Quantitative Magnetization Transfer Imaging of Human Sciatic Nerve at 3 Tesla

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Target Audience: imaging scientists interested in quantitative myelin imaging methods and the White Matter Study Group of the ISMRM

Purpose: To develop a quantitative magnetization transfer (qMT) imaging sequence for mapping of the macromolecular-to-free proton pool size ratio (*PSR*) in human sciatic nerve *in vivo*. Previous work [1] has demonstrated that *PSR* is related to myelin content in white matter, yet no studies have reported *PSR* mapping in peripheral nerve *in vivo*. This can be attributed to the challenges of nerve imaging, including the influence of fat and the need for higher resolution. Proximal nerves are inaccessible via current techniques (e.g., electrophysiology); thus, this study focuses on developing qMT approaches for the currently inaccessible sciatic nerves of healthy controls as a baseline for future studies in neuropathy patients.

Methods: Data Acquisition: Five healthy volunteers (24-37 y.o), Gd-DTPA phantoms (0.05-0.5 mM), and bovine serum albumin (BSA: 5-15%) phantoms were imaged at 3.0 T (Philips Achieva). A two-channel body coil and a six-channel cardiac coil were used for excitation and reception. Axial volumes were acquired from the knee to the middle of the thigh (192×192×96 mm^3). For qMT imaging, an MT-prepared (20-ms sinc-Gauss pulse), segmented EPI sequence (5 lines/shot) with a water-selective excitation pulse (1331, 6°) and flow-compensation was employed. Data were collected at four MT offset frequencies (1-16 kHz) using three MT pulse angles (350-850° and 0° for normalization), resulting in 16 volumes. Additional parameters included: acquired (reconstructed) resolution = 1×1×6 mm^3 (0.75×0.75×3 mm^3), TR/TE = 55/12 ms, SENSE factor = 1.5, and scan time ≈ 9 min. The qMT model requires independent T_1, RF transmit (B_1^+), and main magnetic field (ΔB_0) estimates. T_1 was estimated using both multiple flip angle (MFA: qMT sequence, flip angle/TR = 6–30°/25 ms) and inversion recovery approaches (IR: SPGR readout, TI = 0.1–5 sec). The MFA approach yields rapid, high-resolution T_1 maps, but is susceptible to bias [2]; therefore, the phantom IR data served to calibrate the MFA data. B_1^+ was measured using a Bloch-Siegert method [3]. ΔB_0 was measured using a dual-gradient echo method [4] with fat and water protons in phase. Phantom Data: T_1 was estimated in the Gd-DTPA phantoms from the MFA and IR data [5]. Previous work [2] has demonstrated a linear relationship between MFA-derived and true T_1 values; therefore, the MFA- and IR-derived T_1 values were linearly regressed and the resulting slope and intercept were used to correct MFA-derived values. To test this method, the correction factors were applied in BSA phantoms (and a volunteer) and qMT analysis was performed. Human Data: All data were rigidly co-registered via FSL [6]. ROIs were defined in the reference qMT volume for the sciatic nerve and manually adjusted in other volumes to account for non-rigid motion. B_1^+ and ΔB_0 maps were estimated and smoothed with a 9 × 9 × 9 mm^3 median filter. T_1 was measured from MFA data. For the qMT analysis, median B_1^+, ΔB_0, and T_1 values across all slices were used to minimize error propagation. In addition, mean ROI qMT values were binned into four groups of six contiguous slices, and mean group values were fit to a two-pool MT model [7], yielding estimates of *PSR*, the MT rate (k_{mf}), the R_1 of the free pool (R_{1f}), and T_2 (T_{2f}, T_{2m}).

Results and Discussion: Phantom Data: Fig. 1 shows IR- versus MFA-derived T_1 measurements in Gd-DTPA phantoms along with the linear fit. Note that the values in BSA and sciatic nerve also fall close to this line, indicating that the Gd-DTPA-derived correction factors are applicable in tissue. To further validate our methods, *PSR*/(*PSR*+1)*100% values were linearly regressed against BSA concentration; and the resulting slope (0.77) and offset (<0.01%) values were similar to published values [8]. Human Data: The mean (± SD) SNR across individuals was 100 ± 30, where SNR is defined as the 1/SD of the qMT residuals. Monte Carlo simulations indicate that this is sufficient to fit *PSR* values with an uncertainty of ≈6%. Fig. 2 shows sample data, while Table 1 summarizes mean parameters across all slices and subjects. *PSR*, k_{mf}, and T_{2m} were similar to values reported in white matter [7], while R_{1f} and T_{2f} were consistent with reported relaxation measurements in median nerve [9]. Also, *PSR* variability was ≈3× the simulated value, implying that a large portion of the observed variability is related to inter-subject differences in *PSR*. Note that while structurally similar to white matter, peripheral nerve contains larger, less densely packed axons and an abundance of collagen, both of which affect *PSR*.

Conclusions: qMT parameters can be robustly estimated in human sciatic nerve *in vivo* using the methods outlined herein. Note that ΔB_0 mapping may be eliminated in the future to reduce scan times, as ΔB_0 values were consistently close to zero. Additionally, previous work [10] has shown that the product $R_{1f}T_{2f}$ and the qMT parameters k_{mf} and T_{2f} and relatively constant in normal and diseased white matter. If this holds in sciatic nerve, scan times may be further reduced by eliminating the need for T_1 measurements and/or reducing the required number of points for the qMT analysis [10]. Future work includes: *i*) determining the effect of neuropathy on qMT parameters and *ii*) optimizing qMT acquisitions based upon these findings.

References: [1] Schmierer. *JMRI* **26**:41 (2007). [2] Preibisch *MRM* **61**:125 (2009). [3] Jankiewicz. *JMR* **226**:79 (2013). [4] Skinner. *MRM* **37**:628 (1997). [5] Dortch. *Quantitative MRI in Cancer*: 53 (2011). [6] Jenkinson. *Neuroimage* **17**:825 (2002). [7] Underhill *Neuroimage* **47**:1568 (2009). [8] Mossahebi. *MRM* (Available online). [9] Gamborata *JMRI* **29**:982 (2009). [10] Yarnykh. *MRM* **68**:166 (2012). **Acknowledgements:** Will Grissom for input on B_1^+ mapping and K25 EB013659 for funding.

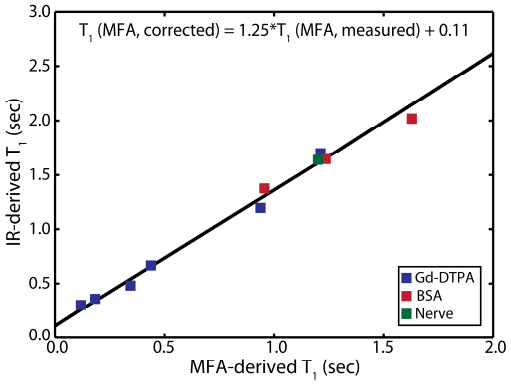

Fig. 1. IR- versus MFA-derived T_1 values in Gd-DTPA phantoms, BSA phantoms, and sciatic nerve.

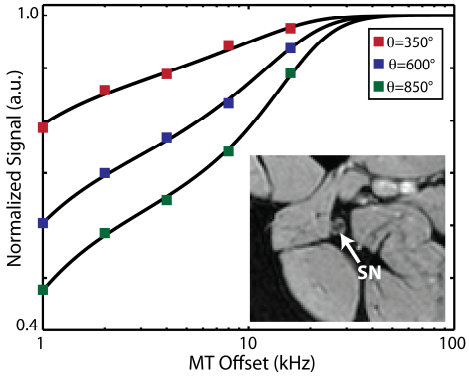

Fig. 2. Sample zoomed qMT image (SN = sciatic nerve) along with group mean qMT data and fit.

Table I. Mean (± SD) fit parameters.

Parameter	Mean ± SD
PSR (%)	10.8 ± 1.9
k_{mf} (s^{-1})	12.8 ± 4.7
R_{1f} (s^{-1})	0.61 ± 0.06
T_{2f} (ms)	30.4 ± 4.3
T_{2m} (μs)	7.3 ± 0.4
B_1^+ (actual/nominal)	1.04 ± 0.09
ΔB_0 (Hz)	5.6 ± 3.4