T_1\rho$ is inversely proportional to the pH value (Fig. 2). The results presented in Fig. 2 were calculated in a 5x5mm square ROI placed manually near the center of the phantom. Fig. 3 (a) shows $T_1\rho$ mouse brain image obtained with a 10ms spin-lock time. The fiber optic sensor for recording pH is shown in the cortex (red arrow). Measurements were obtained from the end of the signal void to reflect the area where the sensor was acquiring its measurements. $T_1\rho$ times were consistent with the brain having elevated pH (basic) following HCO3$^-$ injection (Fig. 3b) as compared to the baseline condition (Fig. 3c). During the administration of 20% CO_2, $T_1\rho$ times were longer in the area surrounding the pH sensor indicating the region was more acidic and consistent with the lower pH detected from the sensor (Fig. 3d). Fig. 4 shows the relationship between $T_1\rho$ and pH measured across all four of the mice.

Discussion and Conclusions

The phantom study shows that $T_1\rho$ imaging is sensitive to pH changes and can be modeled linearly across the physiological range of pH. In vivo imaging in the mouse model, supported by real time direct fiber optic pH measurements, demonstrates a similar negative relationship between $T_1\rho$ and pH to that of our phantom study, with expected differences in relaxivity values. Within the in vivo data, however, observed relaxivity was consistent across the small mouse population we tested. We found that 20% CO_2 altered mean $T_1\rho$ times by amounts consistent with an average pH reduction of ~0.4 units. In contrast, HCO3$^-$ injection altered $T_1\rho$ times by values consistent with a pH increase of ~0.3 units. The ability to measure pH dynamics in vivo using $T_1\rho$ MRI could be a valuable tool for future work in human imaging.

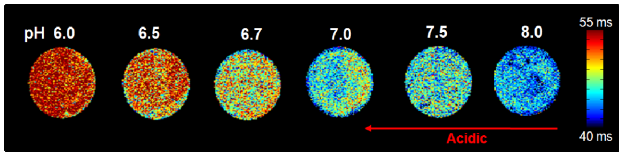

Fig. 1. $T_1\rho$ maps of pH agar phantoms

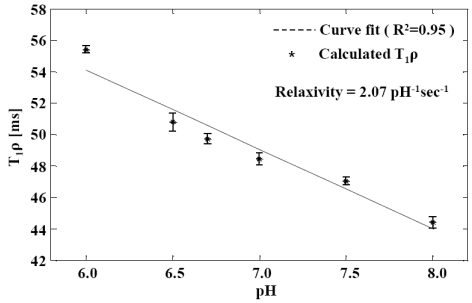

Fig. 2. $T_1\rho$ as a function of the pH measured in the agar phantom

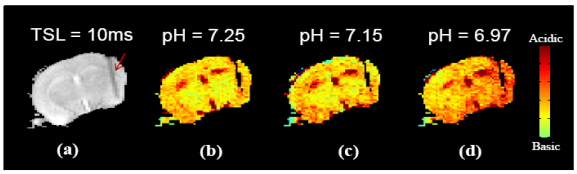

Fig. 3. Detecting pH changes with $T_1\rho$ in the brain of an anesthetized mouse.

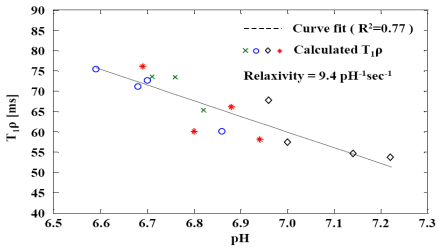

Fig. 4. $T_1\rho$ as a function of the pH measured in the brain of four anesthetized mice.