# DTI at 3T in patients with clinically isolated syndrome – early progression to multiple sclerosis is related to changes in FA and ADC of normal appearing white matter

C. Krautmacher[1], M. P. Wattjes[1], M. Harzheim[2], O. Gür[1], J. Gieseke[1,3], G. Lutterbey[1], T. Klockgether[2], H. H. Schild[1]

[1]Department of Radiology, University of Bonn, Bonn, Germany, [2]Department of Neurology, University of Bonn, Bonn, Germany, [3]Philips Medical Systems, Best, Netherlands

## Introduction

Recent studies have demonstrated significant changes in fractional anisotropy (FA), mean diffusivity and/or trace in normal appearing white matter (NAWM) of patients with clinically definite multiple sclerosis (MS). These changes are thought to represent occult white matter injury due to Wallerian degeneration from distant lesions[1-3]. So far, all respective studies have been performed in patients with definite MS. The shortest median disease duration (MDD) of any study group was 1.6 years[2]; other groups had much longer MDD (e.g. 13 years[3]). The purpose of this study was to examine whether patients presenting with clinically isolated syndrome (CIS) show similar changes in FA and apparent diffusion coefficient (ADC) measurements. In these patients, determining predictors of the development of clinically definite MS is of great interest. Patients with initial CIS who developed clinically definite MS within the first four months of our longitudinal study were compared to patients who did not progress to MS within that period.

## Materials and Methods

We examined 20 patients with CIS and 8 healthy controls with DTI at 3T. Patients were examined at the time of first presentation. Patients did not receive any treatment before MRI. Extended clinical disability status scale (EDSS) scores ranged between 0 and 3.5 (mean 2.2). DTI was performed using a fat-suppressed single-shot SE EPI sequence acquiring b-values of 0 and 600s/mm$^2$. Sequence parameters were TR 12634ms, TE 63ms, SENSE factor 2.2, 60 slices, measured voxel size 2x2x2mm, FOV 256mm$^2$. ADC and FA maps were calculated. ADC and FA were evaluated by ROI-analysis of different parts of the corpus callosum (CC) and frontal and occipital white matter (FWM/OWM). ROI were manually placed to only include NAWM. Results of patients who developed definite MS within four months and results of patients who did not develop definite MS were compared by Student's t-Test. $p<0.05$ indicated statistical significance.

## Results

Four of the 20 patients with initial CIS developed clinically definite MS within the first four months after initial presentation (20%). Comparing all 20 patients to controls showed no significant differences in both FA and ADC in all white matter regions. The 4 patients who developed MS showed significantly lower FA values in the CC compared to the 16 patients who did not develop MS (p=0.020). ADC values in the 4 patients' OWM were significantly higher than in OWM of the 16 patients who did not progress to MS (p=0.005). This difference was also significant compared to controls (mean ADC in OWM of controls 0.43, p=0.016).

| patients who… | …developed MS | | …did not develop MS | | p | |
|---|---|---|---|---|---|---|
| (means) | FA | *ADC* | FA | *ADC* | FA | *ADC* |
| CC | **0.70** | *0.51* | **0.76** | *0.48* | **0.020** | *0.133* |
| FWM | 0.36 | *0.45* | 0.38 | *0.43* | 0.357 | *0.195* |
| OWM | 0.37 | ***0.50*** | 0.41 | ***0.44*** | 0.192 | ***0.005*** |

## Conclusion

This is the first study to show that DTI detects significant changes in FA and ADC of patients with CIS who develop clinically definite MS within a few months after first symptoms compared to patients with CIS who do not progress to MS during that period. Patients who progress to MS seem to exhibit more severe diffuse injury of their white matter already at the onset of the disease. DTI may prove to be a valuable predictor of early progression of CIS to definite MS.

## References

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