Toward Rapid Macromolecular Pool Size Mapping via Selective Inversion Recovery

Richard D. Dortch[1,2], Ke Li[1,2], Daniel F. Gochberg[1,2], John C. Gore[1,2], and Seth A. Smith[1,2]

[1]*Radiology and Radiological Sciences, Vanderbilt University, Nashville, TN, United States,* [2]*Vanderbilt University Institute of Imaging Science, Vanderbilt University, Nashville, TN, United States*

Target Audience: 1) imaging scientists interested in optimizing quantitative imaging methods and 2) the White Matter Study Group of the ISMRM

Purpose: To optimize the selective inversion recovery (SIR) quantitative magnetization transfer (qMT) imaging sequence for mapping of the macromolecular-to-free proton pool size ratio ($PSR = M_{0m}/M_{0f}$). Previous work has demonstrated that *PSR* in white matter is related to myelin content [1] and can be reliably quantified in humans using the SIR approach [2,3]. Despite this promise, the time required to acquire SIR data (and qMT data in general) can be prohibitively long for clinical applications, especially applications that require high resolution and/or large anatomical coverage. SIR scan times can be reduced with optimized sampling schemes [4]. Alternatively, certain model parameters in the analysis may be fixed (to reduce the number of required samples), a method that has been applied to reduce pulse saturation qMT imaging times [5]. Here, we apply a similar approach to SIR where we fix the rate of MT exchange and choose a sampling strategy that minimizes the bias in the estimated *PSR*.

Theory: The observed signal following an inversion pulse recovers as a biexponential function when MT is present [6]; therefore, two-pool MT model parameters may be estimated by sampling this recovery at multiple inversion times (TI). Using the standard SIR analysis [4], this results in a model with five independent parameters: 1) the size of the free pool (M_{0f}), 2) the size of the macromolecular pool (M_{0m}), 3) the rate of MT from the free to macromolecular pool ($k_{mf} = k_{fm}/PSR$), 4) the R_1 of the free pool ($R_{1f} = R_{1m}$), and 5) the inversion efficiency of the free pool (S_f). The saturation effect of the inversion pulse on the macromolecular pool (S_m) must also be accounted for, but can be numerically estimated prior to fitting [4].

Methods: Simulations: To find TI values where the SIR signal (M_{zf}) is insensitive to k_{mf}, the percent sensitivity (S_p) of M_{zf} to each model parameter was numerically estimated over a range of TI values from: $S_{p,i}(TI) = (\partial M_{zf}/\partial p_i)*(p_i/M_{0f})*100\%$, where $\mathbf{p} = [M_{0m}\ M_{0f}\ k_{mf}\ R_{1f}\ S_f]^T$ is a vector of parameter values. Data Acquisition: Eight healthy volunteers (27–37 y.o.) and one relapsing-remitting multiple sclerosis patient (RRMS, 52 y.o.) were imaged using a 3.0-T Philips Achieva MR scanner. A quadrature body coil and a 16-channel neurovascular coil were used for signal excitation and reception, respectively. A 5-mm axial slice was selected in each volunteer and SIR data were collected with: TI = 0.01–2 s (15 log-spaced values) and TI = 10 s, predelay (TD) = 2.5 s, TSE factor = 24, echo spacing = 5.9 ms, TE = 74 ms, SENSE factor = 2, in-plane resolution = 2 × 2 mm^2, and two acquistions. Data Analysis: Two analyses were performed: 1) a 16-point fit using the standard analysis [4] and 2) a 4-point fit with k_{mf} = 13 s^{-1} (mean value from the 16-point). For the 4-point analysis, the subset of four TI values was chosen from the 16-point data to maximize the signal-to-noise (SNR) of the estimated *PSR* values (from Cramér-Rao lower bound (CRLB) theory [4]), while minimizing the sensitivity of the signal to k_{mf} (from sensitivity analysis). ROIs were defined as described in [2] and a paired *t*-test was performed to test for differences between the analyses.

Results and Discussion: Numerical: Fig. 1 shows the percent sensitivity of the SIR signal to each MT model parameter as a function of TI. Note that the SIR signal is sensitive to k_{mf} (black line) over a limited range of TI values (gray box from TI = 11–300 ms). Fortuitously, the SIR signal exhibits sensitivity to the other MT parameters [see M_{0m} (red line)] outside of the regime; therefore, it may be possible to fix k_{mf} without biasing the other parameters by choosing TI values that are outside of the gray box. Using this approach, the optimal subset of four TI values (from the 16 values listed in *Data Acquisition*) was found to be TI = 0.01, 0.301, 1.37, and 10 s. CRLB theory predicts only a small decrease ($\approx$7%) in the SNR of *PSR* estimates from this 4-point analysis relative to the 16-point analysis. Experimental: Fig. 2 shows parameter maps generated from each analysis method in a representative healthy control and an RRMS patient. In both cases, unbiased estimates of the qMT parameters can be obtained from the 4-point method at a similar SNR to the 16-point method. This is consistent with the results from the paired *t*-test in healthy controls, which found no significant difference between the analyses (p = 0.93 for *PSR*, p = 0.99 for R_{1f}). In addition, *PSR* estimates from the 4-point method were less sensitive to partial-volume interference by CSF, which does not exhibit an MT effect, than the 16-point method (see *PSR* map around the ventricles).

Conclusions: By fixing k_{mf}, which is generally not sensitive to pathology [7], one can significantly reduce SIR scan times (with a negligible SNR penalty). Our previous work at 7 T [3] has indicated that whole-brain qMT can be performed in approximately 20 minutes using the full SIR technique; thus, the optimized technique herein may allow for whole-brain SIR imaging in clinically feasible times. For small structures outside of the brain (e.g., peripheral nerve), this may also be of significant value as the time required for high-resolution SIR imaging is currently prohibitive. This may require additional gains in efficiency, which are likely to be achieved by optimizing over the entire TI–TD space [4].

References: [1] Odrobina. *NMR Biomed* **18**: 277 (2005). [2] Dortch. *MRM* **66**:1346 (2011). [3] Dortch. *Neuroimage* **64**:640 (2012). [4] Li. *MRM* **64**: 491 (2010). [5] Yarnykh. *MRM* **68**: 166 (2012). [6] Edzes. *Nature* **254**: 521 (1977). [7] Smith. *MRM* **61**: 22 (2009). **Acknowledgements:** K25 EB013659-01 for funding.

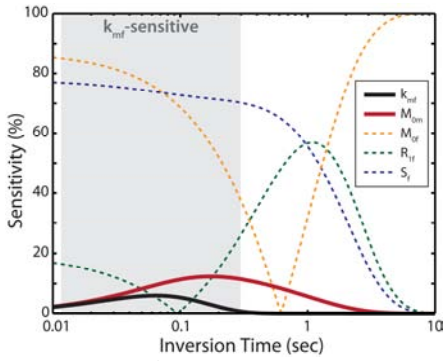

Fig. 1. Sensitivity of the SIR signal to the model parameters as a function of TI. The gray box denotes the k_{mf}-sensitive region. Parameters used [2]: M_{0m} = 0.12, M_{0f} = 1.00, k_{mf} = 13 s^{-1}, $R_{1f} = R_{1m}$ = 1 s^{-1}, S_f = –0.95, S_m = 0.83, and TD = 2.5 s.

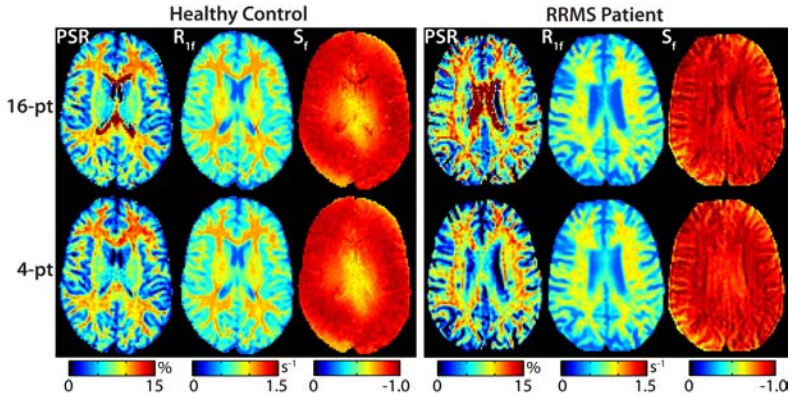

Fig. 2. Representative qMT parameter maps (*PSR*, R_{1f}, and S_f) for the standard 16-point analysis (top) and the 4-point analysis with k_{mf} fixed at 13 s^{-1} (bottom). Shown are results from a healthy control (left) and an RRMS patient (right).