Quantitative Diffusion Tensor Tractography (DTT) of Motor and Sensory White Matter Pathways in Cerebral palsy

R. Trivedi[1], S. Agarwal[2], V. Shah[3], V. K. Paliwal[4], R. K. Rathore[2], and R. K. Gupta[1]

[1]Department of Radiodiagnosis, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India, [2]Department of Mathematics and Statistics, Indian Institute of Technology, Kanpur, India, [3]Pediatric Orthopedic Surgery unit, Bhargava Nursing Home, Lucknow, India, [4]Department of Neurology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India

Introduction: Cerebral palsy (CP) is the term used to describe a variety of neurologic syndromes with disordered movement or posture; mental retardation and seizures may also be present. This condition results from damage to the developing brain from causes such as hypoxia or infection, but in many cases no definitive cause can be ascertained. The pyramidal tract and the somatosensory radiation are among the first white matter tracts to mature. During brain maturation, these two important white matter tracts are susceptible to injury leading to neurological deficits, often resulting in the classic clinical presentation of spastic diplegia / quadriplegia in children born preterm (1). Conventional magnetic resonance imaging (MRI) cannot delineate the white matter pathway of human brain precisely and is of limited use in identifying individual white matter tracts involved in this condition (2). Diffusion tensor imaging (DTI) can demonstrate the orientation and integrity of white matter tracts *in vivo*. Diffusion tensor tractography (DTT) of white matter fibers is a non-invasive method of delineating specific neuronal pathways in three dimensions (3). Besides qualitative localization, DTT also allows individual neuronal pathways to be quantified across regions of the brain where manual segmentation would not be possible. This study investigates the feasibility of both localizing and quantitatively assessing motor and sensory pathways in patients with spastic quadriparesis to understand the microstructural brain damage underlying the motor disability.

Methods and Materials: 39 children with CP (30 males, 8 years mean age) as well as 14 age/sex matched healthy controls were included in this study. Inclusion criteria for the patients group were spastic quadriparesis with or without clinical sensory involvement. All subjects underwent a thorough, video recorded neurological examination by a pediatric surgeon to confirm the findings in patients and to exclude any deficits in controls. Whole brain conventional MRI [T2, T1 and fluid attenuated inversion recovery (FLAIR)] and DTI were performed on a 1.5-Tesla GE MRI system. All imaging was performed in the axial plane and had identical geometrical parameters: field of view (FOV) = 240 × 240 mm^2, slice thickness = 3 mm, interslice gap = 0 and number of slices = 36. DTI data were acquired using a single-shot echo-planar dual spin-echo sequence with ramp sampling. Tracking has been done using FACT algorithm (4). The software enables to select region of interests (ROI)s from the plane orthogonal to the orientation of fiber bundle associated with the thickest part of the fiber bundle. The interface incorporates a number of plug-in for the operations of add/delete selected fibers, morphological trimming operations , adding fibers from another ROI and gathering statistics on the obtained fiber volume or parts of it. The central sulcus was identified and marked on sagittal surface image reconstructed by 3D surface randering of b0 image stack (**Fig a**). By using 3 dimensional cross connectivity between three planes central sulcus was displayed on axial images. Free hand ROIs for FA and MD quantitation were drawn on axial T2 image near the brain's vertex on the precentral and postcentral gyri, and were defined as motor or sensory tracts, respectively **(Fig b, c, and d).** Multiple comparisons using Bonferroni, Post Hoc test was performed to determine the changes in fractional anisotropy (FA) and mean diffusivity (MD) values among controls and patient groups. A p value ≤ 0.05 was considered to be significant.

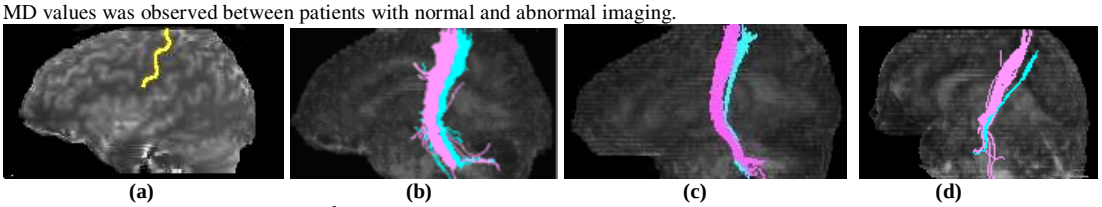
Results: Based on the conventional MRI findings, patients were grouped into normal (n=15) and abnormal (n=24) conventional imaging for the purpose of quantitative DTT analysis. Mean FA and MD values in whole fiber bundles of motor and sensory pathways are summarized in table.

Motor pathway

Significantly decreased FA values were observed in patients with abnormal imaging compared to both controls as well as patients with normal imaging in motor pathway. No significant change in FA values was observed between controls and patients with normal imaging. Significantly increased MD values were observed in both patient groups compared to healthy controls.

Sensory pathway

Significantly decreased FA and increased MD values were observed in both patient groups compared to controls in sensory pathway. No significant change in FA and MD values was observed between patients with normal and abnormal imaging.



(a) **(b)** **(c)** **(d)**

Fig. (a) 3D surface rendering of 7 year old control showing central sulcus (yellow line). **Fig. (b-d)** Projection of motor and sensory fibers on mid sagittal plane in control **(b)**, patient with normal imaging **(C)**, and patient with abnormal imaging **(d)**. Motor tracks (red) are anterior to the sensory (blue) fiber tracks.

Table: Summary of FA and MD ($\times 10^{-3}$) values of whole fiber bundles of motor and sensory pathway from patient groups and controls

Region		Control	Patients with normal imaging	Patients with abnormal imaging	P value
Motor tracts	**FA**	0.32 ± 0.02	0.30 ± 0.02	0.27 ± 0.04	< 0.01
	MD	0.75 ± 0.05	0.81 ± 0.04	0.84 ± 0.07	< 0.01
Sensory tracts	**FA**	0.31 ± 0.02	0.28 ± 0.03	0.27 ± 0.04	< 0.01
	MD	0.75 ± 0.04	0.82 ± 0.05	0.84 ± 0.06	< 0.01

Discussion: This study demonstrates the feasibility of performing DTI fiber tracking for quantitative assessment of motor and sensory pathways in CP patients with normal as well as abnormal imaging. This approach allows 3D delineation of functionally specific white matter tracts across multiple levels of the cerebrum. The descending motor pathway is known to be located in the middle third of the cerebral peduncle and the posterior limb of the internal capsule. Similarly, the somatosensory radiation is known to pass through the internal capsule posterior to the motor tract. However, the motor tract and somatosensory radiation cannot easily be defined or differentiated from other white matter tracts on conventional MR at the level of the corona radiata or centrum semiovale. Based on the present study, it appears that patients with CP with normal imaging on conventional MRI have microstructural damage predominately in the sensory pathway. The degeneration of various motor and sensory pathways appears to be important in understanding of pathophysiological mechanisms in patients with CP. These observations of decreased FA along with increased MD in motor and sensory pathway of patients with normal and abnormal imaging suggest a net loss and disorganization of the structural barriers to molecular diffusion of water. In the patients with normal as well as abnormal imaging, significantly decreased FA with increased MD values was observed in sensory pathway compared to controls. However, significantly decreased FA values in motor pathway compared to controls were observed only in patients with abnormal imaging, which suggest that the abnormality on conventional imaging appears with involvement of sensory along with motor pathways. In conclusion, this quantitative DTT characterizes the trends in spatially averaged diffusivity and FA for the CP patients with normal as well as abnormal imaging in motor and sensory tracts.

Reference: (1) Berman et al. NeuroImage 2005,27:862– 871; (2) Thomas B, et al. Brain 2005;128:2562-2577; (3) Basser et al. Magn Reson Med 2000,44:625– 632; (4) Mori et al. Ann Neurol 1999,45:265–69.