

ASSOCIATIONS BETWEEN DTI MEASURES, CONVENTIONAL MRI MEASURES, AND FUNCTIONAL IMPAIRMENT IN MS PATIENTS TRANSPLANTED WITH AUTOLOGOUS MESENCHYMAL STEM CELLS

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Introduction

- Diffusion tensor imaging (DTI) is a sensitive imaging technique that may provide a more sensitive assessment of tissue injury than conventional MRI measures in patients with multiple sclerosis (MS).^{1,2}
- Autologous mesenchymal stem cell (MSC) transplantation is under investigation as a potential neuroprotective/repair-promoting strategy in MS.³

Objective

To examine the association between DTI, conventional MRI, and functional impairment measures before and after autologous MSC transplantation

Methods

- 24 patients with MS were enrolled in a Phase I study of autologous MSC transplantation. All participants had significant clinical or radiographical disease activity in the two years prior to enrollment and optic nerve involvement.
- Participant characteristics:

Characteristic	Participants (n=24)
Age in years – mean ± SD	46.5 ± 15.4
Sex	16 F/8 M
Disease Course	10 RRMS/14 SPMS
Years of Symptoms: mean ± SD	15.1 ± 9.5
EDSS – median (range)	6.0 (3.0 – 6.5)

- Participants underwent serial assessments at Months (M) -2 (screening), M -1, M 0 (baseline, followed by transplantation), M 1, M 2, M 3, and M 6. Select measures collected include:
- Conventional MRI measures:** T2 Lesion Volume [T2LV], whole-brain and regional atrophy measures (Brain Parenchymal Fraction [BPF], Gray Matter Fraction [GMF], and Cortical Thickness)
- DTI measures of the corticospinal tract (CST) and defined lesional areas:** Mean [MD], Longitudinal [LD], and Transverse [TD] Diffusivity and Fractional Anisotropy [FA]
- Measures of functional impairment:** Expanded Disability Status Scale (EDSS), Timed 25-Foot Walk, 9-Hole Peg Test
- DTI parameters were extracted from previously completed CST probabilistic tractography. Pearson correlations with Bonferroni correction (significance at $p < 0.001$) and linear mixed effect modeling with likelihood ratio test (significance at $p < 0.01$) were performed to assess longitudinal change in metrics pre- and post-transplant and relation of DTI indices to functional impairment at baseline. Fixed effects included age, sex, and years of disease. Random effects included subject and month. A null model was created for the likelihood ratio test containing these factors. T2LV and DTI indices were added as fixed effects in Table 2.

Results

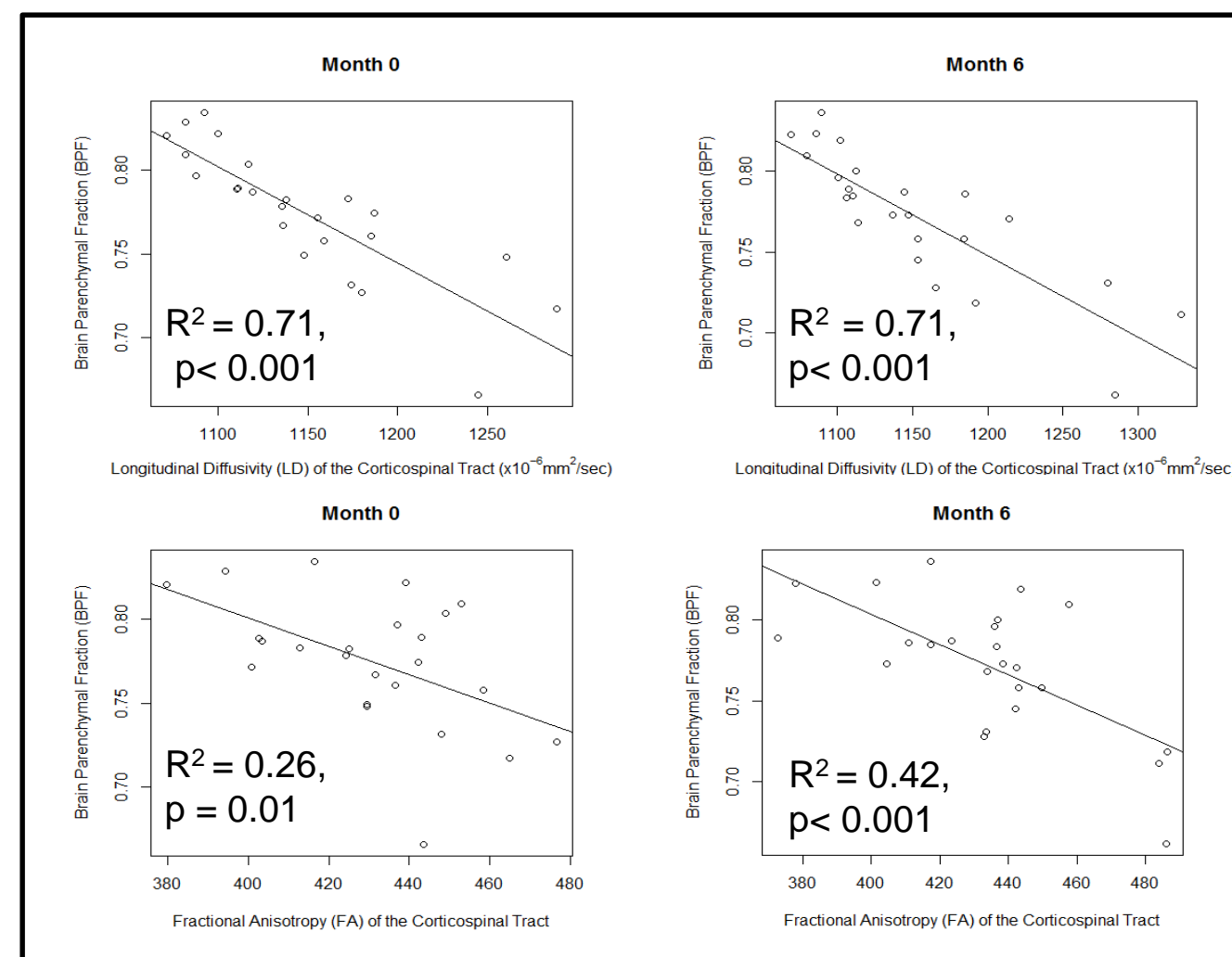


Figure 1. Graphical representation of Pearson correlations between CST LD, CST FA, and BPF at M 0 and M 6. LD in particular demonstrated consistent correlation with conventional MRI measures.

Pearson Product-Moment Correlation Matrix	Month 0 pre-transplant			Month 6 post-transplant		
	BPF	GMF	T2LV	BPF	GMF	T2LV
CST MD	-0.66*	-0.61	0.80*	-0.62	-0.59	0.73*
CST LD	-0.84*	-0.82*	0.79*	-0.84*	-0.83*	0.76*
CST TD	-0.26	-0.33	0.63*	-0.18	-0.12	0.47
CST FA	-0.51	-0.58	0.17	-0.65*	-0.71*	0.34
Cortical Thickness	0.91*	0.86*	-0.62	0.87*	0.91*	-0.61

Table 1. Pearson correlations between DTI indices and conventional MRI measures are shown. * Indicates $p < 0.001$. No significant correlations were found between DTI indices and functional impairment, or lesional DTI measures, conventional MRI, and functional impairment measures.

Predictive ability of DTI indices on functional impairment	DTI indices that predict functional impairment over null model	DTI Indices that provide additional information to predictions by T2LV
EDSS	CST TD (left-side)* CST MD (left-side)*	CST TD (left-side)* CST MD (left-side)*
9-Hole Peg Test	None	None
Timed 25-Foot Walk	None	None

Table 2. Mixed linear models showing the predictive ability of DTI indices for measures of functional impairment pre-transplant. * Indicates $p < 0.01$

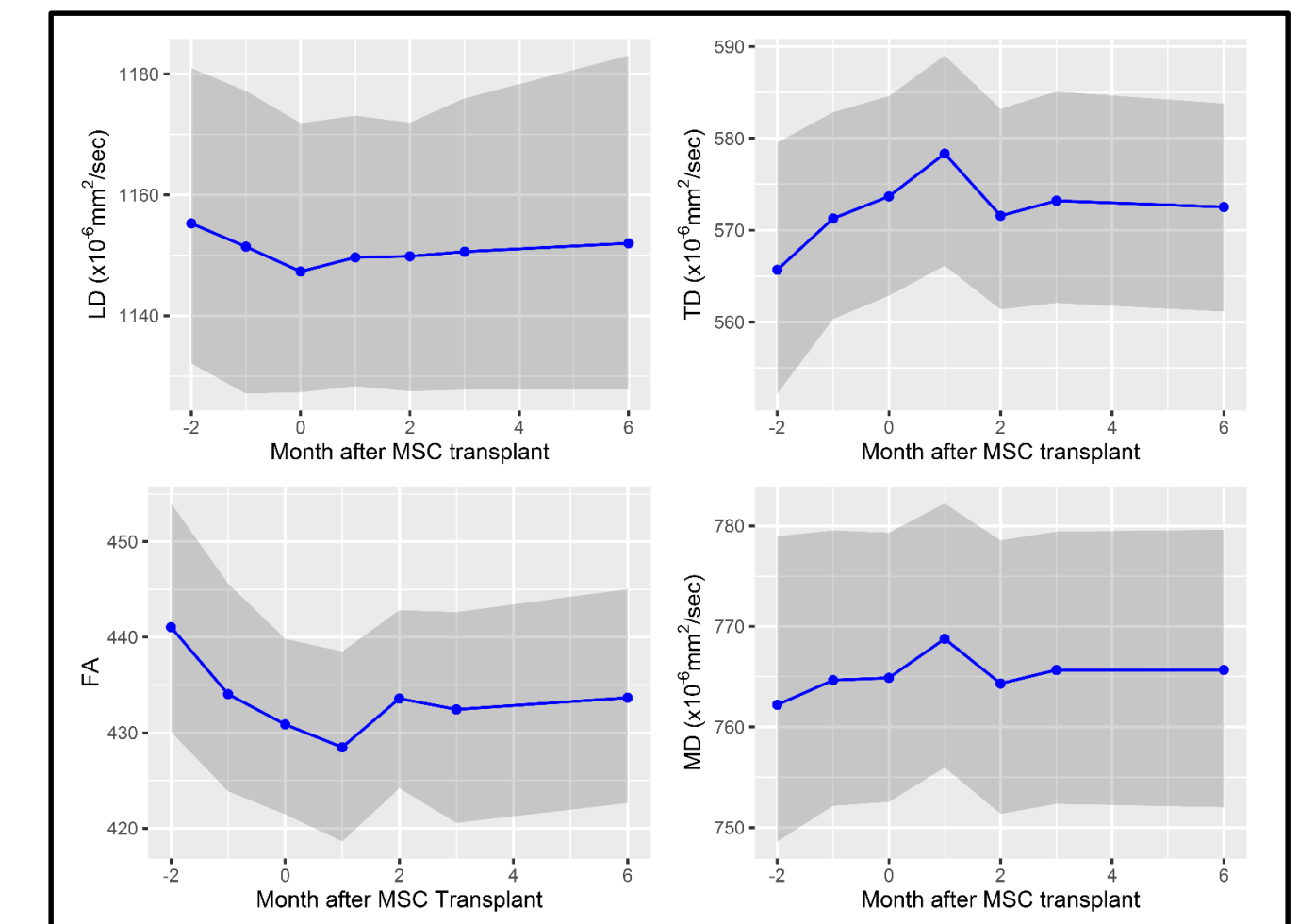


Figure 2. DTI indices over time pre- and post-transplant. Trends in DTI indices were observed before and after transplant but were not statistically significant ($p > 0.01$).

Conclusions

- CST LD consistently correlated with whole-brain atrophy measures and T2LV at baseline and six months after transplantation. Notably, LD showed a consistent positive relationship with T2LV and an inverse relationship with BPF and GMF. While increased LD has been proposed to indicate increased axonal integrity,⁴ results of this study show further research is warranted.
- CST TD lacked consistent correlation with conventional MRI measures but predicted EDSS score at baseline better than conventional MRI measures alone. This supports TD as a unique indicator of tissue and functional change.
- Significant changes in CST DTI indices before and after MSC transplantation were not found. Significant changes may occur only in selective tracts or defined lesional areas.

ACKNOWLEDGEMENTS

This project was funded through a grant from the Foundation of the Consortium of Multiple Sclerosis Centers MS Workforce of the Future program.

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