Correlation of Diffusion Measures with Multicomponent T2-Relaxation Data in Multiple Sclerosis Lesions and Normal Appearing White Matter

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Introduction

In demyelinating diseases such as Multiple Sclerosis (MS), the mechanisms of myelin pathology must be well understood before steps can be taken to prevent, slow, or stop demyelination and promote remyelination. One possible way to investigate myelin integrity is to use diffusion imaging, which allows for tracking of the mobility of water associated with different brain structures. In regions of white matter, myelinated fibres exert strong anisotropic effects, therefore measuring a decrease in diffusion anisotropy could indicate structural breakdown. Alternatively, the amount of myelin in a given region can be determined by analyzing T_2 relaxation distributions. From the T_2 decay curves obtained using a multi-echo CPMG imaging sequence, the relative contributions from water in different environments can be resolved (in particular the water trapped between the myelin bilayers, with $T_2 < 50$ ms). The ratio of myelin associated water to the total water present provides a quantitative measure of the myelin water fraction (MWF) [1]. MWF has recently been validated as a marker for myelin through quantitative correspondence with histopathology [2]. As both MWF and diffusion measures such as fractional anistropy (FA) are believed to indirectly measure myelin, they are expected to be related to each other. It has indeed been shown for healthy volunteers that there is a significant correlation between MWF and FA [3]. The goal of this study was to determine whether MWF and measures of diffusion are also related in MS lesions and contralateral normal appearing white matter (cNAWM).

Methods

MRI measurements were performed on 14 MS patients (4 men, 10 women; mean age 39.4 years (range: 25-54 years); median EDSS of 2.5 (range 1.0-6.5), 11 relapsing remitting, 2 secondary progressive, 1 benign) on a GE Signa 1.5T system. T_2 relaxation measurements were acquired using a 48-echo CPMG experiment (variable TR=3800-2120ms, acquisition matrix 256x128, echo spacing: first 32 echoes=10ms, last 16 echoes=50ms, slice thickness=5cm, FOV=22cm) [4]. Diffusion Tensor Imaging (DTI) was performed with a single shot pulsed-field gradient EPI sequence (TR=3-4 RR, TE=85ms, gradient duration=25ms, observation time=38ms, 3 b-values between 0 and 1000 s/mm^2, 4 averages, slice thickness=5cm, FOV=22cm). Regions of interest (ROIs) were drawn around lesions and cNAWM. The data was compared to values obtained from a previous study for normal white matter (NWM) and normal grey matter (NGM) from healthy volunteers [3].

Results and Discussion

A weak but significant correlation was found between FA and MWF for MS lesions (R^2=0.207, $p<0.0001$) and for cNAWM (R^2=0.151, $p<0.001$). The MWF was approximately 17% lower in cNAWM than in NWM, consistent with previous work [5]. The FA was approximately 27% lower in cNAWM than in NWM, which is a greater difference than that reported in the literature [6,7], which may be due to variation in NWM ROI selection. As seen in figure 1, the relative changes in FA and in MWF are not the same, indicating that myelin water imaging and diffusion tensor imaging provide different but complimentary information. Both FA and MWF were more reduced in MS lesions compared to cNAWM; the FA was reduced to approximately the same value as for NGM, while the MWF was much higher than that for NGM. This suggests that while lesions have a large effect on anisotropy, a significant amount (~ 65% compared to cNAWM) of myelin remains.

In MS lesions, the trace of the diffusion tensor, which reflects the magnitude of diffusion and hence is larger where there are fewer impediments to diffusion, was more variable (i.e. higher standard deviation) for lower MWF values. This could be due to increased heterogeneity in the lesions where little myelin remains. The trace was found to be significantly larger for both NAWM and lesions than for NWM, which is in agreement with the literature [6,7].

Conclusions

While MWF and FA both offer information related to the amount and state of myelin within a region of the brain, this information is not redundant but complimentary. Use of both of these tools provides a more complete description of the integrity of myelin in the CNS.

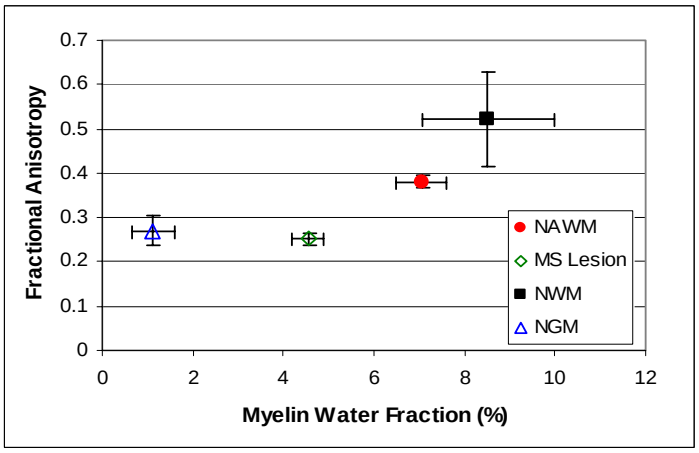

Figure 1: Mean values of FA and MWF for NAWM, MS Lesions, NWM and NGM with error bars representing standard error. A large amount of variation in both FA and MWF was observed in NWM as ROIs were drawn in various brain structures.

Acknowledgments

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