In-Vivo and Numerical Studies of Myelin Water Fraction in Rat Spinal Cord

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Introduction

Mutli-exponential T2 (MET2) analysis has revealed the existence of two T2 components in white matter – a fast component believed to originate from water associated with myelin and a longer-lived component believed to originate from water in both the extracellular and inter-axonal spaces [1]. Myelin water fraction (MWF) estimated from MET2 analysis has been shown to be an effective marker of myelin in tissue, but a recent study found evidence from ex-vivo samples of rat spinal cord that MWF is significantly biased due to the exchange of water between the myelin and surrounding anatomical compartments in white matter [2]. The present work extends these findings to in-vivo measurements of MWF and investigates the biophysical tissue characteristics necessary to explain the previous observations.

Methods

MET2 Imaging was performed on a 9.4T Varian scanner with a 38 mm Doty quad coil used for transmission and reception. A 1.5 mm slice was chosen transverse to the spinal cord of anesthetized rats, with 128x128 sampling over a 25.6 x 25.6 mm^2 FOV. Twenty-four TEs were evenly spaced 9 ms apart between 6.8 ms and 172.2 ms, with another eight TEs spaced at 50 ms increments, TR = 2000 ms, NEX = 16. A finite difference model of water diffusion and relaxation was used to simulate T2 decay within cell geometries defined by segmented light microscopy images of six white matter regions within rat spinal cord. A T2 spectrum from each MET2 experiment and simulation was obtained via NNLS analysis. The T2 spectra derived from numerical simulations in each of the six regions were collectively fit to experimental T2 spectra (collected ex-vivo [2]) from corresponding white matter regions.

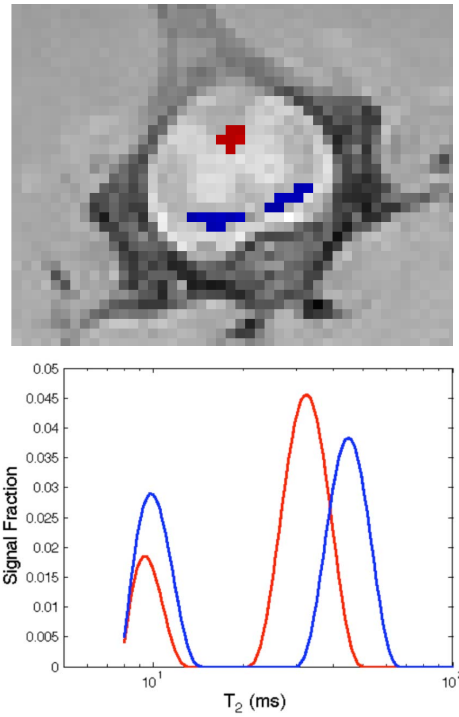

Fig. 1: T2-weighted image of the rat spinal cord, where the vestibulospinal tract (VST) and dorsal corticospinal tract (dCST) are marked in blue and red, respectively. The T2 spectrum from both ROIs is also given. The MWF of the dCST is much lower than that of the VST, despite a constant underlying myelin volume faction.

Results and Discussion

Fig. 1 shows a cropped image of the spinal cord and an example T2 spectrum from ROIs within the vestibulospinal tract (VST) and dorsal corticospinal tract (dCST). The MWF is 38.9% in the VST and 20.5% in the dCST even though the myelin fraction is known to be similar within these regions. An underestimation of the MWF could be caused by differences in water exchange within regions of physiologically different axon sizes. Light microscopy images of the VST and dCST are shown in **Fig. 2**, and demonstrate a large difference in the average axon size within these regions. Simulations of T2 decay within six white matter tracts of the spinal cord were fit to experimental T2 spectra, and these fitting results are shown in **Table 1**. Within this model, exchange is necessary to characterize the variation in MWF, and simulations more appropriately characterize the T2 spectra when exchange is mediated by the diffusivity of myelin water rather than a membrane permeability between the myelin and intra + extra axonal spaces. The value of D_m fit in this study is significantly lower than the myelin diffusivity estimated from previous studies [3]. However, if the myelin diffusivity were limited by the permeability of membranes that form myelin, the effective D_m fit here would require a membrane permeability of only 0.28 μm/ms, which is within a reasonable range of membrane permeability.

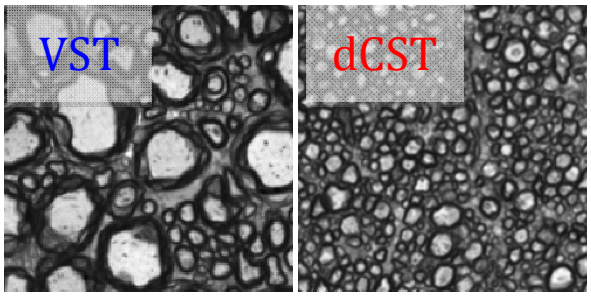

Fig. 2: Light microscopy images of the VST and dCST. Regional variations in the axon size and myelin thickness will influence exchange, and likely causes an under-estimation of the MWF.

Table 1: Fitting Results

Intra-Axonal T2 (ms)	Extra-Axonal T2 (ms)	Myelin T2 (ms)	Myelin Diffusivity (μm²/ms)	Permeability (μm/ms)	Residual
91.3	30.6	11.9	0.00123	n/a	0.5827
94.7	27.3	12.6	n/a	0.00572	1.3151

Conclusion

These results indicate that the MWF may be significantly underestimated by exchange of water associated with myelin and intra + extra-axonal water. Simulations further suggest that exchange is limited by the apparent diffusivity of myelin water, and may not be adequately characterized by a slow-exchange model.

References

1) MacKay et al. MRM 1994; 31:673-677
2) Dula et al. MRM in press
3) Andrews et al. MRM 2006; 52:381-385

Acknowledgements

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