Quantitative improvement in FA values in various fiber bundles is associated with improvement in Clinical Grade of children with Cerebral Palsy following therapy

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Introduction: Cerebral Palsy (CP), a common form of perinatal brain damage, has been defined as a group of disorders of the development of movement and posture. Impairment in the motor functioning of patients with CP is often accompanied by disturbance of sensation, cognition, communication, perception, behavior and/or seizure[1]. Term infants with spastic diplegia manifest a wider variety of MRI abnormalities including periventricular leukomalacia, and porencephaly, or may also present with normal conventional MRI[2]. In most studies, DTI metrics have been obtained using region of interest (ROI) analysis[3]. ROI based morphometric DTI analysis is limited to 2dimensions (D) and does not reflect the changes in whole fiber bundle. The information about the direction of diffusion encoded by the eigenvalues and eigenvectors of the diffusion tensor has been used in DT tractography to investigate the continuity of axonal orientation between voxels, and thus to infer the paths of fiber tracts in 3D. In the present study, we analyzed, fractional anisotropy (FA) and apparent diffusion coefficient (ADC) values in anterior thalamic radiation (ATR), posterior thalamic radiation (PTR), inferior longitudinal fasciculus (ILF), superior longitudinal fasciculus (SLF), corpus callosum (CC), cingulum (CG), sensory and motor tracts of children with spastic diplegia, at baseline and follow up after therapy to look for the possible differences between the two time points and also to see if these metrics correlate with gross motor function measurement (GMFM) scores.

Materials and Methods: We examined 10 CP children twice (10 base line and 10 follow up at 6 month; 8 boys and 2 girls) (mean age=6 years) who had spastic diplegia. All these children were born at term (37 to 40 weeks gestational age) and had no history of seizures. The diagnosis of CP was based on clinical observations: delayed motor milestones, abnormal neurologic examination, persistence of primitive reflexes, and abnormal postural reactions. All patients were assessed through standard clinical examination, GMFM scale[4] and modified Ashworth scale (to measure spasticity) by an experienced physiotherapist. Only those children were included who had GMFM score ranging from 50-60 and grade II on Ashworth scale. Whole brain conventional MRI (T2, T1 and FLAIR) and DTI were performed on a 3-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=3mm, interslice gap=0 and number of slices=46. DTI data were acquired using a single-shot echo-planar dual spin-echo sequence with ramp sampling. The diffusion tensor encoding used was a vender supplied DTI scheme with 30 uniformly distributed directions and a b-factor=1000s/mm^2. Fiber assignment by continuous tracking (FACT) algorithm was used for reconstruction of fibers. The white matter fiber tracts were generated as described in detail elsewhere[5]. **Statistical analysis:** Paired t- test was performed to measure difference in DTI metrics and GMFM score of baseline and follow-up. Bivariate analysis of correlation was performed to study the relationship between DTI metrics and GMFM score.

Results: Significant mean differences were observed between FA values of baseline [left motor (0.37±0.04), left sensory (0.35±0.04), CG (0.32±0.06), ATR (0.32±0.03), PTR (0.36±0.03)] and follow-up in left motor (0.42±0.04,p=0.003), left sensory (0.39±0.04,p=0.007), CG (0.37±0.06,p=0.01), ATR (0.35±0.03,p=0.019), PTR (0.38±0.03,p=0.02) (fig.1). A significant positive correlation was found between GMFM scores and FA values of left motor (r=0.723, p<0.001), left sensory (r=0.609, p=0.004), CG (r=0.787, p<0.001) and ATR (r=0.420, p=0.065) (fig.2). The ADC values of any region and also FA values of rest of the regions did not correlate significantly with GMFM score. Though not significant, there was an increase in GMFM scores on followup as compared to the baseline (fig.3). In 8 of the ten children studied, there was an asymmetrical spasticity (predominantly right sided), and rest of the two were having symmetric spasticity.
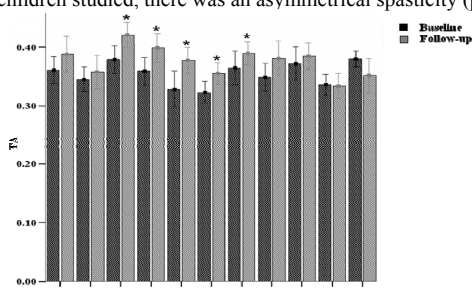

Fig 1: Bar diagram (left to right) showing differences in FA values of right motor&sensory, left motor& sensory, cingulum, anterior, posterior& superior thalamic radiation, superior&inferior longitudinal fasciculus between baseline and followup study. *Represents significant difference
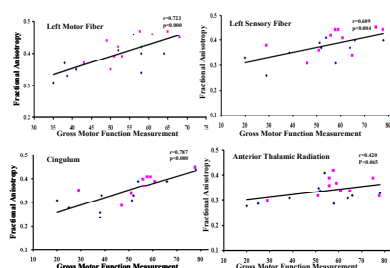

Fig 2: Scatter plots showing correlation of FA values of fibre bundles from left motor & sensory, cingulum and anterior thalamic radiation regions with GMFM scores.
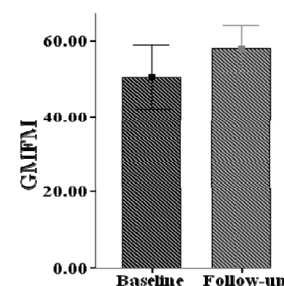

Fig 3: Bar diagram showing differences in gross motor function measurement (GMFM) scores in baseline and followup study.

Discussion: It is well known that FA represents the integrity of white matter tracts. In a previous study using ROI method to quantify DTI metrics, improvement in FA values in white matter regions of CP patients following treatment has been reported[3]. They suggested that it is due to use-dependent plasticity in these regions that is further confirmed by improved clinical staging. Similarly, in this study we observed an increase in FA values of left motor & sensory, CG, ATR and PTR region fibers on follow-up as compared to the baseline. We have also observed a significant positive correlation of FA values in left motor & sensory and CG fibres with GMFM scores obtained at both the time points indicating that improvement in FA values coincide with clinical improvement in these regions. The improvement in FA values at follow-up further suggests the reorganization of these white matter tracts with treatment.

References : 1) Bax et al. *Dev Med Child Neurol* 1964;6:295-97. **2**) Menkes et al. *Child Neurology*. Philadelphia, Lippincott Williams & Wilkins, 2000;401-66. **3**)Trivedi et al. Pediatr Neurol 2008;39:341-49.**4**) Bohannon et al. *Phys Ther* 1987;67:206-7.**5**) Rathore et al. *Magn Reson Imaging*. 2011;29:1088-100.