Temporal Changes of Fractional Anisotropy in DTI of the Corpus Callosum in Secondary Progressive Multiple Sclerosis: a Putative Marker of Accumulating Tissue Damage

W. TIAN[1], J. Zhong[1], X. Liu[1], P. Rao[2], B. M. Segal[2], and S. Ekholm[1]

[1]Department of Imaging Sciences, University of Rochester Medical Center, Rochester, NY, United States, [2]Department of Neurology, University of Michigan, Ann Arbor, MI, United States

Introduction: Conventional MRI looking at lesion load has not been very helpful in evaluating and monitoring brain tissue damage in secondary progressive MS (SPMS), which is characterized by gradually accumulating neurological disability. Even though enhanced lesions on the postcontrast images indicate a more active phase, the relationship between these radiological measures, and clinical disability and progression is unclear and discrepant. However, diffusion tensor imaging (DTI) can detect and quantitatively analyze occult injuries in brain tissues, including corpus callosum (CC)[1]. Our purpose is dedicated to investigate the diffusion changes of CC in patients with SPMS and evaluate the potentials of the diffusion changes of CC in predicting severity and activity of SPMS by a preliminary one-year period longitudinal DTI study.

Methods: The study includes 11 untreated patients (55±8 yrs) with clinically definite SPMS, who completed 6 bimonthly MRI scans and included 5 matched healthy controls who were scanned 3 times with 1.5 months interval. MRI examinations were performed on a GE Signa Excite 1.5 T scanner and included axial post contrast T1WI (only patients) and DTI (TR/TE=10800/80ms, FOV= 24cm, matrix 128x128 , NEX=2; 21 diffusion directions, b=1000, 3mm slice thick). Based on the presence of T1 enhancing lesions during the one-year study period, patients were divided into an enhancing and a non-enhancing group, 5 and 6 patients respectively. The Fractional anisotropy (FA) and Mean Diffusivity (MD) values of genu, body and splenium of CC were measured at every time point using a region of interest (ROI) method with a home-built software. The differences of FA and MD change over time were evaluated for each group as well as between groups using repeated measures analysis of variance (ANOVA) with SPSS15 [2.3].

Results: Disease duration (DD), mean FA and MD of CC in the 1st MR scan were comparable between the groups. Although the patients with enhancing lesions tended to have a higher EDSS score than the non-enhancing, there was no significant difference between groups which indicates a similarity of severity in the SPMS patients at the beginning of the study. The statistical analysis of temporal diffusion changes of inter/intra-group comparisons are shown in Table 1 and Fig 1.

Our results showed a significant difference for FA changes over time in body CC (P=0.006) and splenium (P=0.003) between enhancing and non-enhancing groups by 'Time X group' interaction analysis; The enhancing patients group also showed a significant progressive decline in FA over the 6 time points in body CC (P=0.001) and splenium (P=0.003); which was not noted for the non-enhancing group and the controls (Table 1 and Figure 1). There was no significant difference for MD change between groups over time, P>0.05.

Conclusion: Our longitudinal DTI study indicates that the SPMS patients with enhancing lesion(s) had a significant progressive FA decrease trend in CC over a one-year follow up, as opposed to the non-enhancing group. So, temporal FA changes in the body and splenium of CC could potentially be used as a putative marker in predicting severity and activity of SPMS, and thus helpful in studying treatment effects.

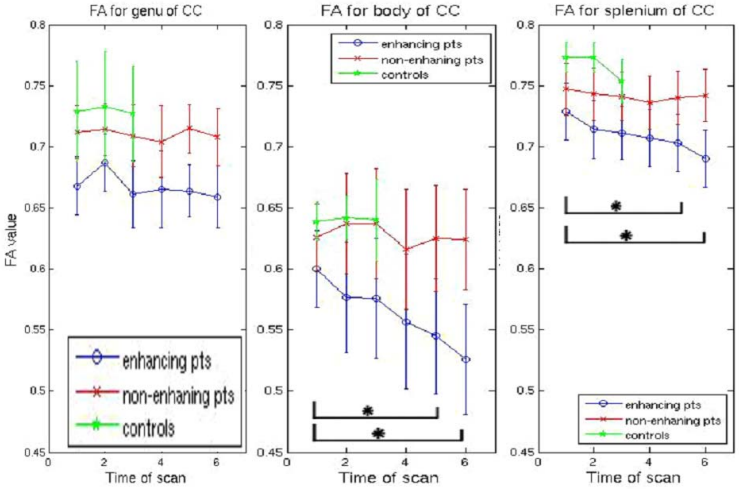

Fig 1: Time-Course trend of mean FA changes in 3 regions of CC of 3 groups, star represents statistical significant at 5th, 6th compared to the 1st time point in enhancing group. Error bars represent 95% confidence interval. Blue line = enhancing pats group, red line=non-enhancing patients group, green line=Controls. * indicates P<0.05.

	Region	patients group	p for each group	p for 2 group	p for 'timeXgroup' interaction of 2 groups
FA	genu	Gd+	0.116		
		Gd-	0.836	0.428	0.675
	Body	Gd+	0.001*		
		Gd-	0.397	0.003*	0.006*
	splenium	Gd+	0.003*		
		Gd-	0.495	0.001*	0.003*
MD	genu	Gd+	0.371		
		Gd-	0.062	0.12	0.338
	body	Gd+	0.007*		
		Gd-	0.059	0.018*	0.967
	Splenium	Gd+	0.193		
		Gd-	0.093	0.018*	0.968

Table 1: Comparison of mean FA, MD changes over time in CC of intra/inter groups. * indicates P<0.05. Gd+ =with gadolinium-enhancing patients group , Gd- = nonenhancing patients group

References: 1) Hansan MK et.al. JMRI 21:735-743, 2005. 2) Agosta F et. al. Brain, 130: 2211-2219,2007. 3) Gupta RK et. al. JMRI, 24: 549-555, 2006. **Acknowledgment:** This work was supported by an Autoimmunity Center of Excellence grant (1 U19 AI056390-01; Project 2) from the NIAID, NIH (to B.M.S.). Tong Zhu provided substantial help on DTI data processing.