Detection of demyelination and remyelination in multiple sclerosis by analysis of T2* relaxation at 7T

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Target audience: Pre-clinical scientists, Clinicians.

Purpose: Investigate the evolution of focal myelin loss in multiple sclerosis (MS) using fitting of a three-component model to T_2^* decay curves at 7T.

Methods: Based on the identification of enhancing lesions in scheduled examinations at 3T, five women relapsing-remitting MS patients (ages 33-59 years, and average age 42 years) were scanned at 7T. Follow-up scans were performed after approximately 3 and 6 months. Multi-gradient-echo data (15 slices, TR 1s, FA 70°) were acquired with isotropic 1.5mm resolution (38 echoes, TEs of 2.3-62.7ms, echo spacing 1.6ms, 5 averages). The slices were parallel to the plane of the anterior and posterior commissure line and captured much of the corpus callosum. ROIs were chosen in enhancing and non-enhancing lesions identified from pre- and post-gadolinium T_1-weighted MRI. In addition, control ROIs were chosen in normal-appearing white matter (NAWM) in homologous locations contralateral to the lesions. Similarly to our previous study[1], a three-component model allowing for variable offset frequencies of the components was used to fit the T_2^* decay curves of the mean ROI signal. Statistical analysis was carried out using ANOVA to investigate the significance of changes in the three-component fitting results among the three scans for these three ROI types.

Results: Eleven enhancing lesions and thirteen non-enhancing lesions were analyzed. In the follow-up scans, none of the initially enhancing lesions showed enhancement. The three-component fitting results for lesions and NAWM are shown in Table 1. A_n is the amplitude, $R_{2,n}^*$ the relaxation rate, and Δf_n the frequency shift of the component n. Components 1, 2 and 3 were assigned to myelin, axonal and interstitial water respectively.[1,2] The $R_{2,1}^*$ and Δf_1 of lesions were fixed with the value from contralateral NAWM as the myelin water signal in lesions is too small to determine these independently. In both lesions types, the amount of myelin water (A_1) was found to be significantly decreased relative to the contralateral NAWM (Table 1), suggesting demyelination.[3] The accompanying increased axonal water (A_2), decreased R_2^* of axonal and interstitial water ($R_{2,2}^*$ and $R_{2,3}^*$) and small frequency shift of axonal water (Δf_2) are also consistent with the myelin loss.[1] A significant further increase in R_2^* of axonal water was found in enhancing lesions (p = 0.01, Fig 1), which might indicate the progression of remyelination. In line with this, in follow-up scans of enhancing lesions compared to baseline, trends of increasing both in frequency shift of axonal water (Δf_2) and amplitude of myelin water (A_2) were observed (Table 1, Fig 1), which also suggested remyelination. No significant changes were observed among the three scans in non-enhancing lesions and NAWM.

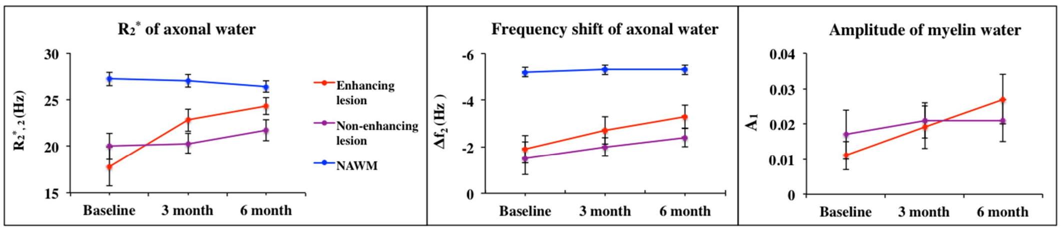

Fig 1. The R_2^* of axonal water ($R_{2,2}^*$), frequency shift of axonal water (Δf_2) and amplitude of myelin water (A_1) at baseline and during follow-up scans in lesions and NAWM. Data are represented as mean ± standard error (mean±SE). R_2^* of axonal water in enhancing lesions showed significant increase (p = 0.01).

Discussion and Conclusion: The mechanisms underlying the progression of MS and the relationship to pathology are still poorly understood. Gadolinium enhancement is thought to be a radiological sign of a new inflamed white matter lesion. The changes over time that we observed in enhancing lesions are consistent with the presence of ongoing demyelination and repair, whereas these processes appear to be more stable in non-enhancing lesions and NAWM. These findings suggest that the fitting of a three-component model to the T_2^* decay curves at high magnetic field can be used to characterize the dynamics of these processes and possibly to detect response to remyelinating and neuroprotective therapies.

References:

1. Sati, P. et al. Micro-compartment specific T_2^* relaxation in the brain. Neuroimage. 2013; 77: 268–78.
2. van Gelderen, P. et al. Nonexponential T_2^* decay in white matter. Magn Reson Med. 2012; 67: 110–7.
3. Yao, B. et al. Chronic Multiple Sclerosis Lesions: Characterization with High-Field-Strength MR Imaging. Neuroradiology. 2012; 262: 206–215.

Table 1. ROI-based fitting of a three-component model to the T_2^* decay curve for enhancing and non-enhancing lesions and normal-appearing white matter (NAWM) in baseline and 3 and 6 month follow-up scans. A_n is the amplitude, $R_{2,n}^*$ the relaxation rate (Hz), and Δf_n the frequency shift (Hz) of component *n*. Mean values and the standard deviation (SD) over *N* ROIs are shown. The $R_{2,1}^*$ and Δf_1 of lesions were fixed with the value from contralateral NAWM as the myelin water signal in lesions is too small to determine these independently.

ROI	N		Myelin water			Axonal water			Interstitial water	
			A_1	$R_{2,1}^*$(Hz)	Δf_1(Hz)	A_2	$R_{2,2}^*$ (Hz)	Δf_2 (Hz)	A_3	$R_{2,3}^*$ (Hz)
Enhancing lesion	11	Baseline	0.011 (0.014)	----	----	0.528 (0.076)	17.8 (6.9)	-1.9 (1.9)	0.497 (0.058)	16.1 (4.9)
		3 month	0.019 (0.019)	----	----	0.541 (0.062)	22.4 (4.0)	-2.7 (2.1)	0.489 (0.047)	21.3 (5.5)
		6 month	0.027 (0.022)	----	----	0.546 (0.068)	24.3 (3.0)	-3.3 (1.6)	0.483 (0.067)	19.6 (7.3)
Non-enhancing lesion	13	Baseline	0.017 (0.025)	----	----	0.540 (0.064)	20.0 (5.0)	-1.5 (2.4)	0.490 (0.035)	18.4 (4.8)
		3 month	0.021 (0.018)	----	----	0.546 (0.051)	20.3 (4.1)	-2.0 (1.5)	0.464 (0.049)	17.0 (5.2)
		6 month	0.021 (0.022)	----	----	0.552 (0.048)	21.7 (4.0)	-2.4 (1.5)	0.476 (0.057)	16.4 (4.7)
NAWM	24	Baseline	0.096 (0.027)	140 (30)	17.0 (9.9)	0.470 (0.034)	27.2 (3.4)	-5.2 (0.9)	0.497 (0.037)	26.1 (2.2)
		3 month	0.102 (0.026)	145 (27)	17.1 (8.1)	0.473 (0.031)	27.0 (3.2)	-5.3 (0.9)	0.484 (0.037)	25.6 (2.3)
		6 month	0.109 (0.027)	140 (28)	13.3 (7.2)	0.466 (0.029)	26.4 (3.0)	-5.3 (0.9)	0.487 (0.048)	25.8 (2.7)