# COMPARISON BETWEEN THE SINGLE-COMPARTMENT AND TWO-COMPARTMENT PARAMETERS DERIVED FROM DIFFUSION KURTOSIS IMAGING IN ASSESSING THE AXON GROWTH

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**Target audience:** pediatric researchers and clinicians.

**Purpose**

During the postnatal period, white matter fibers are undergoing structural changes both in the intra-axonal and extra-axonal spaces [1]. Conventional diffusion tensor imaging (DTI) is developed based on single compartment with the hypothesis that water diffusion is Gaussian. However, the water diffusion in biologic tissues is non-Gaussian. And the signal decay is not monoexponential when applying high b-value [2]. Diffusion kurtosis imaging (DKI) [3] may be able to solve the above problems. Specific parameters of white matter model for DKI are proposed based on two compartments, including intra-axonal ($D_a$), extra-axonal axial ($D_{e,//}$) and radial ($D_{e,\perp}$) diffusivities [2]. The purpose of this study was to compare the performances of the single-compartment and the two-compartment parameters in assessing the axon growth.

**Methods**

The study was approved by the local Ethics Committee. Written informed consents were obtained from the parents of the neonates and the adults. In this study, 44 subjects were examined, including 22 term neonates (11 males and 11 females; gestational age (GA) range: 38 ~ 41 weeks, median = 39 weeks; postmenstrual age (PMA): 39 ~ 44 weeks, median = 40 weeks) and 22 adults (11 males and 11 females; GA range: 37 ~ 40 weeks, median = 39 weeks; postnatal age: 18 ~ 26 years, median = 22 years). There were no significant differences in sex, or gestational age between neonates and adults. Subjects who were confirmed or suspected to have congenital malformations of central nervous system, congenital infections, metabolic disorders, abnormal appearances in conventional MRI were all excluded.

The neonates were all sedated with oral chloral hydrate before MRI scan. DKI by single short echo planar imaging sequence was performed in a 3T scanner (Signa HDxt, General Electric Medical System, Milwaukee, WI, USA) with an 8-channel RF head coil. DKI was carried out with the following variables: b values = 500, 1000, 2000, 2500 s/mm$^2$; 18 gradient directions; TR = 8000 ~ 11000 ms; TE = 91.7 ~ 126.1 ms; 20 ~ 33 axial slices with thickness = 4 mm without gap; field of view = 180 × 180 mm$^2$ for neonates and 240 × 240 mm$^2$ for adults; acquisition matrix size = 128 × 128 for neonates and 172 × 172 for adults. Artifact-corrupted diffusion weighted images were excluded by using an automated method [4]. Diffusion tensor and kurtosis tensor were estimated by using constrained weighted linear least squares (CWLLS) [5]. Parametric maps of fractional anisotropy (FA) were derived from the diffusion tensor. $D_a$, $D_{e,//}$, and $D_{e,\perp}$ were subsequently calculated according to the white matter model for DKI [2].

The FA images of neonates and adults were normalized to the neonatal FA template of Johns Hopkins University [6] and the adult FA template in FSL [7], respectively. Fourteen regions of interests (ROIs) were selected by using the white matter labels (as shown in Figure 1). The ROIs included: the projection fibers: anterior limb of internal capsule (ALIC), posterior limb of internal capsule (PLIC), retrolenticular part of internal capsule (RLIC), anterior corona radiata (ACR), superior corona radiata (SCR), posterior corona radiata (PCR), posterior thalamic radiation (PTR); the commissural fibers: corpus callosum (CC); the association fibers: superior longitudinal fasciculus (SLF), external capsule (EC), superior fronto-occipital fasciculus (SFO), uncinate fasciculus (UNC); and the limbic fibers: cingulum cingular part (CGC), cingulum hippocampal part (CGH).

Inter-group differences of the regional values were tested by using the Wilcoxon Signed Rank Test on SPSS version 13.0 (SPSS Inc., Chicago, IL, USA).

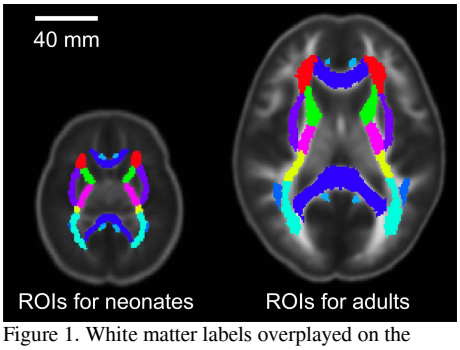


Figure 1. White matter labels overplayed on the mean FA maps.

**Results and discussion**

In this study, we investigated changes of the intra-axonal and extra-axonal diffusivities, as well as the single-compartment fractional anisotropy (FA) through the comparison between the neonates and adults. FA was more sensitive than the diffusivity parameters in DTI [8]. However, FA was not a specific parameter. White matter model for DKI provided specific parameters for different compartments. $D_a$ was a biomarker specific to structural changes in the intra-axonal space. $D_a$ demonstrated largest relative changes in adults (as shown in Figure 2). This was in agreement with the fact that the myelinated axon was more than twice the axon caliber of the unmyelinated axon [1]. The developmental increase of the axon caliber made the intra-axonal water diffusion or axoplasmic motion easier, causing the increase of $D_a$. With regard to the extra-axonal space, many physiological changes could influence the diffusivities. The increasing alignment degree of fibers and the gilial cells proliferation were two counteracting factors influencing the changes of diffusivity on the axial direction. Therefore few significant changes of $D_{e,//}$ were found. On the radial direction, the decrease of $D_{e,\perp}$ was mainly caused by the gilial cell proliferation and myelination.

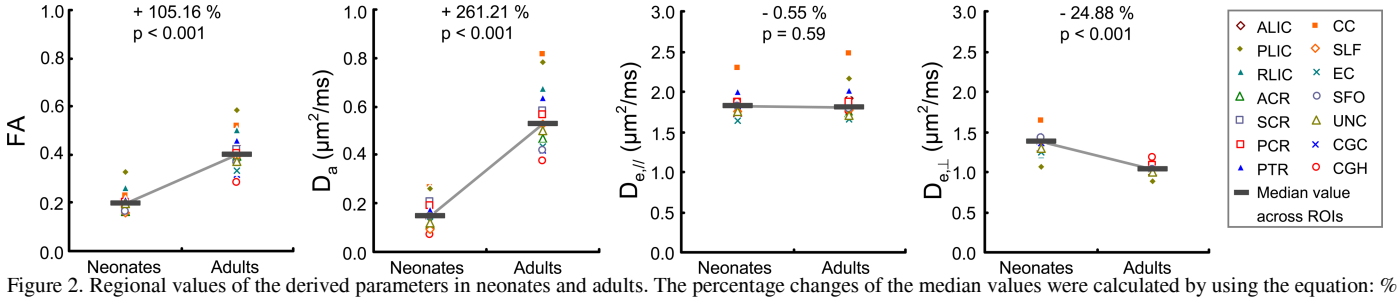


Figure 2. Regional values of the derived parameters in neonates and adults. The percentage changes of the median values were calculated by using the equation: % changes = (values of adults - values of neonates) / values of neonates.

**Conclusion**

The intra-axonal diffusivity was a sensitive biomarker for the assessment of the axon growth. White matter model for DKI provided more detail information for investigating the white matter development.

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