Rapid Three-Dimensional Myelin Water Fraction Imaging of the Cervical Spinal Cord

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INTRODUCTION: The ability to non-invasively and quantitatively assess myelin content in the spinal cord would improve our understanding of a variety of spinal cord-related conditions, as well as enhance our ability to differentially diagnose, treat and monitor them. Currently, little is known about the pathology of myelin in spinal cord disease due to the technical challenges of measuring myelin noninvasively. Multi-component relaxometry can be used to estimate the myelin water fraction (MWF)[1], which has been shown to relate to myelin content[2]. However, imaging a single slice takes between 15 and 25 minutes using conventional multiple-echo spin-echo based techniques[3,4] (though recent advancements have increased the coverage to 4 or 5 useable 5-mm axial slices[5]). Moreover, these spin-echo methods are sensitive to the in-flow affects of cerebral spinal fluid and off-resonance conditions associated with the multiple air-tissue and bone-tissue interfaces and respiratory motion.

mcDESPOT (multi-component Driven Equilibrium Single Pulse Observation of T_1 and T_2)[6] offers a promising alternative to conventional spin-echo multi-component relaxation imaging techniques. The goal of this study was to assess the efficacy of mcDESPOT for obtaining high spatial resolution spinal cord MWF data covering the entire cervical spinal cord. Further, we characterized the relaxation parameters, and their reproducibility, along the cervical spine.

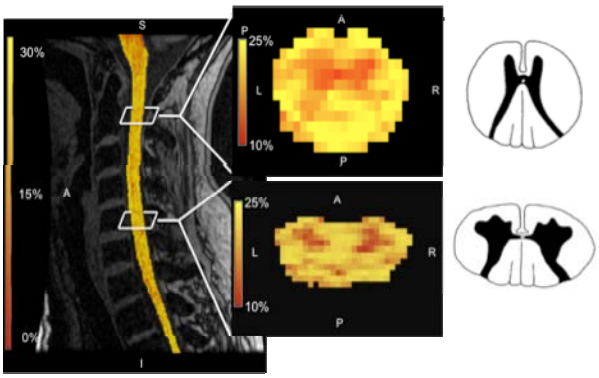

Figure 1: Sagittal myelin water fraction map of the spinal cord with axial cross-sections at C2 and C5 showing the central grey matter butterfly.

METHODS: Sagittal mcDESPOT data were acquired of 7 healthy individuals at 1.5T using an 8-channel torso-array RF coil with the following scan parameters: FOV = 12 x 12 x 18 cm, resolution = 1 x 1 x 1.5 mm; SPGR: TE / TR = 2.2 / 5.0 ms, α = {2, 4, 6, 8, 10, 12, 14, 16, 18, 20}°, BW = ± 25 kHz; SSFP: TE / TR = 1.7 / 3.5 ms, α = {7, 14, 21, 28, 35, 42, 49, 56, 63, 70}°, BW = ± 62.5 kHz, acquired with phase-cycling increments of ϕ = 0° and 180° (for correction of off-resonance effects[7]); IR-SPGR data: TE / TR = 2.1 / 4.6 ms, TI = 350, 450 ms, α = 5°, BW = ± 25 kHz (for correction of flip angle variations[8], acquired with half the spatial resolution in both phase-encode directions to reduce acquisition time). Total acquisition time for each SPGR / SSFP flip angle image was 59 s / 39 s, for a total exam time of approximately 26 minutes. Five of the subjects underwent a repeat scan on a separate occasion.

Data for each volunteer were linearly co-registered to account for intra-scan motion[9], non-spinal cord pixels were masked using a semi-automated fuzzy connection approach[10], and the MWF, residence time, and T_1 and T_2 of the intra/extracellular (free) water and myelin water were calculated voxel-wise using mcDESPOT analysis[6]. The spinal cord pixels were manually segmented by vertebral level for the cervical spine (C1-C7) and upper thoracic spine (T1). The coefficient of variation (CV = standard deviation / mean) was calculated for each variable in cervical spine for repeated scans.

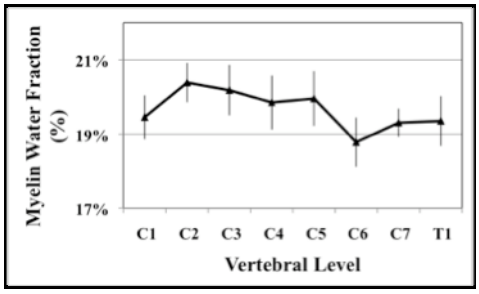

Figure 2: Average myelin water fraction values by vertebral level. Error bars represent standard error.

RESULTS and DISCUSSION: A representative MWF map for one sagittal slice overlaid on an anatomical SPGR image (α=6°) is shown in Figure 1. Axial cross-sections through the C2 and C5 levels show reduced MWF values where the grey matter "butterfly" is expected.

The average MWF along the length of the imaged spine is shown in Figure 2. The lower values in the lower cervical spine are consistent with the reduced proportion of white matter in the cervical enlargement[11].

Average relaxation parameter values in cervical spine are given in Table 1. The MWF value of 19.8% is similar to, though slightly lower than, past measurements (ranging from 21.8 to 26.4%[3,4]). However, whilst our measurements encompassed the entire cervical spinal cord, prior literature values are derived from a single imaging slice likely containing a smaller proportion of grey matter, and sensitive to intra-acquisition through-plane motion and differential partial volume effects.

	Average (se)	CV
Myelin water fraction (%)	**19.8% (0.6%)**	**0.03**
T_1 of free water (ms)	**970 (20)**	**0.05**
T_2 of free water (ms)	**88 (2)**	**0.08**
T_1 of myelin water (ms)	**392 (7)**	**0.06**
T_2 of myelin water (ms)	**7.2 (0.3)**	**0.03**
Myelin residence time (ms)	**118 (1)**	**0.06**

Table 1: Average relaxation parameter values across 7 volunteers, with standard error in parentheses, and average coefficients of variation (CV) for the 5 subjects who underwent 2 scans.

The MWF and myelin residence times obtained in the cord were both higher than measured in brain white matter[6], reflecting the greater myelin thickness in the spinal cord[12].

The reproducibility of the mcDESPOT measures was also examined (Table 1 gives the average CV for repeated scan measures), with an average CV for MWF of 3%. In contrast, Wu et al[3] reported an average MWF CV of 7%. The superior reproducibility of mcDESPOT to spin-echo based methods could, again, be related to its lower sensitivity to intra-acquisition motion, partial volume effects, and main magnetic field inhomogeneities.

CONCLUSIONS: Our results demonstrate the ability to reliably acquire high quality, high spatial resolution multi-component relaxation data in the spinal cord using the mcDESPOT method. Compared with alternatives, mcDESPOT provides far greater volumetric coverage per unit scan time, which is particularly important in spinal imaging applications as the cord does not lie in a flat plane. Additional information such as the residence time and multi-component T_1 values provided by mcDESPOT analysis may also be of value in characterizing myelin thickness and pathology.

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