Application of a dipolar model to inhomogeneous magnetization transfer (ihMT)

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Target audience Researchers interested in advanced magnetization transfer methods or myelin imaging.

Purpose and Theory Selective imaging of magnetization transfer from inhomogeneously broadened (ihMT) lines has demonstrated signal almost exclusively in myelinated tissues [1]. The method involves subtraction of magnetization transfer images obtained with simultaneous saturation at positive and negative frequency offsets from those obtained with single frequency saturation at the same total power. The origin of inhomogeneous broadening in myelin has been attributed to dipolar interactions within relatively isolated methylene pairs in membrane lipids [1] that behave as a dipolar reservoir [2], but a full, quantitative model has not been developed. Previously a quantitative MT model of tissue including a dipolar reservoir based on Redfield-Provotorov theory [3] was evaluated [4]. Though this model did not substantially improve upon fits to data from single frequency irradiation without a dipolar reservoir [4], the possibility of dual frequency irradiation was not considered. Adding the effect of dual frequency saturation as derived from Provotorov theory by Goldman [5], differential equations for the dipolar reservoir and bound pool, M^B magnetization may be written in a form similar to [3] (Fig.1a). From these modified equations one can see that for the case when Δ_1=-Δ_2, dM^B/dt becomes independent of the dipolar reservoir as characterized by B, the inverse spin temperature associated with the dipolar order. Thus for dual frequency saturation, the equations that describe the magnetizations' evolution reduce to the two-pool model of MT [4]. The steady-state ihMT signal may thus be described by the difference between the free pool magnetization, M^A solutions to the two-pool model and two-pool model with a dipolar reservoir (Fig. 1b).

a) $$\frac{dB}{dt} = \frac{R_{rfB}}{2}\left(\frac{2\pi}{D}\right)^2(\Delta_1+\Delta_2)M^B(t) - \left[\frac{R_{rfB}}{2}\left(\frac{2\pi}{D}\right)^2(\Delta_1^2+\Delta_2^2)+\frac{1}{T_D}\right]B(t)$$

$$\frac{dM^B}{dt} = R_B(M_0^B - M^B(t)) - RM_0^A M^B(t) + RM_0^B M^A(t) - \frac{R_{rfB}}{2}(\Delta_1+\Delta_2)M^B(t) + \pi R_{rfB}(\Delta_1+\Delta_2)B(t)$$

b) $$\text{ihMT} = -\frac{4\pi^2 R_{rfB}^2 T_D (T-SU)\Delta^2}{(T+R_{rfB}U)(D^2(T+R_{rfB}U)+4\pi^2 R_{rfB}T_D\Delta^2 T)}$$

Figure 1 Equations describing: a) derivative of B and M^B with respect to time; and b) ihMT signal, with definitions as in [4].

Methods ihMT data was obtained from experiments conducted at multiple frequency offsets for varying powers. Preclinical experiments were conducted on a mouse maintained at physiological temperature within a 11.7T vertical bore scanner (Avance, Bruker) using pulsed RF saturation applied for 900ms prior to a RARE acquisition ($B_{1,RMS}$=5.0, 8.4μT; Δ=6-20kHz in 2kHz steps, 25kHz, 30kHz; 64x64 matrix; NSA=30; 1mm slice): Human brain data was collected using a 3T scanner (Signa, GE Healthcare) using 2s pulsed RF within a 2D single-shot EPI sequence ($B_{1,RMS}$=2.5, 5.0μT; Δ=5-17kHz in 3kHz steps; FOV=24x24cm^2; NSA=6; 6mm slice; TE/TR=24/8000ms). ihMT data were processed and quantified within ROIs containing different tissues (IC=internal capsule; CC=corpus callosum; GM=grey matter; Mu=muscle) and then fit using a non-linear least squares method (Matlab, Mathworks). Data from the dual frequency experiments was initially processed using the two-pool model steady-state solution. As in [3], the value for R^B was fixed at 1s^{-1}. The complete ihMT dataset was then used to ascertain T_D, the relaxation time of dipolar order, with $T_{2,B}$, the bound pool's transverse relaxation time, also allowed to vary.

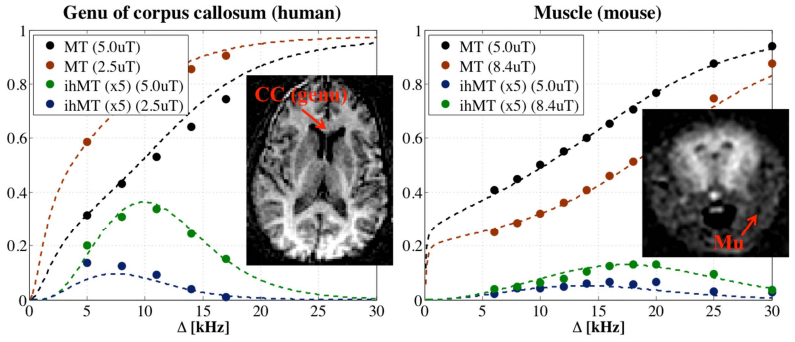

Figure 2 Sample plots of MT and ihMT(x5) data, from a) human CC and b) mouse Mu (ihMT images inlaid for reference), with lines from model fitting.

ROI		T_D [ms]
Preclinical:	IC	2.5
	CC	2.1
	GM	1.4
	Mu	1.0
Human:	frontal WM	8.3
	CC (genu)	7.3
	IC	11.7
	CC (splenium)	13.9
	posterior WM	12.4

Table 1 Values for dipolar relaxation time, T_D from fits to ROI data.

Results and Discussion The model provided an excellent fit to both the dual frequency MT and ihMT difference signals (Fig. 2). White matter (WM) T_D values were found to be shorter in mice than in human data (Table 1). This, along with an even shorter T_D value in muscle relative to WM, might provide the basis behind a stronger ihMT signal from human WM than in mice, and negligible ihMT in surrounding tissue [1].

Conclusions A model for ihMT has been presented based on modification of previous spin-bath models derived using spin temperature concepts. Fits of the data indicate that longer T_D, perhaps reflecting reduced bending mobility in membrane lipid methylene chains, is primarily responsible for the much higher ihMT signal in myelinated tissues.

References [1] Varma et al. Magn. Reson Med (2014); [2] Girard et al. Magn Reson Med (2014); [3] Yeung et al. J Magn Reson A (1994) 106:37-45; [4] Morrison et al. J Magn Reson B (1995) 108:103-113; [5] Goldman M, Spin Temperature and NMR in Solids (1970).