Quantification of Myelin Water in Human Cervical Spinal Cord in vivo

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INTRODUCTION

The cervical spinal cord is a common site of pathology in multiple sclerosis (MS) and lesions in this location are an important source of disability. Such lesions might be amenable to novel therapies aimed at myelin repair if the axonal substrate remains intact. Success will critically depend on myelin-specific, *in vivo* imaging techniques to guide patient selection and track therapeutic results. Measurement of T_2 distributions (specifically, the fast T_2 component) is thought to allow quantitation of the intramyelinic water compartment and this approach has been used in the brain (1-2). In spinal cord imaging, CSF related artifacts become essential. In this work, an optimized inversion-recovery (IR), multiple spin-echo (ME) pulse sequence was developed to quantify the myelin water in human cervical spinal cord. Our preliminary results show promising consistency.

MATERIALS AND METHODS

An optimized IR, multiple spin-echo pulse sequence with descending, alternating crushers and composite 180° refocusing pulses (2-3) was used to collect 32 echoes at increasing TEs. For reproducibility testing, five normal volunteers underwent a total of 8 sagittal and 5 axial single-slice scans. A whole-body coil was used for radio frequency transmission, and a single-element posterior cervical spine coil for signal reception. Imaging parameters were TI = 1500 ms, TR = 3000 ms, slice thickness = 4 mm (sagittal) / 5 mm (axial), echo spacing = 7.2 ms, 128x128 acquisition matrix, and two averages to improve the SNR. All data were collected on a 1.5T GE Signa system (General Electric Medical Systems, Milwaukee, WI). T_2 distributions were calculated voxel-by-voxel from the decay curves by using the nonnegative least-squares (NNLS) algorithm (1,4). Myelin Water Fraction (MWF) was defined as $MWF = S_s/(S_s+S_m)$, where S_s, and S_m are the signal amplitudes with short (10–50ms), and medium (50–150ms) T_2 times, respectively. Since most signals from the CSF have been suppressed by the IR pulse, the long T_2 component is not considered here. Mean Myelin Water Fraction (*MMWF*) is estimated by taking the average of *MWF* over the voxels that have a short T_2 component ($S_s \neq 0$).

Six normal volunteers and four MS patients with visible cord lesions then underwent a series of comprehensive MR studies including magnetization transfer (MT), diffusion tensor (DTI) and myelin water imaging. An interleaved 3D MT sequence was used to reduce motion bias (5). A PROPELLER fast spin-echo (FSE) pulse sequence was used for DTI (6).

RESULTS AND DISCUSSION

Fig. 1 shows a representative *in vivo* T_2 decay curve (a) and its T_2 distribution (b) in the spinal cord of a normal volunteer. The measured decay curve is reasonably good although there is some noise fluctuation during the later echoes. Fig. 1c shows a first-echo image with a region of interest (ROI) obtained by thresholding. The IR pulse successfully suppressed CSF related artifacts. Fig. 2a is a scatter plot showing the results of the reproducibility study including multiple subjects and scans (sagittal and axial plane). The results were very consistent both across subjects and within subjects across different days. The mean T_2 components through all experiments were 19.3 ± 3.2 ms for the short T_2 and 88.9 ± 14.4 ms for the medium T_2. The mean myelin water fraction (*MMWF*) through all experiments was 26.4% ± 2%. The coefficient of variation as a measure of day-to-day reproducibility for the subjects (control 1, 2, and 3) who have repeated scans on different days was 7%, 2.6%, and 10%, respectively. There was no significant difference between sagittal and axial plane measurements.

Figs. 2b and 2c show the correlation of MWF with MTR and FA, respectively. The correlation coefficients over all subjects (including the controls and the MS patients) are 0.64 (p=0.048) for MTR and 0.88 (p=0.001) for FA, respectively. However, MTR was not found to correlate significantly with MWF within subject groups (e.g., for either controls or MS patients only), while FA remained correlated with MWF even within groups.

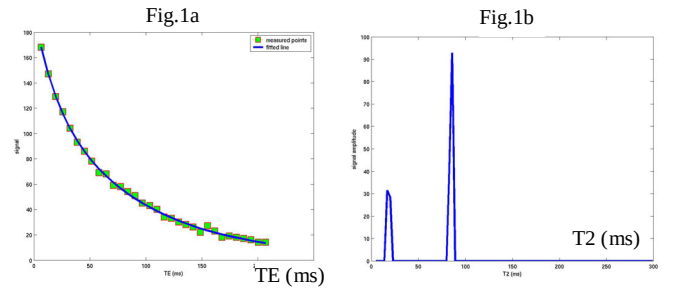

Figure 1. a: Representative measured (squares) and fitted (line) *in vivo* T_2 decay curves. b: corresponding T_2 distribution in the spinal cord of a normal volunteer. c: first echo image with ROI obtained by thresholding.

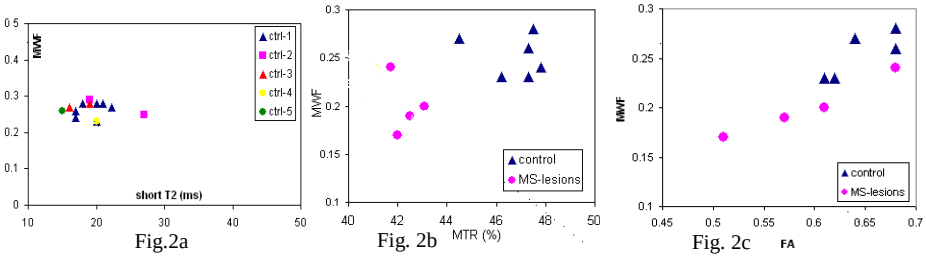

Fig.2a Fig. 2b Fig. 2c

Figure 2.a: Scatter plot showing good inter- and intra-subject reproducibility. Different symbols represent different subjects. b and c: scatter plots showing significantly different MWF between controls and MS patients. Both MTR and FA are correlated with MWF over all subjects but only FA remains correlated with MWF even within groups.

CONCLUSIONS

Our preliminary results demonstrate the feasibility and reproducibility of myelin water quantitation in the cervical spinal cord *in vivo*. The difference of the MWF between the control group and the MS patients with visible cord lesions is significant at p=0.011. This technique may be useful in guiding novel therapies aimed at myelin repair. The comprehensive MR studies show good correlation of MWF with both MTR and FA over all subjects, but only with FA within subject groups. Study with more subjects is ongoing.

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