Study of Bound Proton T2 and Magnetization Transfer using Pulsed MT

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Introduction

Magnetization Transfer (MT) contrast has been used to study brain myelination and relies on selectively saturating bound (non-water) protons based on their rapid T_2-relaxation. Optimization of this selectivity and quantification of MT contrast requires knowledge of the bound proton T_2, which has proven difficult to measure. The range of reported estimates (10 to 30 μs(1–6)) is rather large, likely due to differences in experimental conditions, measurement method and sample type. With the goal of optimizing measurement of the exchangeable bound proton fraction through a pulsed MT experiment(7), we set out to determine the bound proton T_2 in white matter, grey mater and muscle *in vivo*.

Methods

The effect of a binomial MT pulse(8) on bound proton magnetization was studied as a function of post-saturation delay Δ (measured from the center of the pulse) using a multi-gradient echo sequence, after which the amplitude of the saturation effect and its dependence on MT pulse amplitude were calculated and compared with simulated values to determine bound proton T_2. The MT pulse was 2ms long and consisted of 10 subpulses of flip angles 0.5x, -x, x …, -x, 0.5x(x is an arbitrary angle). Reference signal level was measured by omitting the MT pulse.

Two *in vivo* scans of two common marmosets (*Callithrix jacchus*) were performed on a Bruker 7T scanner. MT pulse amplitude was varied from 500-2000Hz in 500Hz steps, Δ ranged from 2.2 to 399ms. Other parameters: 0.297mm isotropic resolution, TE 2.4ms, TR 3s, nominal excitation flip angle 90°. For *ex vivo* scans, two formalin fixed common marmoset brains were scanned on a Bruker 4.7T scanner. MT pulse amplitude was varied from 500-3500Hz in 500Hz steps, Δ ranged from 2.4 to 120ms. Other parameters: 0.281mm isotropic resolution, TE 2.8ms, TR 8s, nominal excitation flip angle 90°. For both experiments, a reference scan (Ref) without saturation pulse was also obtained.

A region of interest (ROI) in white matter was selected (see example in Fig. 1(d)). The average signal amplitude $A(\Delta)$ in the ROI and further the saturation fraction of the water protons S_w: $S_w = 1 - A(\Delta)/A_{Ref}$ were calculated. To estimate the saturation fraction of the bound protons (S_b), S_w was normalized to its value found at maximum pulse amplitude (this amplitude was more than sufficient to achieve maximum saturation).

This estimate of S_b was then compared with the simulated dependence of longitudinal magnetization (after the MT pulse) on T_2 and RF pulse amplitude (Fig.2), assuming a single (average) T_2 of the bound protons, obtained from simulations of the Bloch equations. Measured saturation fractions were fit to this model (Fig. 3) to find T_2 bound protons in white matter, grey matter and muscle respectively.

We then proceeded to estimate the exchangeable bound pool fraction V_b (relative to that of water protons) and exchange rate k from water to bound protons based on a 2-pool exchange model with $S_w = A_1 e^{-R_1 t} + A_2 e^{-(R_1 + k(1+V_b)/V_b)t}$ with R_1 is the apparent longitudinal relaxation rate.

Table 1. Fitting results for T_2, in μs.

Scans \ Tissues	White Matter	Grey Matter	Muscle
in vivo 1	29±6	19±5	13±1
in vivo 2	25±4	16±5	14±1
ex vivo 1	31±4	26±6	N/A
ex vivo 2	30±8	25±8	N/A

Results

The estimated values for bound proton T_2 are shown in Table 1. T_2 was found to be somewhat longer in white matter than in grey matter and muscle; also the *ex vivo* values were longer than the *in vivo* values. All values are at the long end of the range found previously with other approaches (1-6). From the 2-pool model fitting (Fig. 4), we found k to be 13±2s^{-1}, 30±3s^{-1}, and 47±9s^{-1} for white matter, grey matter and muscle respectively and V_b to be 21%, 6%, and 11% respectively. Fig. 1 shows the fractional difference between images at two delays ($Im(\Delta = 2.2\text{ms}) - Im(\Delta = 99\text{ms}))/Im(Ref)$ for different powers levels(500Hz, 1000Hz, 1500Hz, and 2000Hz). It demonstrates that at the highest power (2000Hz), we can saturate all the bound protons.

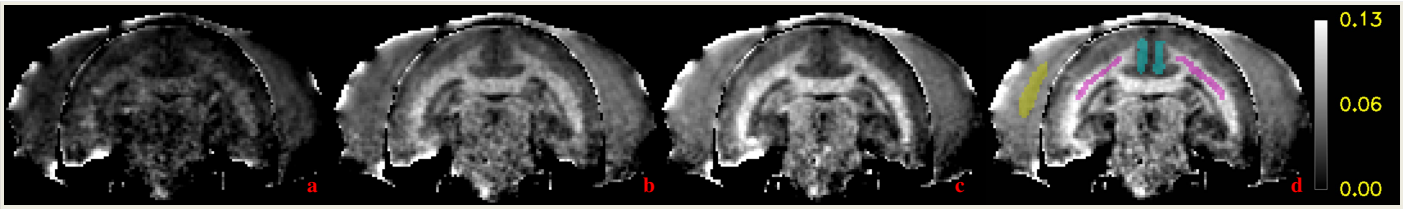

Figure 1. Fractional difference between images at two delays ($Im(\Delta = 2.2\text{ms}) - Im(\Delta = 99\text{ms}))/Im(Ref)$ for power of 500Hz(a), 1000Hz(b), 1500Hz(c), and 2000Hz(d) for the second *in vivo* scans.

Discussion

The binomial MT pulse proved to be an efficient way to selectively saturate bound protons in white matter within only 2ms and under clinically available peak RF pulse amplitude. This short pulse duration is advantageous to study exchange effects as it minimizes the exchange during the saturation, which would otherwise complicate interpretation. Our simulation shows that by changing pulse duration, number of sub-pulses, and amplitude, one can change the saturation of short T_2 protons without altering that of long T_2 protons. This specificity can be appreciated from Fig. 1, where the differing bound proton concentrations of white and grey matter create very strong contrast.

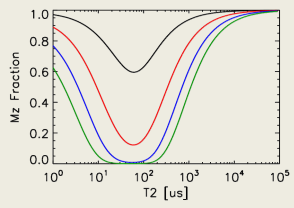

Figure 2. Residual Mz after a MT pulse as function of T_2 for four different power levels: 500Hz(black), 1000Hz(red), 1500Hz(blue), and 2000Hz(green). Results obtained from simulations of the Bloch equations.

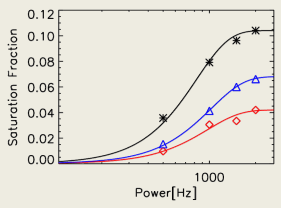

Figure 3. Measured (points) and fitted (lines) saturation fractions of bound protons S_b as function of power for white matter (black), grey matter (red) and muscle (blue) for the second *in vivo* scan.

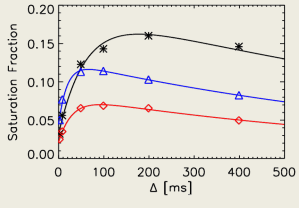

Figure 4. Measured (points) and fitted (lines) saturation fraction for white matter (black), grey matter (red) and muscle (blue) as a function of delay time for the first *in vivo* scan.

These findings indicate that pulsed MT could readily be implemented on human high field systems, within their constraints of RF peak amplitude and power deposition. This opens the way to study exchange characteristics and bound pool fractions in a sensitive manner, and it is practical for clinical application.

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