Exploring a Flexible Pulse Design for Studying Magnetization Transfer

Peter van Gelderen[1], Xu Jiang[1], and Jeff H Duyn[1]
[1]*AMRI, LFMI, NINDS, National Institutes of Health, Bethesda, MD, United States*

Purpose of study: To investigate a simple pulse design for MT contrast.

Although magnetization transfer (MT [1]) has been used widely to study various neurological disorders because of its sensitivity to brain myelin content, the extraction of quantitative, reproducible parameters has proven difficult due to the complexity of the contrast mechanism. Pulsed MT experiments, in which MT kinetics are studied in response to an RF pulse that selectively saturates bound (non-water) protons, may be easier to interpret and allow for measurement of parameters such as the fraction and transfer rate of bound protons [2]. However, practical implementation of the pulsed MT experiment is hampered by the finite duration of the MT pulse, limitations on RF peak power, and the requirement to minimize the effect on mobile (water) protons. Here we explore a simple variation on the binominal pulse design that allows a flexible trade-off between these constraints [3,4].

Theory

The general pulse scheme used for bound proton saturation is based on T_2 selectivity and consists of a train of N hard pulses, played out on-resonance, with a B_1 amplitude modulation of +1,-1,+1,….,-1,1 (or a phase of 0,π,0,π….) and a (relative) length of 1,2,2…2,1, resulting in flip angles of α,-2α,2α…..-2α,α (Fig. 1). B_1 amplitude, total pulse width PW, and N can be varied to maximize the saturation of short T_2 (~20μs) bound protons and minimize that of long T_2 (>20ms) water protons. (Fig. 2).

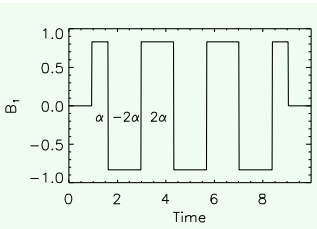

Figure 1. Example of the type of MT pulse used.

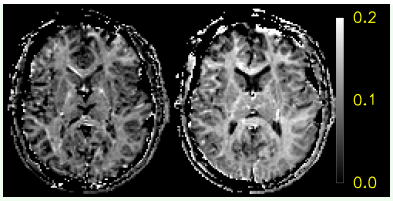

Figure 4. Saturation effects 100ms after two different MT pulses: left 1.28ms, right 10ms long, designed to have a similar long T_2 pool effect, but different short T_2 pool saturation. Acquired with EPI at 3T, 20 averages, 1.6mm resolution.

Methods

This class of MT pulses was tested on healthy subjects, scanned under a local IRB approved protocol on a Siemens Magnetom at 7T (n=11) and a Siemens Skyra at 3T (n=9). Following a time TD from the MT pulse, the signal M(TD) was measured with EPI as follows: 240x180 mm^2 FOV, 144x108 resolution, 5 2mm slices (1.5mm gap), sense rate 2 (with external gradient echo based reference), 3s TR, 24/30ms TE (for 7/3 T), 5-10 repetitions. TD was varied from 5-600ms in 5-10 steps, and 2-4 repetitions without MT pulse were acquired as reference (R) to the determine MT-induced fractional saturation: S=1-M(TD)/R. All MT pulses had 833Hz B_1 amplitude, close to the maximum available at both scanners. The slices were acquired sequentially following the MT pulse with the slice positions rotating through five of the TDs (as in [5]), two of these cycles were acquired when measuring 10 TDs. To investigate the potential effects of a third (hidden) pool interacting with the bound protons and the EPI-visible water, a double pulse MT experiment was performed on some of the subjects, with varying delays both between the two pulse trains and after the second pulse. The signals were averaged over an ROI selecting the splenium of the corpus callosum. A two-pool exchange model was fitted to the MT induced saturation data to estimate the individual saturation levels of the bound (S_B) and mobile (S_W) protons and their exchange time.

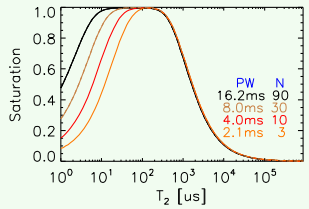

Figure 2a. Simulation of the saturation effect of various MT pulses as function of T_2. The four pulses were designed to have similar effects on long T_2 species. The B_1 was 833Hz.

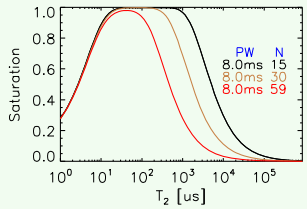

Figure 2b. The simulated saturation effect of three MT pulses with similar short T_2 suppression.

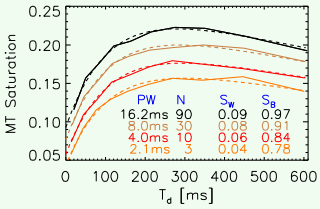

Figure 3a. Saturation levels as function of delay time as measured in a SCC ROI at 7T using the pulses from Fig. 2a, modulating the short T_2 suppression. Solid lines are data, dashed: a 2-pool fit. M_f and M_b indicate the saturation levels estimated with the 2-pool model.

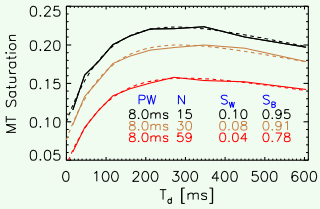

Figure 3b. Saturation levels using the pulses from Fig. 2b, measuring the effect of longer T_2 suppression.

Results & Discussion

An example of the pulse optimization by selectively varying the short or long T_2 saturation is shown in Fig. 2. Associated MT-induced saturation curves are shown in Fig. 3 (7T). 3T data (Fig. 4) illustrate the difference in MT saturation effects between 1.3ms and 10ms MT pulses with similar long T_2 effects, and thus attributed to differential saturation of bound protons. The 2-pool model fitting of the data from 10 subjects indicated a bound pool fraction of 16-20% and a lifetime of 90-120ms .The dependence of bound pool saturation on pulse length (c.f. Fig. 3a) indicated a bound pool T_2 of around 30μs.

Data from the double MT pulse experiment was well explained by the 2-pool model and led to the same bound pool fraction and lifetime. This suggests that much of a potential third, intermediary, pool (e.g. myelin water protons invisible to EPI) exchanges relatively fast with the visible proton pool (axonal and interstitial water). This pool is expected to play a role as most of the bound pool protons are located in the myelin layers and would have to transfer through the myelin water to enter the free-water pool (axonal or interstitial space). The lack of evidence of a separate myelin water pool in the double pulse data indicates the exchange with either the bound pool or the free pool is fast (ms range), effectively unifying two of the three pools, or exchange time of myelin water has a broad distribution and myelin water is not a single pool in this context. The intermediate T_2 of myelin water (~10ms) makes it invisible in these experiments, but it could contribute to what appears as the bound pool, which would explain dependence on N of the bound pool saturation seen in Fig. 3b.

References:
1. Wolff & Balaban, MRM **10**:135 (1989)
2. Kalantari et.al., MRM **66**:1142 (2011).
3. Forster et.al., MAGMA **3**:83 (1995).
4. Henkelman, Stanisz & Graham, NMR in Biomed **14**:57.
5. Clare & Jezzard, MRM **45**:630 (2001)