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ORIGINAL ARTICLE

# Applications of MR fiber tractography imaging in multiple sclerosis

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**KEYWORDS**

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**Abstract** *Aim of the study:* To evaluate role of fiber tractography in the assessment of white matter (WM) fiber tract affection in patient with multiple sclerosis (MS).
*Patient and methods:* Using fiber tractography, WM tract fibers were evaluated in 12 patients with MS and 8 healthy controls in correlation with motor disability in variants of MS, ages range 35–50 years, mean 40.9 ± 5.2. MRI imaging was obtained by using 1.5 T whole-body scanner. Fiber tractography was acquired after routine sequences. Data postprocessing and fiber tracking method were applied including fractional anisotropy (FA) and mean diffusivity (MD) for three regions.
*Results:* Bilateral WM tract fiber affection was detected in 7 patients, however only 3 showed left sided lesion and 2 patients on right side. WM tract fiber was decreased in all patients; FA and MD for patients were significantly lowered compared to control on all regions (mean values of control $FA = 1.07 \pm 0.34$, $MD = 1.27 \pm 0.36$, with $P < 0.05$ for all differences).
*Conclusion:* Fiber tractography is a promising non-invasive method for assessing the WM tract affection in patients with MS. It provides an accurate characterization of tissue injury including demyelination and axonal injury.


## 1. Introduction

Multiple Sclerosis (MS) is a chronic inflammatory-demyelinating and neurodegenerative disease of the central nervous system (CNS) and is considered as the most common cause of non-traumatic disability in young and middle-age adults (1)). The clinical course of MS is extremely variable; about 85% of cases present with a clinically isolated syndrome involving the optic nerve, brainstem, or spinal cord In these patients,

*Abbreviations:* DTI, diffusion tensor imaging; FA, fractional anisotropy; FT, fiber tractography; FLAIR, fluid-attenuated inversion-recovery; IC, internal capsule; MD, mean diffusivity; MS, multiple sclerosis; NAWM, normal appearing white matter; ROI, region of interest; RRMS, relapsing-remitting MS; PPMS, primary progressive MS; WM, white matter.

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symptoms and signs typically evolve over a period of several days, stabilize, and then often improve, resulting in a relapsing-remitting (RR) course (2). Persistent signs of CNS dysfunction may develop after a relapse, and the disease may progress between relapses secondary progressive (SPMS). About 15% of patients have primary progressive (PPMS) which is distinguished by a steady progression from the clinical onset, without clear-cut relapses (3). At the initial stage, lesions are typically thin and appear to be linear (Dawson's fingers), these are probably associated with the inflammatory changes around the long axis of the medullary vein that create the dilated periventricular space. Corpus callosum, subcortical region, brain stem, U-fibers, optic nerves, and visual pathway are also regions where lesions are frequently located (4).

The observation that fiber tract loss in the corticospinal tract is associated with distal upstream lesions supports the concept of wallerian degeneration and axonal transection in MS disease (5). Fiber tractography plays a vital role not only in the identification of tracts of interest, but also in the quantification of the degree of axonal loss and demyelination (6). Demyelinating plaques cause destruction of white matter (WM) fibers which are manifested in diffusion tensor imaging (DTI) as increased diffusivity of water molecules (7,8). This can be demonstrated by comparing indices such as the mean diffusivity (MD) and fractional anisotropy (FA) (9). These indices have been successfully applied to study abnormalities in patients with MS by showing reduced FA (increased MD) in MS lesions and the normal appearing WM (NAWM) (10,11). DTI fiber tracking algorithms can be divided into deterministic and probabilistic methods; fiber assignment by continuous tracking is a deterministic method (12,13). FA change gradient has been demonstrated, with lower values being observed close to the plaques and higher values far from the plaques (14,15).

Analysis of tractography results typically involves two approaches; one can measure tract-specific values such as, FA, and mean diffusivity (MD). This approach has found correlation with clinical measures of disability in MS and with functional MRI measures of transcallosal inhibition. The second approach essentially counts streamlines generated by the tractography algorithm. However, this counting approach and the related tract volumetric study demonstrate a relatively high variability and a reduced sensitivity (16,17). Abnormalities in MD and FA in NAWM, cortex, and deep gray matter nuclei are present with the earliest stages of MS and become more pronounced with increasing the disease duration and neurologic impairment (18).

We aimed to study the role of MR fiber tractography in the assessment of WM fiber tract in patients with different grades of MS compared to matched healthy control.

## 2. Patients and methods

This study was approved by the ethics committee of Mansoura University Hospital and a written informed consent was taken from all patients. MRI was performed between February 2013 and March 2014. Patient group includes 12 cases with different clinical grades of MS (9 females and 3 males); mean age was 49.5 years (range 35–50 years). They were clinically classified into 10 RRMS and two PPMS. Eight healthy individuals of matched age (5 females and 3 males) were enrolled as a control group.

Based on history taking and neurologic examination the clinically diagnosed MS cases were subjected firstly to conventional MRI followed by MR tractography.

### 2.1. MRI protocol

MR imaging was performed on a 1.5 T whole-body scanner (Achieva, Philips Medical System, Best, Netherlands). All patients underwent routine pulse sequences, including axial fast spin echo T1, T2 and FLAIR images & coronal T2 and sagittal T1 images: T1-weighted sequences (5 mm slice thickness , no interslice gap, repetition time 450 ms, echo time 15 ms) T2 weighted sequences (repetition time 3963 ms, echo time 110 ms) and FLAIR (repetition time 6000 ms and echo time 120 ms and inversion time 1800 ms).

### 2.2. MRI processing

The processing of Fiber-Tracking Method Anisotropy at each voxel was calculated and color maps were created. A two

**Table 1** Demographic characteristics of the studied patients.

| | |
|---|---|
| Total number | 12 |
| Age (mean ± SD) | 49.5 ± 5.2 |
| Female/male | 9/3 |
| *Symptoms:* | |
| Weakness of UL & LL | 6 (50%) |
| Fatigue | 6 (50%) |
| Visual problems | 3 (25%) |
| Numbness of face | 1 (8.3%) |
| *Side of the lesion* | |
| | Bilateral = 7 |
| | Left = 3 |
| | Right = 2 |
| *Location of the lesions* | |
| | Periventricular WM = 7 |
| | Corona radiate = 2 |
| | Internal capsule = 1 |
| | Frontal region = 1 |
| | Superior cerebellar peduncle = 1 |

UL – upper limb and LL – lower limb.

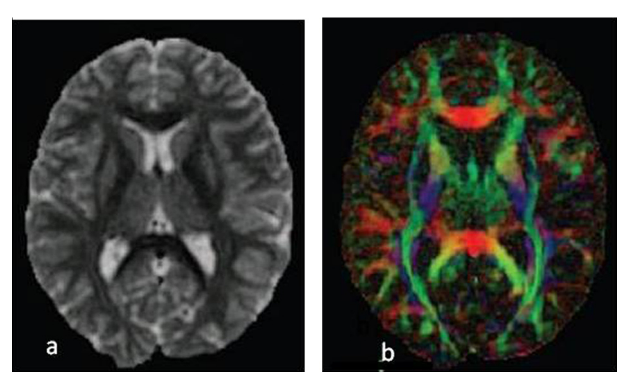


**Fig. 1** Images in 37 years old female healthy control subject (a) conventional MRI T2WI shows normal periventricular WM (b) color map to identify specific WM tracts with red–green–blue color (red fibers with lateral orientation: green antero-posterior: blue, craniocaudal).