Myelin Water Imaging with MRI at 3.0T in the Healthy Human Spinal Cord: Reproducibility and Changes with Age

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Introduction

Multi-echo T_2 relaxation measurements offer a non-invasive technique to investigate myelin content *in vivo* based on the presence of a short T_2 pool of water trapped between myelin's bilayers, called the myelin water fraction[1,2] (MWF), and have been applied to the study of human brain and spinal cord (SC) pathologies[3,4]. The advancement of clinical MRI scanners to 3.0T, combined with the development of a 3D multi-echo acquisition sequence, has led to improvements in both spatial resolution, scan coverage, and signal to noise ratio. The purpose of the present study was to apply a 3D multi-echo sequence to the lower cervical spine region for the measurement of MWF, to test reproducibility of the measurement, and to explore whether the resulting MWFs exhibit a trend with age.

Methods

Subjects: 31 healthy volunteers (12 male, 19 female, mean age 48y, range 21-75) were recruited in accordance with the local ethics review board. Subjects were recruited and into two categories, a group under 30 years of age and a group over 50 years of age.

MR Experiment: Subjects were scanned on a 3.0T MRI system (Philips Healthcare, Best, The Netherlands) with a phased array spine coil using only the first four channels. Multi-echo T_2 relaxation was performed using a 3D 32 echo sequence consisting of a 90° slice selective pulse followed by 32 slab selective 180° pulses (1st echo at 10ms, echo spacing of 10ms, TR=1300ms, six 5mm thick axial slices perpendicular to the spinal cord from levels C4 to C6, 256×128 matrix, FOV 180mm×135mm, single acquisition)[5]. Seven subjects (all over 50y) were rescanned one week later to assess reproducibility.

Data Analysis: One or two slices from each scan were excluded due to phase wrap artifact in the image plane that overlapped with the spinal cord signal, while data from one male subject could not be used due to phase-wrap artifact in all slices. For each pixel, the 32-echo decay curve was decomposed into an unspecified number of exponentials using a regularized non-negative least squares (NNLS) algorithm with 120 input relaxation times spaced logarithmically from 15ms to 2s[1,2]. The MWF was defined as the fraction of the T_2 signal between 15 – 35ms relative to the total T_2 signal, and a myelin map was produced by displaying the MWF for each pixel in the spinal cord. For each slice, ROIs were drawn well within the dorsal and right/left lateral column white matter on myelin maps for the under 30 years age group, while ROIs were drawn on registered T_2 weighted images (T2WI) for subjects over 50 years of age (ROIs could not be drawn on myelin maps because of lack of structural details, so T2WI were added). Volumes of interest (VOI) were created by combining all ROIs from the same column across all slices. All errors are expressed as standard errors.

Results

Two subjects' repeat scans could not be included in the reproducibility analysis, one due to motion artifact, and the other to poor fitting of the NNLS algorithm. For the remaining 5 cases, the mean absolute difference (mean (SE)) was 0.064(0.005), and the mean relative difference was 26%(2%). Scan-rescan reproducibility is shown in Figure 1, with the identity line shown for comparison.

MWF in the cervical spinal cord show a negative trend with increasing age; the Spearman's rank coefficient for this trend was significant for all ROIs pooled together (Figure 2, rho = -0.250), as was a linear relationship (p = 0.007). Significant trends were also found for the dorsal (rho = -0.416, p = 0.023) and left lateral (rho = -0.352, p = 0.107) columns independently.
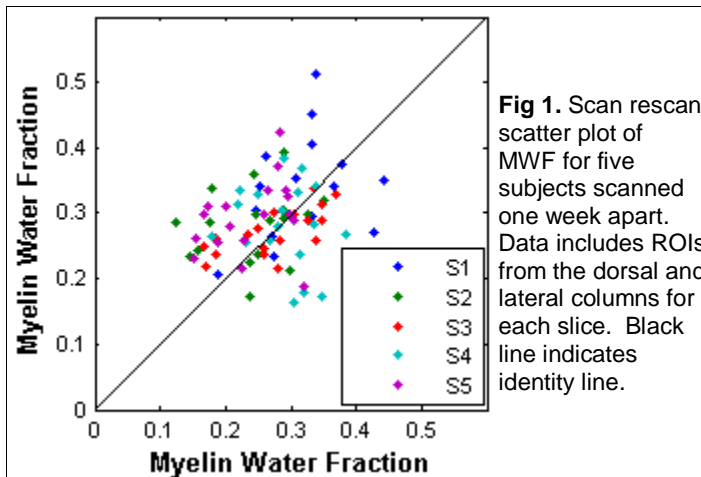
Fig 1. Scan rescan scatter plot of MWF for five subjects scanned one week apart. Data includes ROIs from the dorsal and lateral columns for each slice. Black line indicates identity line.
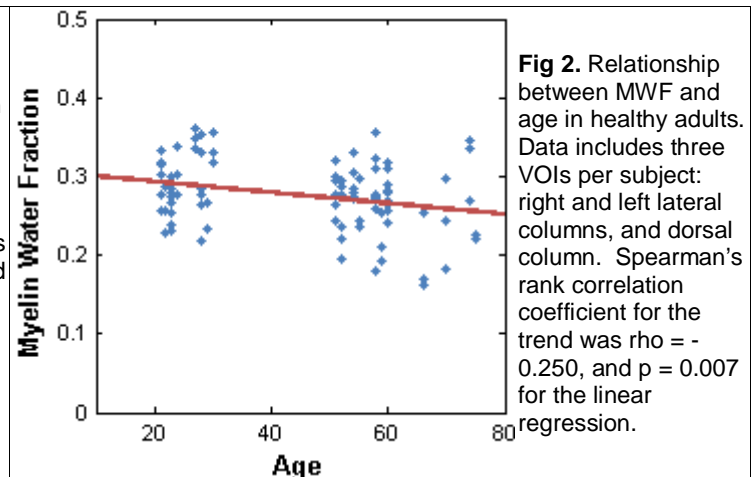
Fig 2. Relationship between MWF and age in healthy adults. Data includes three VOIs per subject: right and left lateral columns, and dorsal column. Spearman's rank correlation coefficient for the trend was rho = -0.250, and p = 0.007 for the linear regression.

Conclusions

Myelin water imaging with MRI at 3.0T indicates that white matter myelin content in the cervical spinal cord decreases with age. These findings are in agreement with photomicrograph studies that detected a decrease in myelinated fibre density with age in the lateral cortical spinal tracts[6], and support the use of myelin water imaging as an *in vivo* tool to track changes in white matter myelin content in the cervical spinal cord.

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