Analytical Method for Correction of B1 Errors in High-Field Magnetization Transfer Ratio Mapping

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Introduction Magnetization transfer ratio (MTR) is a widely used simple empiric quantitative measure of the magnetization transfer (MT) effect in tissues. One serious limitation of MTR applications in high magnetic fields is its sensitivity to B_1 non-uniformities (1,2). Two B_1 correction techniques based on empirical linear regression models were suggested (1,2). These approaches, however, do not take into account the theoretical background of the effect of B_1 variations on MTR. This study proposes a new analytical theory explaining MTR errors caused by B_1 inhomogeneity and demonstrates an alternative theory-driven method for correction of MTR maps.

Theory As a starting point, we use the approximated MTR equation derived for a spoiled gradient-echo sequence with MT prepulse (MT-GRE) based on the pulsed MT theory (3). This theory considers periodic pulsed saturation applied to the two-pool model with cross-relaxation, where the tissue is presented as a system containing free water protons (free pool) and macromolecular protons (bound pool). Assuming that saturation is selectively applied to the bound pool and the TR of the sequence is sufficiently short to satisfy the first-order approximation, the basic MTR equation (3) can be rewritten as

$$\mathrm{MTR} \approx \frac{kf\,(t_m/\mathrm{TR})W^B}{k(R_1-(1-f)\ln\cos(\alpha)/\mathrm{TR})+f\,(t_m/\mathrm{TR})W^B(R_1+k-\ln\cos(\alpha)/\mathrm{TR})} \quad [1]$$

where k is the cross-relaxation rate constant defined for the free to bound pool transfer, f is the bound pool fraction, $R_1=1/T_1$ is the observed longitudinal relaxation rate assumed to be equal to relaxation rates for both pools ($R_1^F=R_1^B=R_1$), α is the flip angle (FA) of the excitation pulse, t_m is the duration of the saturation pulse, and W^B is the saturation rate for the bound pool. W^B is calculated as $W^B=\pi\omega_{1rms}^2 g^{SL}(\Delta,T_2^B)$, where ω_{1rms} is the root-mean-square amplitude and Δ is the offset frequency of the saturation pulse, and g^{SL} is the superLorentzian absorption lineshape describing saturation of macromolecular protons with their transverse relaxation time T_2^B (4). Now let us assume that the observed MTR_{obs} is obtained in the presence of RF inhomogeneity with an actual $B_1=cB_{1nom}$, where B_{1nom} is the nominal value corresponding to formal scanner settings, and c is the scaling coefficient, which can be independently measured using any B_1 mapping sequence. Correspondingly, actual values for the saturation rate and FA are $W^B=c^2W^B{}_{nom}$ and $\alpha=c\alpha_{nom}$. The goal of the correction procedure is to calculate a corrected value MTR_{cor}, which would correspond to nominal values $W^B{}_{nom}$ and α_{nom}. Applying Eq. [1] to calculate MTR_{obs} and MTR_{cor}, introducing the reverse rate constant (similar to the notation in Ref. (4)) $R=k(1-f)/f$, and assuming that $R_1/R\ll1$ (based on the literature (4,5)) and $f\mathrm{TR}^{-1}|\ln(\cos\alpha)|\ll R_1$ (holds well for small FA), the correction equation can be derived:

$$\mathrm{MTR}_{cor}=\frac{A(c)B(c)\mathrm{MTR}_{obs}}{1-(1-A(c)B(c))\mathrm{MTR}_{obs}}, \quad [2]$$

where $A(c)=\dfrac{R\mathrm{TR}+c^2t_mW^B_{nom}}{c^2(R\mathrm{TR}+t_mW^B_{nom})}$ and $B(c)=\dfrac{R_1\mathrm{TR}-\ln\cos(c\alpha_{nom})}{R_1\mathrm{TR}-\ln\cos(\alpha_{nom})}$

The B_1 dependence of MTR mainly arises from the saturation effect (term A) and, to a lesser extent, from the effect of excitation FA (term B). It is important to emphasize that the parameters R and T_2^B entering into the term A are characterized by a very small variability in brain tissues (4,5), and for practical neuriomaging applications the constant values R=30 s^{-1} and T_2^B=11 μs can be chosen. For small excitation FA, the term B slowly varies with R_1, and therefore, an approximately average R_1 value can be chosen for a group of tissues with close T_1. For the brain at 3T, R_1=1 s^{-1} was used in the proposed algorithm.

Methods ***Simulations:*** Dependences of MTR on B_1 were simulated using the transient full Bloch model with cross-relaxation and effective saturation of the bound pool described by the SuperLorentzian function (3). Iterative solution of differential equations was repeated until the pulsed steady state was achieved. The correction algorithm (Eq. [2]) was then applied to simulated MTR values. Simulations were performed for average data sets corresponding to white matter (WM) and gray matter (GM) (5) with the parameters of the experimental pulse sequence listed below.

Imaging and processing: Images were obtained from four healthy subjects on a 3T whole-body scanner (Philips Achieva) using a transmit-receive quadrature head coil. For whole-brain MTR mapping, scans with and without off-resonance saturation were acquired using a spoiled 3D GRE sequence with TR/TE = 43/2.3 ms, α_{nom} =10°, one signal average, and spatial resolution 1.5x1.5x3.0 mm (scan time 6 min 40 s). A single-lobe sinc saturation pulse with Gaussian apodization was applied at t_m=19 ms, Δ=2 kHz, and nominal effective FA 990° ($\omega_{1rms}/2\pi$=167.1 Hz). For B_1 mapping, the actual flip-angle imaging (AFI) sequence (6) was used with $\mathrm{TR}_1/\mathrm{TR}_2/\mathrm{TE}$ = 25/125/2.3 ms, α_{nom} = 60°, one signal average, and spatial resolution 3.0x4.5x6.0 mm (scan time 3 min). Uncorrected MTR maps were calculated from signal intensities with (S_{mt}) and without (S_{ref}) saturation as MTR= $100(S_{ref}-S_{mt})/S_{ref}$. Then, the correction algorithm given by Eq. [2] was applied with constants R=30 s^{-1}, T_2^B=11 μs (resulting in $W^B{}_{nom}$=35.85 s^{-1} at Δ=2 kHz), and R_1=1 s^{-1}. Extracranial tissues were removed using Brain Extraction Tool (BET) software (7). MTR histograms of the brain were calculated with the bin size of 0.5% and normalized to the total number of voxels.

Results ***Simulations:*** Simulations show that the correction algorithm effectively removes MTR dependence on B_1 (Fig. 1). While simultaneously applied with the standardized parameter set (i.e. R, T_2^B, and R_1) to WM and GM, the correction is uniform across a wide range of B_1 inhomogeneities with a very minor tissue-dependent bias (<1% across 50-140% c range).

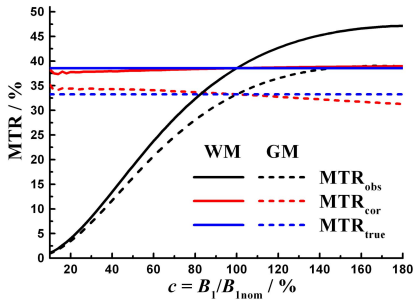

Fig. 1. Numerical simulations of MTR correction: MTR_{cor} plots are calculated from simulated MTR_{obs}. True value MTR_{true} corresponds to c=100%.

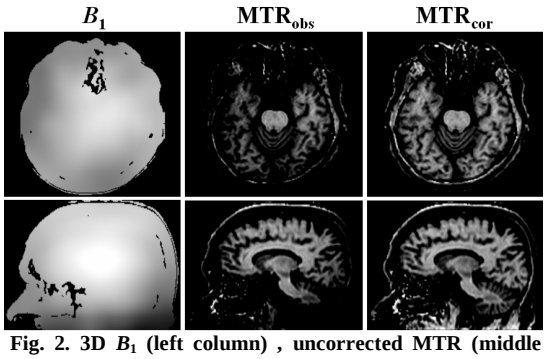

Fig. 2. 3D B_1 (left column) , uncorrected MTR (middle column), and corrected MTR (right column) maps of the human head in axial and sagittal planes. All MTR maps are presented with the same window settings.

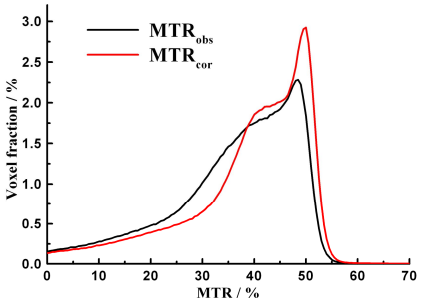

Fig. 3. Uncorrected (black) and corrected (red) whole-brain MTR histograms averaged for a group of 4 healthy subjects.

MTR imaging: AFI B_1 maps demonstrated strong RF inhomogeneity across the human brain (c range 55-110%, Fig. 2a). This non-uniformity translates into a marked variability of MTR values (Fig 2b). Considerable improvement of MTR uniformity was achieved after correction (Fig 2c). This is further exemplified by comparison between corrected and uncorrected MTR histograms (Fig 3). The correction procedure results in reducing the spread of MTR values and better separation of WM and GM peaks.

Conclusions The developed MTR correction algorithm is simple and highly accurate across a wide range of B_1 non-uniformities. Combination of this algorithm with the fast AFI B_1 mapping technique enables whole-brain MTR mapping and histogram analysis on high-field scanners for a variety of neuroimaging applications.

References **(1)** Ropele S, et al. *MRM* 2005;53:134. **(2)** Samson RS, et al. *MRI* 2006;24:255. **(3)** Yarnykh VL. *MRM* 2002;47:929. **(4)** Morrison C, Henkelman RM. *MRM* 1995;33:475. **(5)** Sled JG, et al. *MRM* 2004;51:299. **(6)** Yarnykh VL. *MRM* 2007,57:192. **(7)** Smith SM. *Hum Brain Mapp* 2002;17:143.