Extracting a robust inhomogeneous magnetization transfer (ihMT) rate parameter, ihMT-R_{ex}

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Target audience Researchers interested in quantitative measures of myelin using the inhomogeneous magnetization transfer (ihMT) effect.

Purpose and Theory The recently reported ihMT technique shows promise for characterizing myelinated tissues[1], but the ihMT signal difference may be modulated by factors such as T_1 and/or B_1 amplitude non-uniformity that are less specific to myelin. In particular, B_1 dependence has been observed in the quantitative measurement of the ihMT ratio (ihMTR)[1-2], one potential surrogate measure of myelin content. An alternative to the ihMTR is use of the inverse of the saturated signal, similar to corrections of quantitative ratios employed in other saturation-based techniques[3-4]. In particular, use of a metric based on the inverse Z-spectrum in steady-state pulsed CEST-MRI is relatable to an exchange-dependent relaxation rate[3]. Taking the steady-state signal, S for a spoiled gradient echo (SPGR) sequence under the assumption of a low flip angle, α and $R_1\mathrm{TR}<<1$[4], the normalized magnetization, M_0 and relaxation rate, R_1 may be considered to change following saturation/exchange to $M_{0,sat}$ and $R_{1,ex}$ respectively, such that $M_{0,sat}R_{1,ex}=M_0R_1$. The resulting signal with saturation, S_{sat} shows an inverse dependence on the rate parameter $R_{1,ex}$ (Fig. 1a). If the inverse of S_{sat} is taken, subtraction at two saturation rates, i.e. for the single and dual frequency experiments used to calculated ihMT, preserves the linearity in $R_{1,ex}$ (Fig. 1b). The influence from T_1 may be reduced by normalization with S_C from an unsaturated SPGR sequence with α increased by a factor C, such that $C^2\alpha^2/2>>R_1\mathrm{TR}$ (Fig. 1c). Although the resulting signal equation relating to ihMT via $\Delta R_{1,ex}$, hereon referred to as ihMT-R_{ex}, contains an α^2 term in the denominator, any B_1 dependence is assumed to be removed for cases where ihMT-R_{ex} is also linearly proportional to power. This work aims to investigate the case(s) in which these assumptions hold true, thus allowing a more reliable ihMT measure.

a) $$S = M_0\frac{\alpha R_1\mathrm{TR}}{R_1\mathrm{TR}+\frac{\alpha^2}{2}} \rightarrow S_{sat} = M_{0,sat}\frac{\alpha R_{1,ex}\mathrm{TR}}{R_{1,ex}\mathrm{TR}+\frac{\alpha^2}{2}}$$

b) $$\frac{1}{S_{sat}} = \frac{1}{M_0}\frac{R_{1,ex}\mathrm{TR}+\frac{\alpha^2}{2}}{\alpha R_1\mathrm{TR}} \rightarrow \Delta\left(\frac{1}{S_{sat}}\right) = \frac{1}{M_0}\frac{\Delta\left(R_{1,ex}\right)\mathrm{TR}}{\alpha R_1\mathrm{TR}}$$

c) $$S_C = M_0\frac{C\alpha R_1\mathrm{TR}}{R_1\mathrm{TR}+\frac{C^2\alpha^2}{2}} \rightarrow S_C\Delta\left(\frac{1}{S_{sat}}\right) = \frac{2\Delta\left(R_{1,ex}\right)\mathrm{TR}}{C\alpha^2}$$

Figure 1 Low α steady-state signal, S: a) with saturation; b) inverted; and c) normalized with S_C.

Methods In order to fully investigate a range of powers used for the ihMT experiments, a 1s SPGR preparation was placed before a 2D single-shot spin-echo EPI acquisition (FOV=24x24cm^2; NSA=8; 6mm slice; TE=24; $\mathrm{TR_{EPI}}\geq7$s) at 3T (Signa, GE Healthcare). Based on a previously described 3D ihMT acquisition[5], the SPGR preparation consisted of 5ms trapezoidal pulses applied ±5kHz off-resonance (cosine modulated for dual frequency saturation), followed by an on-resonance α=10° pulse every $\mathrm{TR_{SPGR}}$. The sequence was applied at the mid-ventricular level for $\mathrm{TR_{SPGR}}$=10ms; 15ms for varying $B_{1,RMS}$ values based on SAR restrictions. For S_C data, $B_{1,RMS}$ was set to zero and α was increased to 40°. Data acquisition was repeated with the transmit gain (TG) decreased by 3dB in order to preliminarily assess B_1 dependence. ROIs were chosen in areas of frontal/posterior white matter (fWM/pWM), and the internal capsule (IC) for analysis.

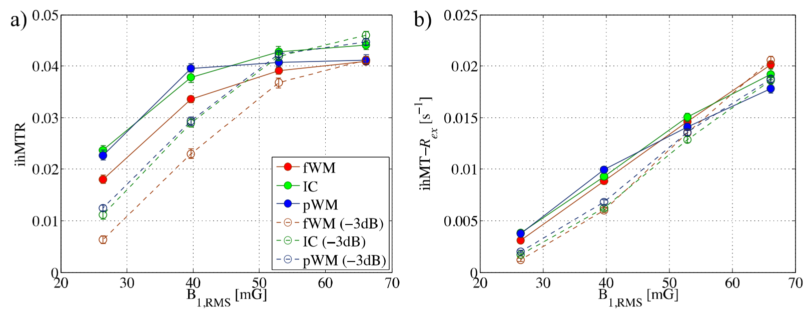

Figure 2 Sample plots of a) ihMTR and b) ihMT-R_{ex} with variation in the amplitude of saturation pulses using data acquired with $\mathrm{TR_{SPGR}/TR_{EPI}}$=10ms/10s.

Results and Discussion ihMTR saturated at different levels and $B_{1,RMS}$ values for each ROI; The ihMT-R_{ex} appeared linear with $B_{1,RMS}$ (Fig. 2). For $B_{1,RMS}\geq50$mG, ihMT-R_{ex} values at regular TG and at half the transmit power overlapped for both $\mathrm{TR_{SPGR}}$s. This is indicative of reduced sensitivity to any B_1 inhomogeneity since the reduction in TG affects S_{sat} and S_C, whereas the change in $B_{1,RMS}$ affects S_{sat} only. ihMTR and ihMT-R_{ex} maps from the same dataset (Fig. 3), show the former to have lower anterior signal in WM where B_1 decreases, whereas the contrast is sharper and signal more uniform in the latter.

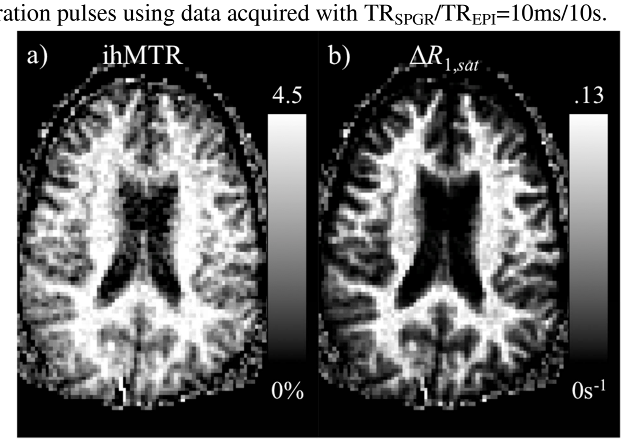

Figure 3 Maps of a) ihMTR and b) $\Delta R_{1,sat}$, using data acquired with $B_{1,RMS}$=53mG and the initial TG.

Conclusions Use of the inverse signal provided maps that appear more uniform in white matter. Although the results translate to a 3D SPGR sequence of relatively high SAR, they may be transferred to lower field, and/or help develop a 3D sequence with a suitable preparation.

References 1. Varma et al., MRM (2014). 2. Girard et al. MRM (2014). 3. Helms et al. MRM (2010) 64:177-185. 4. Zaiss et al. NMR Biomed (2014) 27:240-252. 4. Helms et al. MRM (2008) 59:667-672. 5. Varma et al. Proc ISMRM (2013) 21:4224.