Detection of demyelination in Multiple Sclerosis using analysis of T2* relaxation at 7T

Xiaozhen Li[1,2], Peter van Gelderen[1], Pascal Sati[3], Jacco A. de Zwart[1], Daniel S. Reich[3], and Jeff H. Duyn[1]

[1]Advanced MRI Section, LFMI, NINDS, National Institutes of Health, Bethesda, Maryland, United States, [2]Division of Clinical Geriatrics, NVS Dept., Karolinska Institutet, Huddinge, Stockholm, Sweden, [3]Translational Neuroradiology Unit, Neuroimmunology Branch, NINDS, National Institutes of Health, Bethesda, Maryland, United States

Introduction: Multiple sclerosis (MS) is a chronic disease of the nervous system characterized by focal areas of myelin loss ("lesions"). Recent gradient-echo studies suggest the possibility of obtaining cellular compartment-specific information from multi-component fitting of the T_2^* relaxation decay curve, allowing determination of the relative fractions of myelin water, axonal water and interstitial water [1, 2]. The distinction between these three components may help further understand the pathological changes in MS during evolution of the disease. Specifically, quantification of myelin water may provide a measure of demyelination in MS.

Materials and Methods: Thirteen relapsing-remitting MS patients (2 male, 11 female, ages 25-62, and average age 41) were studied at 7T, five of whom were scanned twice. Multi-gradient-echo data (15 slices, TR 1s, FA 70°) were acquired either with 1.0mm resolution (25 echoes, TEs 2.8-54.4 ms, echo spacing 2.2ms, 3 averages) or 1.5mm resolution (36 echoes, TEs of 2.3-58.3 ms, echo spacing 1.6ms, 5 averages). The slices were parallel to the plane of the anterior and posterior commissure line and captured a section of the corpus callosum. Regions of interest (ROIs) outside lesions were drawn manually in the optic radiations (OR) and the splenium of corpus callosum (SCC), excluding visible veins and lesions. Furthermore, ROIs were chosen in enhancing and two non-enhancing lesions (Figure 1a) identified from gadolinium-enhanced T_1-weighted MRI and non-enhanced T_2-FLAIR imaging respectively. In addition, control ROIs (Figure 1b) were chosen in normal-appearing white matter (NAWM) in homologous locations contralateral to the lesions. Similarly to our previous study [2], 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.

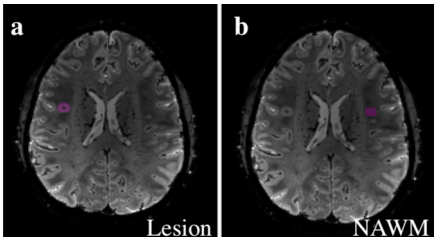

Figure 1 ROI in lesion (a) and NAWM (b).

Results/Discussion: SCC was not included in one study, and the OR ROI could not be drawn in two studies. In total, seven enhancing lesions and 36 non-enhancing lesions were analyzed. The three-component fitting results for SCC, OR, lesions and NAWM are shown in Table 1 and Figure 2. A_i is the relative amplitude (%), $R_{2,i}^*$ the relaxation rate, and Δf_i the frequency shift of the component i. Components 1, 2 and 3 were assigned to myelin, interstitial and axonal water respectively [1, 2]. The fitting results for SCC and OR are consistent with previous results in healthy controls [2]. In both lesions types, the amount of myelin water (A_1) was found to be significantly decreased relative to the contralateral control (Table 1 and 2), suggesting demyelination [3]. The accompanying reduction in R_2^* of myelin water ($R_{2,1}^*$) (Table 1 and 2) and frequency shift of axonal water (Δf_3) are also consistent with myelin loss [2]. Interestingly, in non-enhancing lesions compared to enhancing lesions, a reduction in the fraction of axonal water (A_3) and an increase in the amount of interstitial water (A_2) were observed (Table 1 and 2).

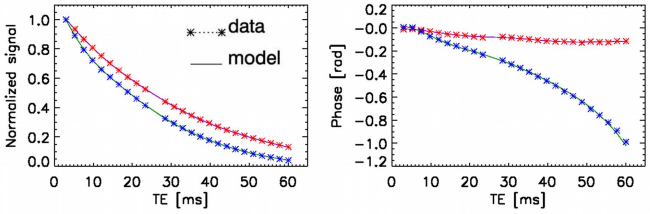

Figure 2 Results of a three-compartment model fit for the same lesion (red) and contralateral NAWM (blue) as in Figure 1.

Conclusions: These findings suggest that three-component fitting of the T_2^* relaxation decay curve in MS lesions may help quantify cumulative myelin loss, and possibly discriminate between chronic and more acute stages of lesion evolution.

Table 1 ROI-based three-component fitting for SCC, OR, lesions and NAWM. A_i is the relative amplitude (%), $R_{2,i}^*$ the relaxation rate (Hz), and Δf_i the frequency shift (Hz) of the component i. Mean values are followed by the standard error over *n* ROIs, shown in parentheses.

		Myelin water			Interstitial water			Axonal water		
	n	A_1 (%)	$R_{2,1}^*$ (Hz)	Δf_1 (Hz)	A_2 (%)	$R_{2,2}^*$ (Hz)	Δf_2 (Hz)	A_3 (%)	$R_{2,3}^*$ (Hz)	Δf_3 (Hz)
SCC	17	13.8 (1.9)	157.4 (11.0)	29.6 (3.4)	46.5 (2.9)	33.7 (3.4)	2.2 (0.7)	39.7 (2.2)	23.2 (2.5)	-4.4 (1.0)
OR	16	14.1 (1.8)	161.6 (17.9)	27.4 (3.4)	41.4 (1.4)	23.9 (2.4)	1.7 (0.4)	44.8 (2.0)	29.5 (2.2)	-4.8 (0.7)
Non-enhancing Lesions	36	2.9 (1.7)	49.4 (21.8)	28.4 (21.2)	51.8 (6.3)	19.6 (4.8)	1.6 (1.2)	45.3 (7.1)	18.0 (7.5)	-1.9 (0.9)
Enhancing Lesions	7	2.7 (2.2)	55.5 (20.6)	20.8 (10.6)	46.6 (3.7)	19.9 (4.6)	1.5 (0.7)	50.6 (3.4)	22.6 (3.5)	-2.5 (0.8)
NAWM	43	10.6 (2.3)	148.9 (24.5)	25.6 (6.0)	44.3 (4.6)	26.2 (5.7)	1.9 (0.9)	45.1 (4.4)	27.8 (3.4)	-3.9 (1.1)

Table 2 Significance of the differences in three-component fitting results between enhancing and non-enhancing lesions, and NAWM.

		p (Myelin water)			*p* (Interstitial water)			*p* (Axonal water)		
	n	A_1	$R_{2,1}^*$	Δf_1	A_2	$R_{2,2}^*$	Δf_2	A_3	$R_{2,3}^*$	Δf_3
Non-enhancing lesion vs NAWM	36	**<0.001**	**<0.001**	0.55	**<0.001**	**<0.001**	0.05	0.84	**<0.001**	**<0.001**
Enhancing lesions vs NAWM	7	**<0.001**	**0.001**	0.78	**0.03**	**0.01**	0.75	**0.02**	0.07	**0.005**
Enhancing vs Non-enhancing lesions	7	0.22	0.81	0.41	**<0.001**	0.85	**0.04**	**<0.001**	**0.05**	0.11

References: [1] van Gelderen et al., MRM (2011); [2] Sati et al., Neuroimage (2013); [3] Yao et al., Radiology (2012).