Fast two-point mapping of the bound pool fraction and cross-relaxation rate constant in the human brain

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Introduction: Quantitative imaging of fundamental parameters determining the magnetization transfer (MT) effect (1-4) provides a new source of information about pathological changes in the brain and offers an attractive alternative to traditional magnetization transfer ratio (MTR) measurements due to the capability of physically meaningful interpretation. Among these parameters, the bound pool fraction (*f*) and cross-relaxation rate constant (*k*) are of major interest due to their key role in the formation of the observed MT effect and high sensitivity to white matter organization (4). A common limitation of the existing methods (1-4) is the time-consuming measurements caused by the need in serial images used to reconstruct parametric maps by fit procedures. This study introduces an alternative method for direct algebraic calculation of the parametric *k* and *f* maps from two experimental measurements and compares this method to the previously reported fit-based technique (4).

Theory: Using the full matrix equation for the pulsed MT in the two-pool system (4) and applying the first-order approximation to exponential matrix terms (2), the equation for the signal acquired with the off-resonance MT-prepared spoiled gradient echo (MT-SPGR) sequence can be presented as:

$$S_{mt} \approx \frac{M_0(1-f)(A+R_1^F\tau W^B)\sin\alpha\exp(-\mathrm{TE}/T_2^*)}{A+(R_1^F+k)\tau W^B-(R_1^B+k(1-f)f^{-1}+\tau W^B)(\tau W^F-\mathrm{TR}^{-1}\ln\cos\alpha)}$$

where the indexes "F" and "B" refer to the free and bound pool, respectively; M_0 is the total equilibrium magnetization; $R_1^{F,B}$ are the longitudinal relaxation rates; $A=R_1^FR_1^B+R_1^Fk(1-f)/f+R_1^Bk$; $W^{F,B}$ are the effective saturation rates; α is the flip angle of the readout pulse; and $\tau=t_{mt}/\mathrm{TR}$ is the duty cycle of the MT saturation pulse with the duration t_{mt}. Off-resonance behavior of the signal is determined by the saturation rates, which depend on the lineshapes *g* of the corresponding pools: $W^{F,B}=\pi\omega_{1rms}^2 g^{F,B}(\Delta,T_2^{F,B})$, where ω_{1rms} is the root-mean-square amplitude, and Δ is the offset frequency of the saturation pulse. According to the common practice (5), the Lorentzian and superLorentzian shapes are assumed for the free and bound pool, respectively. Defining the quantity *Z*,

$$Z=\frac{t_{mt}(W^B-W^F)+\ln\cos\alpha}{(R_1\mathrm{TR}-\ln\cos\alpha)(S_{ref}-S_{mt})S_{mt}^{-1}-t_{mt}W^F}$$

with the use of a reference signal intensity (S_{ref}) measured for the same sequence parameters without MT saturation (to exclude unknown M_0) and an independently determined $R_1=1/T_1$, an approximately linear function of W^B with coefficients $1/k$ and $1/f$ can be derived:

$$Z\approx f^{-1}+k^{-1}t_{mt}\mathrm{TR}^{-1}W^B$$

The derivation is based on the assumptions that $R_1^B<<k/f$, $|\mathrm{TR}^{-1}\ln(\cos\alpha)|<<k/f$, and $R_1^F\approx R_1^B\approx R_1$. Parameters *f* and *k* can be calculated from two measurements of *Z* (Z_1 and Z_2) corresponding to two MT-weighted signal intensities (S_{mt1} and S_{mt2}) obtained at two values of the saturation rate $W^B_{1,2}$:

$$k\approx t_{mt}\mathrm{TR}^{-1}(W_1^B-W_2^B)/(Z_1-Z_2),\ f\approx(W_1^B-W_2^B)/(Z_2W_1^B-Z_1W_2^B)$$

Due to small variability of T_2^B in tissues, W^B can be used as an independent variable, and its values can be calculated for experimental ω_{1rms} and Δ with a uniform T_2^B =11 μs (4). If both measurements are taken sufficiently far from the resonance (Δ>2kHz), W^F is small and can be approximated as $W^F\approx(\omega_{1rms}/2\pi\Delta)^2R_1/0.055$ (4).

Methods: Whole-brain images were acquired on a 1.5 T MR scanner (GE Signa) with a transmit-receive head coil using the 3D MT-SPGR sequence. Four MT-weighted scans were acquired with TR/TE = 32/2.4 ms, α=10°, ω_{1rms}=1557 Hz (single-lobe-sinc MT pulse with t_{mt}=14 ms and effective flip angle 950°), and variable Δ = 3, 6, 9, and 12 kHz. A reference image was obtained with the same sequence parameters and without MT saturation. T_1 relaxometry was performed by the variable flip angle technique using the 3D SPGR sequence with TR/TE = 20/2.4 ms at α = 4, 10, 20, and 30°. All data were acquired with actual resolution of 1.4x2.3x2.8 mm and zero-interpolated before the Fourier transform to obtain an isotropic voxel size of 1.4 mm. The scan time was 3 min for MT-weighted scans and 2 min for variable flip angle scans. To compare the two-point reconstruction technique to the previously described non-linear least square fitting (NLSF) method (4), the same T_1 map and reference scan were used. NLSF reconstruction employed all MT-SPGR data, while for two-point reconstruction, the offset points with Δ=3 and 9 kHz were chosen. Data were obtained from five healthy volunteers (3 male, 2 female, age 25-49 years) and one cerebrovascular disease (CVD) patient (male, 75 year-old) with the history of stroke and right carotid artery occlusion. For all subjects, parametric histograms were calculated and normalized to the total number of voxels.

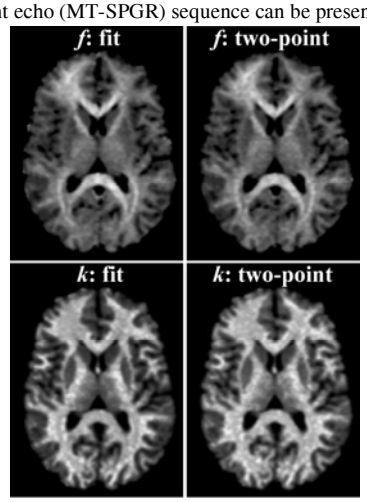

Fig. 1. Parametric *f* (top) and *k* (bottom) maps obtained from a healthy subject and reconstructed by NLSF (left) and two-point (right) methods.

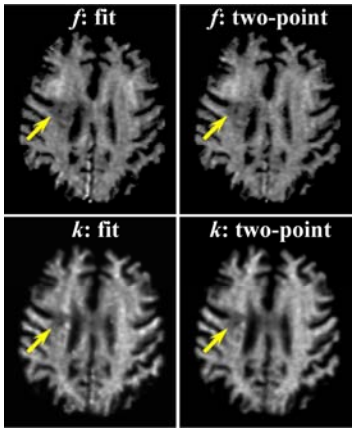

Fig. 2. Parametric *f* (top) and *k* (bottom) maps obtained from a CVD patient and reconstructed by NLSF (left) and two-point (right) methods. A post-infarct lesion in the right centrum semiovale (arrows) with an inhomogeneous decrease of *k* and *f* is visible on all maps.

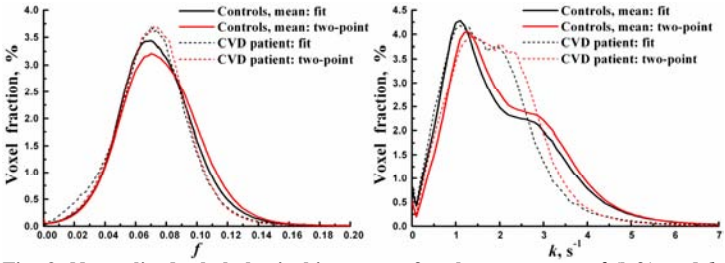

Fig. 3. Normalized whole-brain histograms for the parameters *f* (left) and *k* (right) corresponding to the maps reconstructed by NLSF (black) and two-point (red) methods. The group histograms for healthy subjects (solid lines) and individual histograms for a CVD patient (dashed lines) are presented.

Results: The tissue contrast and appearance of anatomical structures were very similar on fitted and reconstructed by the two-point technique maps (Figs 1, 2). It is noticeable that both fitted and two-point *f* maps reveal a specific type of contrast sensitive to fiber tracts and described in detail previously (4). Both *k* and *f* maps also reveal the sensitivity to pathological changes, as seen on the example images from the CVD patient with ischemic infarct (Fig. 2). Quantitative comparison between two reconstruction techniques is illustrated by parametric histograms in Fig. 3. The histograms from two-point reconstruction represent similar shapes and close quantitative values, although a minor bias is visible. The CVD patient's *k* histograms show the apparent change in shape as compared to healthy controls, which is consistent with systemic brain atrophy and an altered proportion between white and gray matter.

Conclusions: The two-point method represents a simple and time-efficient approach for quantitative imaging of cross-relaxation parameters in vivo. The method provides a reasonable trade-off between complicated multi-point fit techniques and simple but physically meaningless traditional MTR measurements. With an optimized protocol combining two-point MT acquisition, a reference scan, and fast T_1-relaxometric imaging, whole-brain data acquisition can be accomplished within 10-15 min, and thus can be easily implemented in a number of clinical protocols.

References: 1) Sled JG, Pike GB. *MRM* 2001;46:923. 2) Yarnykh VL. *MRM* 2002;47:929. 3) Ramani A, et al. *MRI* 2002;20:721. 4) Yarnykh VL, Yuan C. *NeuroImage* 2004;23:409. 5) Morrison C, Henkelman RM. *MRM* 1995;33:475.