

# BRAIN DEVELOPMENT IN PRETERM INFANTS AT TERM EQUIVALENT AGE: ASSESSMENT USING DTI

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## Introduction

Infant born preterm have a high incidence of neurodevelopmental impairment, comparing with full-term infants. Preterm infants have an increased risk of future neurodevelopmental impairment that is correlated with the degree of prematurity at birth. [1] Development of brain white matter (WM) study based on DTI may allow prediction of later neurodevelopmental outcome. Especially tract-based spatial statistics (TBSS) performed spatial normalization for group analyses in multi-subject diffusion data. In this study, we performed analyses of brain development between full-term infants and preterm infants at equivalent age using TBSS.

## Method

**Subject :** We studied 45 infants who were obtained on 13 full-term control infant and 32 preterm infants at term-equivalent age. Infants were recruited from the Gil Hospital in Korea. Clinical details of the infants are given in **Table 1**. There were no significant differences in age at scanning ( $p=0.14$ ) between the preterm group and the full-term group. **MRI acquisition :** We used a conventional 3.0T MRI (Verio, Siemens) using Siemens matrix coil. Diffusion weighted images were acquired using a spin-echo based single-shot echo-planar diffusion sequence. The DTI sequence parameters were as follows :  $b = 0$  and  $700 \text{ s/mm}^2$ ,  $\text{TR/TE} = 6600/74 \text{ ms}$ , number of diffusion gradient directions = 30, number of excitations = 2,  $\text{FOV} = 230 \text{ mm}$ , matrix =  $128 \times 128$ , slice thickness =  $1.8 \text{ mm}$ , voxel =  $1.8 \times 1.8 \times 1.8 \text{ mm}$ , Flip angle =  $90^\circ$ . The scanning time for the DTI sequence was 7min 36seconds. **Image analysis :** The diffusion weighted images were processed with FMRIB Software Library (FSL, Oxford, United Kingdom). [2] The DTI data was first corrected for eddy current induced spatial distortion using non diffusion weighted ( $b=0$ ) image. Images were brain-extracted by using BET [3] and individual FA, MD maps as well as the eigen-value maps ( $\lambda_1$ ,  $\lambda_2$  and  $\lambda_3$ ) were generated by using DTIFit implemented in FSL [4]. We calculated values of axial ( $\lambda_1$ ) and radial ( $(\lambda_2 + \lambda_3)/2$ ) diffusivity using MATLAB (Math works, Natick, MA). Voxelwise statistical analysis of FA was carried out with Track-Based Spatial Statistics (TBSS). [5] TBSS performed spatial normalization for group analyses. To normalize FA images, all subjects' FA map were aligned into a common space using a non-linear registration algorithm. The normalized FA images of all subjects were combined to create a group specific mean FA image. Then, the mean FA image created a mean FA skeleton which represented the centres of all tracts common to the group. Each subject's aligned FA data were projected onto mean FA skeleton. **ROIs :** Five additional regions of interests (ROIs) were chosen from a TBSS-generated skeleton FA-slice : (1) Corpus callosum, (2) Interior limb of internal capsule, (3) Posterior limb of internal capsule, (4) Optic radiation, (5) Cerebral peduncle.

## Results

Group-wise voxel-based comparisons between full-term infants and preterm infants revealed significantly decreased FA values in preterm infants at term equivalent age. **Figure 1**, shows red-yellow regions showing reduced FA in preterm infants compared to full-term infants ( $p < 0.01$ ; TFCE-corrected). There were significant inter-group differences on corpus callosum ( $p < 0.01$ ), interior limb of internal capsule ( $p < 0.01$ ), posterior limb of internal capsule ( $p < 0.01$ ), optic radiation ( $p < 0.01$ ), cerebral peduncle ( $p < 0.01$ ). There were no white matter regions with increased FA in preterm infants. **Figure 2(A)**, shows FA value for full-term infants and preterm infants in 5ROIs. FA values of full-term infants were significantly higher than FA values of preterm infants for all investigated ROIs ( $p < 0.05$ ). We found that performance gestational age was related to FA values in the corpus callosum (76 voxels), interior limb of internal capsule (14 voxels), posterior limb of internal capsule (34 voxels), optic radiation (39 voxels), cerebral peduncle (6 voxels) (**Fig. 2B-F**). We found FA value in the corpus callosum positively correlated with the GA ( $r = 0.004$  ; **Fig 2B**), FA in the posterior limb of internal capsule positively correlated with the GA ( $r = 0.003$  ; **Fig 2C**), FA in the interior limb of internal capsule positively correlated with the GA ( $r = 0.003$  ; **Fig 2D**), FA in the optic radiation positively correlated with the GA ( $r = 0.005$  ; **Fig 2E**), FA in the cerebral peduncle positively correlated with the GA ( $r = 0.006$  ; **Fig 2F**).

## Discussion

The comparison of FA map between preterm infants and full-term infants at term equivalent age revealed significant differences in FA map corresponding to the cerebral white matter. FA values in the CC, PLIC, ILIC, optic radiation, cerebral peduncle decreased in preterm infants and were positively correlated with gestational age at birth. We show that growth of white matter is gestation dependent. Longitudinal study is needed to define the catch-up growth in preterm infants.

## Reference

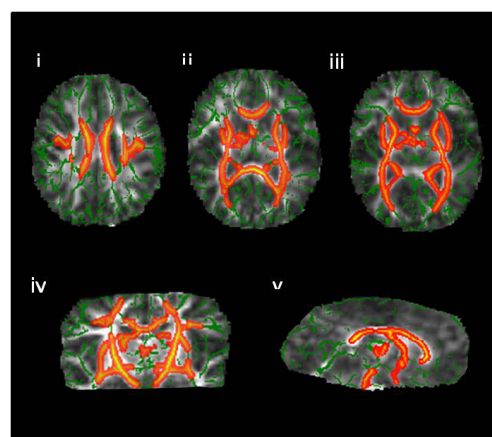
[1] Wood NS, et al. *Arch Dis Child Fetal Neonatal Ed.* 90(2):F134-F140 (2005), [2] Smith, S.M, et al. *Neuroimage.* 23Suppl 1:S208-19 (2004) [3] Smith, S.M, et al. *Hum Brain Mapp.* 17(3):143-55.(2002) [4] Behrens, T.E et al. *Magn Reson Med.* 50(5):1077-88 (2003), [5] Smith, S.M, et al. *Neuroimage.* 31(4):1487-505 (2006).

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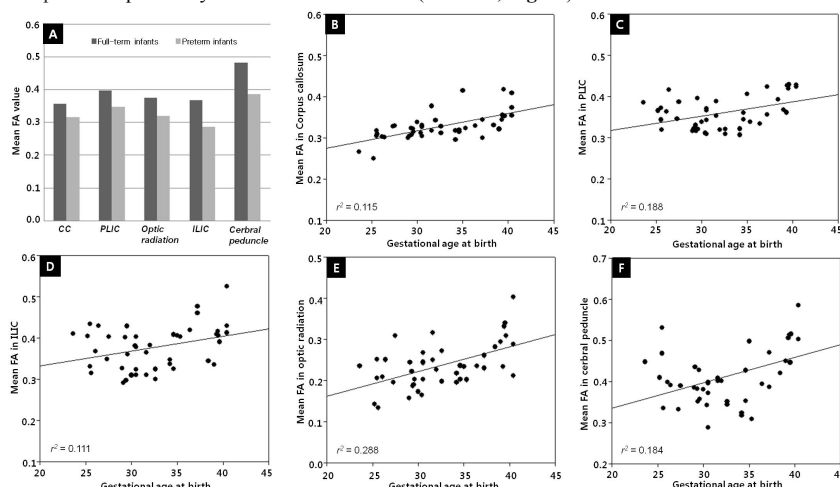
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**Table 1.** Characteristics of all subjects.

demographics	All subjects (n=45)	
	Full-term infant	Preterm infant
Number of participants	13	32
Birth weight, g	3100 (2800 - 4000)	1396 (550 - 2800)
Gestational age, wks	38 <sup>+2</sup> (37 <sup>+0</sup> ~ 40 <sup>+4</sup> )	30 <sup>+1</sup> (23 <sup>+6</sup> ~ 36 <sup>+4</sup> )
Age at MRI	39 <sup>+4</sup> (37 <sup>+4</sup> ~ 42 <sup>+4</sup> )	38 <sup>+2</sup> (34 <sup>+4</sup> ~ 42 <sup>+2</sup> )



**Fig 1.** TBSS analysis of FA map. mean FA skeleton (green) overlaid on mean FA map in axial (i - iii), coronal (iv) and sagittal (v) plane. Areas in red-yellow represent voxels where the FA was significantly lower in the preterm infants. ( $p < 0.01$ ; TFCE-corrected)



**Fig 2.** Comparison to FA values for full-term infants and preterm infants in ROIs (A). (B-F) Graph demonstrating correlation between FA value and gestational age in ROIs shown in the corpus callosum (B), Interior limb of internal capsule (C), Posterior limb of internal capsule (D), Optic radiation (E), Cerebral peduncle (F).