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# Evaluation of cerebral white-matter micro-structural alterations in patients with medically refractory epilepsy using diffusion tensor tractography

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**KEYWORDS**
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**Summary**
*Introduction:* Diffusion tensor tractography (DTT) is a newer magnetic resonance imaging (MRI) technique that helps in evaluation of white matter. Presurgical planning with tractography may be valuable for evaluation of white matter tracts and their relationship with epileptogenic focus and for evaluation of cortical fibres around the epileptogenic zone.
*Methods:* This study was carried out on 33 patients diagnosed with medically refractory epilepsy (males, 27; females, 6) with a mean age of 31.93 (range: 19—50) years. Twenty age and sex matched controls were also included. DTT evaluation was done using a 3.0 TexlaMRI scanner. Single-shot spin-echo echo-planar imaging (with 32-different diffusion gradient directions) was acquired for reconstruction of the white matter tracts. Diffusion metrics within fibre bundles that were reconstructed by a continuous fibre-track algorithm were compared between groups.
*Results:* Patients had either partial seizures (21 patients; simple partial, complex partial or secondarily generalized seizure) or generalized seizures (12 patients; tonic clonic, tonic or myoclonic). Out of the 33 patients, 23 patients were classified into the lesional group and the rest into the non-lesional group. The lesions observed on conventional MRI included focal gliosis, hippocampal sclerosis, post-hypoxic encephalopathy, calcification and post-traumatic cavitation, in various parts of the brain. Significant differences were observed in terms

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of fractional anisotropy and mean diffusivity values amongst controls and patients, as well as on the lesional and non-lesional side of the brain; patients with a normal conventional imaging showed fractional anisotropy and mean diffusivity changes as well.
*Conclusion:* We conclude that widespread diffusion abnormalities occur in the white matter tracts on the side of lesion as well as distant from the epileptic focus.


## Introduction

Epilepsy is one of the most common neurological disorders with a prevalence of 0.5—1% in the general population (Sander and Shorvon, 1996). Approximately, one-third patients with epilepsy evolve into a medically refractory state. The varied aetiology of refractory epilepsy includes malformations of cortical development, low-grade tumours, arterio-venous malformations, calcification, genetic syndromes, hippocampal sclerosis, and gliosis (Saini et al., 2009; Rugg-Gunn et al., 2002).

Diffusion tensor imaging (DTI) is a newer magnetic resonance imaging (MRI)-based method, which evaluates the orientation and integrity of white-matter fibres by assessing the diffusion of water molecules in the neurons. DTI enables the determination of directionality of nerve fibres using anisotropy as well as the magnitude of water diffusion (diffusivity). Diffusion tensor tractography (DTT) is a 3D modelling method used to visually represent neural tracts using data collected by diffusion tensor imaging. DTT is an efficient non-invasive technique, which can delineate white matter tracts in vivo. Tractography is an emerging tool in evaluating individuals with refractory epilepsy in pre-surgical planning in order to minimize postoperative deficits, including memory, language and visual field loss. Diffusion-based MRI determines the microstructural changes in the brain associated with recurrent seizures. Besides, establishing the relationship of white matter tracts with epileptogenic tissue and eloquent cortex, it also serves as the building block for the anatomico-functional construct of the various tracts of the brain (Wieshmann et al., 1997; Powell et al., 2007; Yogarajah and Duncan, 2008; Chen et al., 2009; Yogarajah et al., 2009).

Studies on tractography have shown more pronounced white matter alterations on the ipsilateral side of the lesion in patients with temporal lobe epilepsy (Ahmadi et al., 2009). In this study, we used DTT to understand the chronic pathophysiological effects of recurrent seizures on the brain white-matter tracts in lesional and non-lesional refractory seizures. The lesional (with a definite lesion on conventional MR, like gliosis) and the non-lesional (without a definite lesion on conventional MR) group of patients were compared to look for any differences in the DTT metrics. The null hypothesis in our study was that there were no significant changes in the fractional anisotropy or mean diffusivity in our cohort of refractory epilepsy patients with respect to the external controls (matched population) or the internal controls (lesional versus non-lesional side of cerebral hemisphere).

## Materials and methods

The study was conducted in the department of Neurology, King George Medical University, UP, Lucknow, India, a tertiary care centre, from August 2010 to January 2012. Patients diagnosed with medically refractory epilepsy (as described by Berg and colleagues) attending the neurology out-patient department or admitted to the indoor Department of Neurology, were enrolled in the study (Berg et al., 2006). The terminologies and concepts adopted in this study were in accordance with those laid down by the International League Against Epilepsy (Berg et al., 2010). The institutional ethics committee approved the study protocol. Informed consent was obtained from the patients and controls for the MRI examination. All the patients were assessed by detailed clinical history, neurological examination, including neuropsychological assessment, and anti-epileptic drug history. The patients underwent inter-ictal electroencephalography (EEG) as well as video-electroencephalography (Video-EEG) for the purpose of localization.

This study was carried out on 33 patients diagnosed with medically refractory epilepsy (males, 27; females, 6) with a mean age of 31.93 (range: 19—50) years. Based on the seizure semiology, these patients had either partial seizures (21 patients; simple partial, complex partial or secondarily generalized tonic clonic seizures) or generalized seizures (12 patients; tonic clonic, tonic or myoclonic). The mean duration of epilepsy was 10.94 (4—27) years, with an average of 6—7 seizures per month. MRI was normal in 10 patients, 7 of whom had generalized seizure. The mean age of 20 controls (males, 16; females, 4) was 31.62 (range: 19—52) years.

### MRI protocol

MR imaging was performed on a 3.0 Tesla MR imaging system (Signa; GE Healthcare, Milwaukee, Wisconsin) using an eight-channel head coil in the Department of Radiodiagnosis, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India. The routine MRI sequences included T2 fluid attenuated inversion recovery (FLAIR) with echo time (TE)/repetition time (TR)/inversion time/number of excitations (NEX)/number of slice/slice thickness/FOV = 128 ms/9.000 ms/2200 ms/1/46/3 mm/240 $mm^2$; fast spin echo T2-weighted images with TR/TE/NEX = 6820 ms/71 ms/1 with number of slices/slice thickness/FOV = 46/3 mm/240 $mm^2$; 3D fast spoiled gradient echo brain volume with TE/TR/NEX/inversion time/flip