Quantitative Magnetization Transfer Imaging of Human Cervical Spinal Cord at 3T

R. D. Dortch[1,2], E. B. Welch[2,3], J. C. Gore[1,2], and S. A. Smith[1,2]
[1]Department of Radiology and Radiological Sciences, Vanderbilt University, Nashville, TN, United States, [2]Vanderbilt University Institute of Imaging Science, Vanderbilt University, Nashville, TN, United States, [3]MR Clinical Science, Philips Healthcare, Cleveland, OH, United States

Introduction: The goal of this study was to determine the feasibility of performing quantitative magnetization transfer (qMT) at high resolution in the spinal cord on clinical 3T systems. While magnetization transfer (MT) imaging has been used to assess brain tissue microstructure, similar studies in the human spinal cord have been limited. This can largely be attributed to the difficulties associated with imaging the spinal cord, which include: *i*) high resolution demands (cord diameter ≈ 1.5 cm), *ii*) motion (CSF pulsation and respiration), and *iii*) susceptibility gradients (bone/tissue interfaces). Despite these difficulties, MT has been characterized in the spinal cord via the magnetization transfer ratio normalized to the CSF (MTCSF), a measure that has been shown to be sensitive to myelination changes in patients with adrenomyeloneuropathy (AMN) [1,2]. Unfortunately, MTCSF is also sensitive to changes in tissue relaxation times and flow effects in CSF, making it difficult to discriminate between myelin and inflammation effects. To alleviate this sensitivity, quantitative MT (qMT) approaches have been proposed. Previous work at 1.5T [3] has indicated that the ratio of the macromolecular to free water pool sizes, or pool size ratio (*PSR*), may be sensitive to myelination changes in the spinal cord. Given the resolution demands of imaging the spinal cord, qMT studies of the spinal cord would presumably benefit from the increased SNR at 3T; however, such studies are hampered by the fact that SAR scales according the field strength squared. To address these issues, we have developed a protocol for high resolution qMT imaging of the cervical spinal cord at 3T and here we report data acquired in healthy subjects.

Methods: Four healthy volunteers were imaged using a 3.0T Achieva whole body MR scanner (Philips Healthcare, Best, The Netherlands). A quadrature body coil was used for excitation and a 16-channel SENSE neurovascular coil (Invivo Inc., Gainesville, FL) was used for signal reception. For each volunteer, a transverse volume between C2 and C4 was selected from survey images. Quantitative MT data were acquired in this volume using the 3D MT-prepared spoiled gradient echo sequence originally proposed by Sled and Pike [4]. For MT-preparation, a single-lobe sinc pulse with Gaussian apodization was applied with a duration = 24 ms, nominal flip angles (θ_{MT}) = 700° and 1000°, and offset frequencies (Δ) = 1, 2, 4, 8, 96 kHz, resulting in 10 images of different MT-weighting. Additional imaging parameters included: TR/TE=98/5.8 ms, excitation flip angle = 15° (Proset 1-3-3-1 pulse to suppress fat), SENSE factor = 2, FOV = 150 × 150 × 30 mm^3, acquisition resolution = 1.5 × 1.5 × 3 mm^3, reconstructed resolution = 0.47 × 0.47 × 3 mm^3, and number of acquisitions averaged = 2. B_1 was measured in the same volume using the actual flip angle imaging (AFI) method [5] with TR_1/TR_2 = 100/30 ms and excitation flip angle = 60°. ΔB_0 was also measured from gradient echo phase images acquired with a ΔTE = 10 ms [6]. Total scan time to acquire qMT and field map data was ≈ 11.5 minutes.

Transverse slices were co-registered by determining the 2D affine transformation that minimized the normalized mutual information between slices [7]. Prior to this, each transverse slice was cropped to a 47 × 47 mm^2 window centered about the spinal cord and multiplied by a Gaussian kernel (σ = 23.5 mm). Once co-registered, ROIs were defined for the dorsal column (dc), lateral column (lc), and grey matter (gm) within one slice at the level of C3. Normalized (to Δ = 96 kHz data) mean ROI signal intensities were then fitted [8] to a two-pool model—macromolecular (*m*) and free water proton (*f*) pools—using the mathematical formalism in Ref. [9]. The fits yielded the *PSR* and the exchange rate from the free to macromolecular pool k_{mf}. Previously reported T_1s of white (1 s^{-1}) and grey matter (0.7 s^{-1}) structures in the brain at 3T [9] were used to constrain these fits. As recently suggested [9], it was assumed that $T_2^f R_1^f = 0.024$ and T_2^m = 11 μs. The mean field values (B_1 and ΔB_0) across the cord were used to correct for errors in the fits associated with field inhomogeneities.

Results and Discussion: Sample MT-weighted images as a function of MT pulse frequency offset and power are given in Fig. 1. Note the contrast between white and grey matter, which is especially evident at higher offset frequencies. Sample experimental data from the dorsal column and the corresponding model fit are shown in Fig. 2. Generally speaking, the experimental data fit the model well—the average residual deviation per point was 1.2% for all fits. The qMT parameters for each ROI were tabulated, the results of which are given in Table I. *PSR* values were found to be higher in white matter relative to grey matter and were in good agreement with previously reported values from human cervical spinal cord at 1.5T [3]. Exchange rates (k_{mf}) also differed between white and grey matter, but should be interpreted with caution as they were substantially slower than previously reported values in cervical spinal cord at 1.5T (≈50 s^{-1}) [3]. These differences are presumably a product of the different acquisition parameters used—the previous study acquired data at only one MT pulse power and did not correct for field inhomogeneities—as well as the different model assumptions made in each study. Herein, we chose to constrain the model fits according to previous data in human brain at 3T [9]. Consequentially, our fitted k_{mf} values were closer to previously reported exchange rates in brain [9]. Additional work is needed to ascertain the consequence of these assumptions on the fitted parameters in the spinal cord.

Preliminary results suggest that *PSR* can be robustly quantified in healthy cervical spinal cord at 3T. This is especially promising as *PSR* has been shown to be reduced in the spinal cord of patients with AMN [3], which is thought to reflect a reduction in myelin content in these patients. Future works include: *i*) optimizing acquisition parameters (MT pulse offset frequencies and powers), *ii*) comparing the approach used herein to other qMT approaches, and *iii*) applying qMT imaging of cervical spinal cord to patients with multiple sclerosis.

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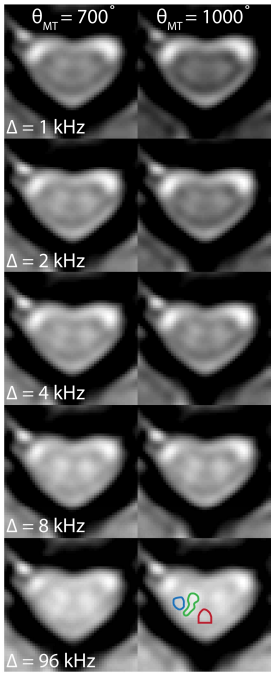

FIG. 1. Sample MT-weighted data. ROIs: dc– red, lc–blue, gm–green.

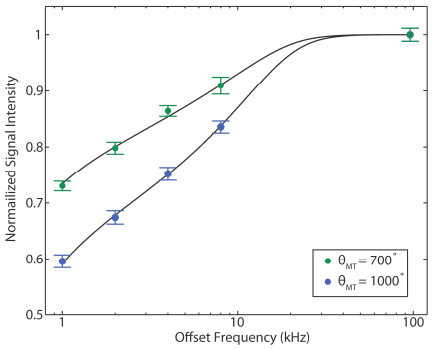

FIG. 2. Sample data and two-pool model fit for the dorsal column. The errorbars represent the SD of the signal intensity within the ROI.

TABLE I. Mean ± SD fitted qMT parameters across volunteers for the ROIs defined in Fig 1.

ROI	*PSR* (%)	k_{mf} (s^{-1})
dc	18.4 ± 2.8	7.5 ± 2.5
lc	17.4 ± 2.5	8.1 ± 2.4
gm	9.8 ± 1.0	14.9 ± 3.3