Analysis of Normal Appearing White Matter of Multiple Sclerosis by Tensor-based Two-Compartment Model of Water Diffusion

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Target audience: Radiologists and physicians interested in diagnosing Multiple Sclerosis, as well as in Diffusion-Weighted MR imaging.

Background and Purpose: Alterations in water diffusion are well assessed in normal appearing white matter (NAWM) of Multiple Sclerosis (MS) patients[1, 2]. However, the two-compartment model[3], which is the one of the major techniques for assessing non-Gaussian water diffusion *in vivo*, has not been well discussed in this field probably due to its large requirement for data acquisition and post-processing. We have designed a novel method to assess the two-compartment model based on diffusion tensor imaging more simply to overcome this problem. The purpose of this study is to evaluate the significance of this method in detecting minimal lesions in NAWM of MS.

Methods: 12 healthy female volunteers and 13 female MS patients were assessed. DWI was acquired by clinical 3T MRI (Achiva, Phillips) with single-shot-EPI, nine b-values (0, 124, 496, 1116, 1983, 3099, 4463, 6074, 7934s/mm^2) with diffusion encoding in 6 directions. For each pixel, the b-value-dependent signal attenuations by imaginary MPGs toward the peculiar axial and radial directions of that pixel (eDWI) were calculated based on the diffusion tensor (Fig.1). This method was as follows: for each b-value, diffusion tensor was calculated from the signal intensity of that b-value (S_b) and b=0 (S_0). Then the maximum eigenvalue of the tensor (L1) was regarded as the axial diffusion coefficient between b=0 and the selected b. Thus, the imaginary signal intensity at the b-value (attenuated by an imaginary MPG toward the axial direction of the pixel) could be estimated from L1 and S0, following the equation

$$S_b = S_0 * \exp(-b * L1). \text{ (See Fig.1)}$$

This procedure was repeated for every b-value to estimate the whole signal attenuation (Fig.1). For the imaginary MPG towards the radial direction, the average of the second and third eigenvalues was applied in the substitution of L1. Finally, bi-exponential fitting, which follows the equation

$$S_b/S_0 = (1 - f_s) * exp(-b * D_f) + f_s * \exp(-b * D_s)$$

was applied to the estimated signal attenuation. The parameters Ds, Df, and fs, which indicate the diffusion coefficient of the slow diffusion, that of fast diffusion, and the fraction of the slow diffusion, respectively, were assessed in this study. Apparent diffusion coefficient (ADC) based on mono-exponential fitting was also calculated by b-value at 0-1116s/mm^2 in both eDWI and the original trace image for comparison. ROI was set at the deep white matter of bilateral centrum semiovale (see Fig.2 for example, the colored pixels were included). Diffusion parameters (Ds, Df, and fs, each axial and radial) as well as ADCs were averaged in the ROI and were compared statistically between control and MS group (Mann-Whitney rank sum test, P<0.01 was considered significant).

Results: Radial Ds map indicated diffuse higher value in MS patients compared to controls (Fig.2). The estimated DWI signal attenuation in the radial direction was larger in MS patients with high b-values (Fig.3). The difference in radial Ds between MS patients and control proved to be statistically significant (Table 1). The differences in other diffusion parameters including ADCs were not significant between the groups.

Discussion: The diffusion parameters discussed in this study require further study to determine their accuracy; however, their usefulness was suggested because a difference with significance was indicated between the groups that could not be done by ADC. In addition, the scan time required for this sequence would be applicable in clinics (approx. 4min). Furthermore, the simple post-processing requires less computing time, and also contributes to the robustness. The mechanism for making the difference in Ds is not clear, but some interaction between water molecule and cell membrane may be considerable because the difference was only seen in the radial direction.

Conclusion: A simple and practical novel method for assessing axial and radial water diffusion based on the two-compartment model was evaluated. The method indicated higher detectability in minor changes in NAWM of MS compared to conventional ADC.

References: 1. Temel S, Kekligkoglu HD, et al Neuroradiol J 26:3-17, 2.Yoshida M, Hori M, et al. Jpn J Radiol 31:50-55,   3. Clark CA, Le Bihan D Magn Reson Med 44:852-859
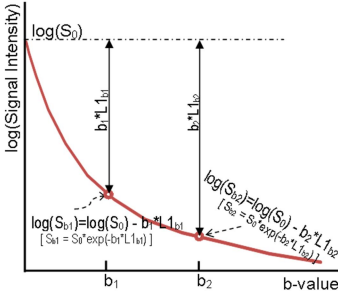
Figure 1. Estimation of the signal attenuation depended on b-value by an imaginary MPG toward the peculiar axial direction (eDWI axial). L1$_{b1}$ is the largest eigenvalue of the diffusion tensor calculated from b = 0 and b$_1$, as is L1$_{b2}$ from b=0 and b$_2$. The signal attenuation (red line) could be estimated by repeating this process at every b-value acquired.
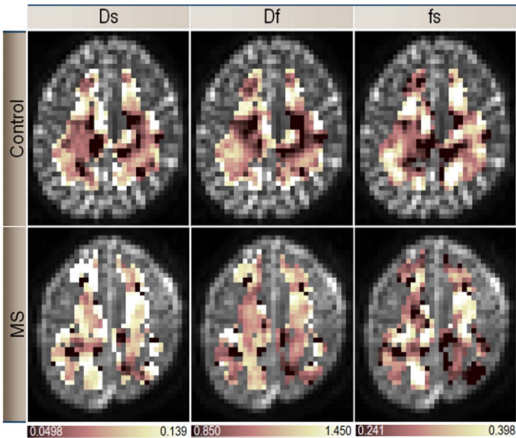
Figure 2. Radial Ds, Df, and fs maps of 52-year-old healthy volunteer and 45-year-old MS patient. Ds was diffusely higher in MS compared to control. Df also seems rather higher in MS, but the difference in Ds was greater (corresponding with statistical results (Table 1)).
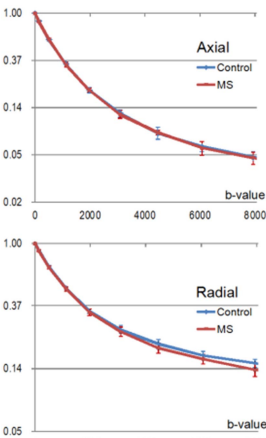
Figure 3. Estimated signal attenuation in the ROI. The difference between the groups was seen only in the high b-value area of radial direction.

	Axial				Radial				
	Ds*	Df*	Fs	ADC*	Ds*	Df*	fs	ADC*	ADC trace*
Control	0.276	2.03	0.280	0.825	0.100	1.09	0.309	0.546	0.733
(min, MAX)	(0.229, 0.378)	(1.75, 2.43)	(0.267, 0.358)	(0.779, 0.885)	(0.0665, 0.119)	(0.966, 1.28)	(0.248, 0.375)	(0.524, 0.564)	(0.697, 0.762)
MS	0.267	1.91	0.288	0.818	0.121	1.16	0.321	0.558	0.739
(min, MAX)	(0.211, 0.403)	(1.49, 6.16)	(0.221, 0.411)	(0.791, 0.858)	(0.0777, 0.154)	(1.04, 1.40)	(0.293, 0.400)	(0.507, 0.606)	(0.708, 0.801)
P-value	0.849	0.644	0.892	0.978	**0.00100**	0.0208	0.1827	0.109	0.314

* x10^{-3}mm^2/sec

Table 1: Median and range of parameters are indicated. P-values were calculated by Mann-Whitney rank sum test (P<0.01 was considered significant to avoid type 1 errors in the multiplicity of statistical analysis). Radial Ds was higher in MS, and the difference was significant. The other parameters did not indicate significant differences.