The physical basis of inhomogeneous magnetization transfer

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Introduction: Magnetization transfer (MT) is usually modeled with a homogeneously broadened, semisolid pool coupled to water by proton exchange or dipolar interactions. Recent work has shown that RF saturation at +/- 10 kHz off-resonance creates additional water suppression in white matter and in certain lipid systems[1,2]. This feature is termed Inhomogeneous MT (ihMT) and may prove useful for selective myelin imaging. The studies presented here outline the chemical and physical properties that create ihMT.

Materials and Methods: Aqueous samples of 1.5% (w/w) agarose, 15% (w/w) gelatin and 15% (w/w) Prolipid 161 (PL161, a lamellar lipid system with MT properties similar to white matter[3]) were prepared in 15 ml centrifuge tubes. MT of the homogeneously broadened components (conventional MT) was generated by broad-band MT (bbMT)[4] (Fig. 1A dashed line). MT enhanced by inhomogeneous broadening was generated by a variant of the bbMT sequence where the gradient direction is reversed to alternatively expose spins to positive and negative RF frequency offsets (Fig. 1A solid line). Gaussian shaped RF pulses (16 µT, 5ms) were repeated 200 times for RF duration of 1s. MT data were normalized to a 1D image with no RF saturation. ihMT was measured as the difference between conventional MT, (+/+) Gz, and enhanced MT, (+/-)Gz. Conventional and enhanced MT spectra in PL161 were collected at 2T as a function of RF power, duration of RF pulse, and sample temperature (Fig. 2A,B).

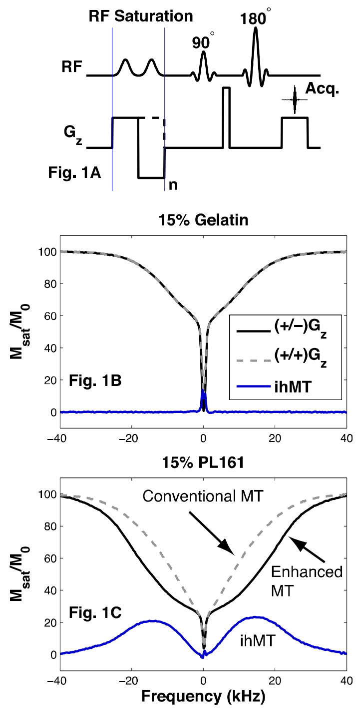

Figure 1. Pulse sequence to generate conventional MT, (+/+)Gz, and enhanced MT, (+/-)Gz. (A). MT and enhanced MT of gelatin are identical and ihMT is zero (B). MT, enhanced MT and ihMT of PL161 at 25 °C (C).

Results: Conventional MT is detected in all samples whereas ihMT is unique to lipids (Figs. 1B vs. 1C). ihMT increases with increased RF amplitude and RF pulse bandwidth (not shown). Raising the temperature of PL161 increases the amount of conventional MT (Fig. 2A), broadens the MT profile, and changes the semisolid lineshape from super-Lorentzian to Gaussian. Enhanced MT (Fig. 2B) also increases with temperature but the lineshape does not broaden and remains Gaussian. At 65 °C (not shown) the enhanced MT becomes nearly identical to conventional MT. The amount of ihMT (Fig. 2C) goes through a maximum around room temperature and gradually decreases with increasing temperature. The frequency of peak ihMT increases with increasing temperature.

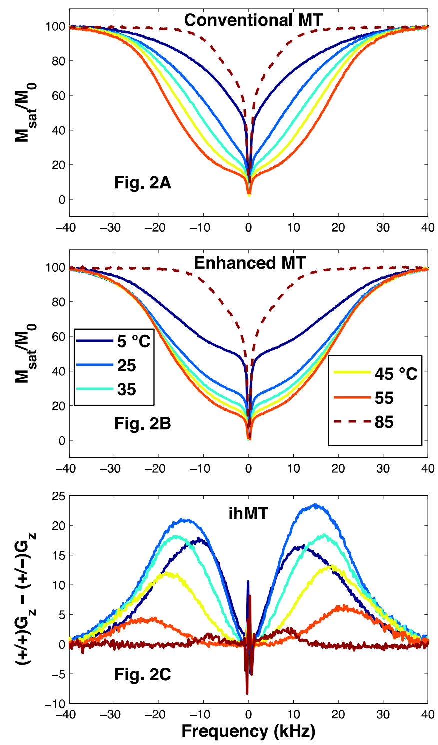

Figure 2. Conventional MT (A), enhanced MT (B), and ihMT (C) in PL161 as a function of temperature from 5°C (blue) to 85 °C (dashed red).

Discussion: Our results provide clues about the molecular mechanism of MT and ihMT. The most interesting finding is the increased broadening of the MT line as the temperature increases, elucidating specific facets of lipid dynamics. In the conventional MT experiment, (+/+) Gz, RF is applied at one frequency offset of the dipolar Pake pattern[5] corresponding to single orientation of semisolid protons. At low temperatures, lipid chain motion is restricted and only a fraction of the spins is saturated. This partial saturation is communicated to remote protons via through-chain nOe and OH-exchange from lipids to water molecules[6] and is observed by conventional MT. Similarly, with (+/-)Gz gradients, RF saturation at two offset frequencies results in “enhanced” MT from ordered lipids. As temperature increases (Fig. 2A), increased motion along the lipid chains reorients the dipolar interaction and creates a time varying frequency for semisolid protons. Via this mechanism, more spins contribute to conventional MT (and less to ihMT) at higher temperatures resulting in a broader saturation profile approaching “enhanced” MT (Fig. 2A). At 85 °C, MT collapses when the rates of incoherent, through-chain motion exceed the strongest dipolar interaction (> 10^5 Hz). Fig. 3C shows that frequency offset of the maximum ihMT grows with increasing temperature, consistent with higher motional rates within lipid membrane.

Conclusions: The revealed nature of the ihMT suggests that this type of MR contrast has enhanced specificity to the dynamic window of motion on the order of dipolar interactions in lipid bilayers. Studies of MT and ihMT in model systems help understand the physical basis of MT *in vivo* related to molecular mechanisms of disease processes.

References: [1]Alsop et al., *Proc. ISMRM* 2004; p2324. [2]Duhamel et al. *Proc. ISMRM* 2013, p2535. [3]Swanson et al, *Proc. ISMRM* 2012; p1378. [4]Swanson, J. Magn. Reson. 1991 **95** (616-618). [5]Pake, *Phys. Rev.* 1948 **74** (1184-8). [6]Malyarenko, et al., *Magn. Res. Med.* 2013 (in press).