Magnetization Transfer from Inhomogeneously Broadened Lines (ihMT): Effect of MT Asymmetry on the ihMT Signal

Guillaume Duhamel[1], Valentin Prevost[1], Gopal Varma[2], David C Alsop[2], and Olivier Girard[1]

[1]*CRMBM, CNRS 7339, Aix-Marseille Université, Marseille, 13005, France,* [2]*Radiology, Beth Israel Deaconess Med. Center, Harvard Medical School, Boston, MA, United States*

Target audience: MR physicists and physicians interested in novel endogenous contrast mechanisms and specific white matter imaging.

Introduction: There are multiple mechanisms in tissues (rotational and translational motion, spin diffusion) which produce fast exchange between the components of a NMR line hence making it homogeneously broadened. However, in large membranes, the main constituent of the myelin sheath, reduced spin diffusion[1] and the absence of the usual mechanisms by which homogeneous broadening is achieved, suggest that inhomogeneous broadening may be present. A recent MT technique, referred as inhomogeneous MT (ihMT) has been able to reveal the inhomogenous component of the MR spectrum[2-6]. It is based on the fact that, if the homogeneous line is symmetric, the effect of applying single frequency irradiation at frequency f, should be identical to that obtained by applying irradiation at both frequency f and $-f$ with the same total energy, whereas it is different for inhomogeneous line[7] because of slow exchange within the line. Then, the difference between a single frequency and a dual frequency MT experiment (Fig 1a and 1c, $ihMT=M^{+f}-M^{+f/-f}$) can be used as an indicator of magnetization transfer from inhomogeneous lines. Unfortunately, asymmetry is present in the MT spectrum[8] and it increases with magnetic field. A first order correction can be performed by using the average of single frequency MT images acquired at positive and negative frequencies in the ihMT subtraction[2,3,6] (Fig. 1a,b and 1c, $ihMT=M^{+f}+M^{-f}-2M^{+f/-f}$). Whereas this double subtraction strategy has allowed obtaining ihMT images with tremendous specificity toward myelinated WM tissue[3,4,6], the contribution and impact of asymmetry on ihMT images has not been addressed. In the present study, we experimentally evaluate the effect of asymmetry on ihMT ratio values and demonstrate that the ihMT effect is not an asymmetry effect.

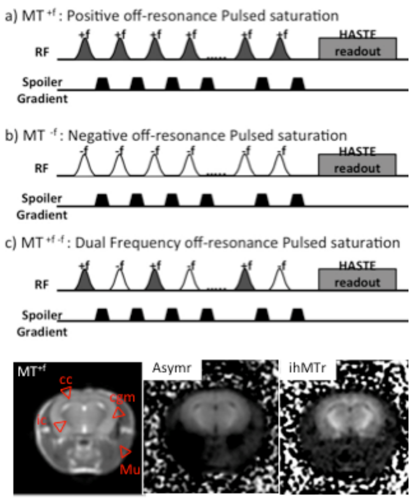

Fig1. ihMT sequence and resulting MT^{+f}, Asymr and ihMTr images for 64 NEX ($\pm f$=±8kHz, f_c=0kHz, Acq.time 15min)

Methods: Experiments were performed at 11.75T (f_0=500MhZ) on a vertical MR system (Bruker, AV 500WB, transmit/receive volume coil: ∅ 2cm, length 3cm) on anaesthetized mice (C57BL/6j, 10 weeks, weight 25±1g). The saturation was performed with 3ms Hann shaped pulses applied every 3.3ms at either positive (*+f=8 kHz*) or negative (*-f=-8 kHz*) frequency offset relative to f_0, during 1.2s (b_1^{peak}=8μT for a total RF energy of 26.2μT^2.s) prior to image acquisition (single-slice TSE readout, 64x64, ST 1mm, FOV 2x2cm^2). Three images were acquired according to the scheme described on Fig 1 in order to derive the ihMT image. An additional image acquired without prior saturation (M_0) was used for calculation of the ihMT ratio ($ihMTr=ihMT/M_0$, Fig. 1). In order to evaluate the asymmetry effect, the experiment was repeated 10 times with saturation offsets $\pm f$=±8kHz relative to a frequency center (f_c) shifted from -4, -3, -2, -1, -0.5, +0.5, +1, +2, +3 and +4 kHz with regards to f_0. 32 NEX were acquired to increase the SNR. ihMT ratios and Asymetry ratios ($Asymr=(M^{+f}-M^{-f})/M_0$, Fig. 1) were evaluated in two areas of white matter (corpus Callosum (CC) and internal capsule (IC)), cortical gray matter (CGM) and muscle (Mu) (Fig. 1, MT^{+f}).

Results: Typical images of MT^{+f}, *Asymr* and *ihMTr* obtained on mouse brain with the proposed sequence and f_c=0kHz are shown on Fig1. Figures 2 and 3 show the effect of shifting f_c on *Asymr* and *ihMTr* images/values. The signal of *Asymr* images tended to cancel for f_c=-1kHz in the brain and for f_c=0kHz in the muscle. For these f_c values, the *ihMTr* image clearly highlighted myelinated white matter brain structures (IC and CC) relative to gray matter structure and muscle. Signal of the *Asymr* and *ihMTr* images increased with higher f_c shifts ($|f_c| \geq$1kHz), but a loss of specificity toward myelinated tissues was clearly evidenced on *ihMTr* images, as illustrated by the strong signal in the muscle area (e.g. for f_c=2kHz). These observations are evidenced on the quantitative analyses (Fig. 3). For each structure (IC, GM and Muscle), the measured asymmetry ratio linearly varied with the shift of f_c, and canceled at $f_c \approx$-0.8kHz for GM/WM brain structures and at $f_c \approx$-0.2kHz for muscle. *ihMTr* followed a different dynamics. In the brain, *ihMTr* values were minimal but non-zero for f_c shifts values that cancel the *Asymr* values ($f_c \approx$-0.8kHz), thus demonstrating that the ihMT effect is not an asymmetry effect. Interestingly, in the regime of weak asymmetry ($|Asymr|$<2% obtained for small shifts -1kHz ≤ f_c≤ -0.5kHz), the *ihMTr* values remained constant (~3% for IC and CC (data not shown) and ~1.7% for GM). For high asymmetry conditions, biased over-estimated *ihMTr* values were obtained (e.g. for f_c=2kHz, *Asymr*(IC)>8%) along with a loss of specificity (*ihMTr*(Mu)>2% against *ihMTr*(Mu)<0.7% for f_c=-0.8kHz).

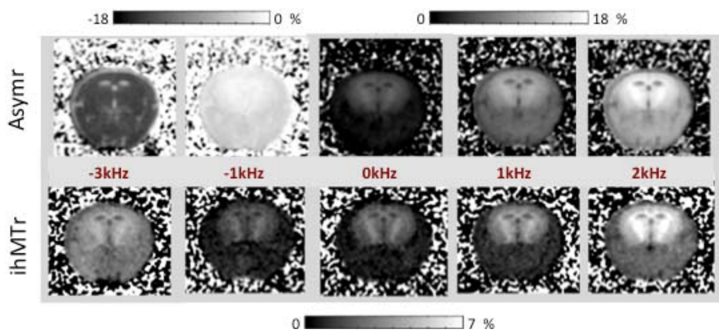

Fig2. Asymr and ihMTr as a function of fc values

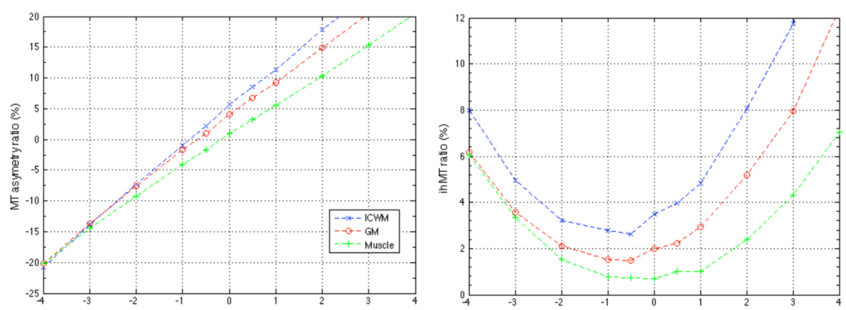

Fig3. Quantitative Asymr and ihMTr values as a function of fc values, in IC, GM and Mu

Conclusion: This work clearly evidenced that ihMT effect is not due to the asymmetry of the MR line since a slight shift of f_c (-0.8kHz) allowed cancelling the asymmetry while preserving non-zero *ihMTr* values. The double subtraction approach showed efficient ihMT imaging with first order correction of asymmetry effects in the limits of *Asymr*=±2%, which were obtained in the range of -1kHz<f_c<-0.8kHz on the mouse brain at 11.75T.

References*: [1]** *Huster D, J Am Chem Soc* 2002. ***[2] *Alsop et al, Proc. ISMRM 2004;p2324.* ***[3]*** *Alsop et al, Proc. ISMRM 2005;p2224.* ***[4]*** *Girard et al, Proc. ISMRM 2013;p2506.* ***[5]*** *Duhamel et al, Proc. ISMRM 2013;p2535.* ***[6]*** *Varma et al, Magn Reson Med, in revision.* ***[7]*** *Bloembergen N et al*, Physical Review 1948. ***[8]*** *Pekar J et al, Magn Reson Med 1996.*