

## Diffusion changes in early brain development beyond diffusion tensor imaging

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### Introduction

Early brain development has been well documented with diffusion tensor imaging (DTI) for the initial increase in fractional anisotropy (FA) and decrease in mean diffusivity. But a single tensor model based representation of diffusion profiles only provides a limited view on the development of complex white matter structures not assuming a cylindrical diffusion profile such as kissing, crossing or fanning. Thus, high angular resolution diffusion imaging (HARDI) [1] and diffusion spectrum imaging (DSI) [2] are strategically advantageous than DTI in quantifying complex diffusion patterns. To move the early brain developmental study beyond DTI, we have performed a large scale longitudinal study on diffusion profiles obtained with HARDI.

### Methods

This study was approved by our institutional review board. We have included a total of 241 datasets from 168 subjects (91 males, 77 females) repeatedly scanned at early after birth (92 datasets, ages:  $0.072 \pm 0.044$  years), 1 year (78 datasets, ages:  $1.056 \pm 0.068$  years) or 2 years (71 datasets, ages:  $2.064 \pm 0.089$ ) after birth. Diffusion weighted images (DWI) were acquired with 42 diffusion encoding directions. Registrations towards a template FA image (not included in the statistical analysis) were performed with a similarity metric derived from geometrical momentum attributes of FA images [3]. Each subject's diffusion profiles represented with spherical harmonics (SH) were reoriented towards the template with a global reorientation matrix computed as a rotational approximation to the affine transformation from the subject towards the template [4]. DWI signals were fitted with even ordered SH up to the 6<sup>th</sup> order so that the diffusion profile at each voxel was represented with a total of 28 coefficients ( $c_{i,j}$  representing the  $j^{\text{th}}$  coefficient of order  $i$  SH ( $i=0,2,4,6; j=-i, -i+1, \dots, i$ )). Longitudinal analysis was performed with generalized estimating equations (GEE) based Wald statistics [5] to detect brain regions under significant age effect in a series of SH parameters ( $y = a0 + a1 * \text{age}$ ). To focus on the diffusion properties not available to DTI, we have examined 1) the power of the diffusion represented by the 4<sup>th</sup> ( $P_4 = \sum_{j=-4}^4 c_{4,j}^2$ ), and 6<sup>th</sup> ( $P_6 = \sum_{j=-6}^6 c_{6,j}^2$ ) ordered SH [6], 2) a multi-fiber index within a voxel ( $R_{\text{multi}} = \sum_{i \geq 4, j} |c_{i,j}| / \sum_{i,j} |c_{i,j}|$ ) [7], and 3) 4<sup>th</sup> order SH coefficients ( $c_{4,-4}, c_{4,-3}, \dots, c_{4,4}$ ).

### Results

At the slice location indicated by the template FA image (A), growth velocities of  $P_4$  (B) and  $P_6$  (C) were spatially inhomogeneous even in major white matter tracts, increasing in genu and posterior limbs of internal capsule while decreasing in splenium (red cross,  $P_4$ :  $-0.358/\text{year}$ ,  $P_6$ :  $-0.062/\text{year}$ ).  $R_{\text{multi}}$  increased in most white matter regions including major white matter tracts ( $\sim 0.05/\text{year}$  in splenium). Significant temporal changes were detected in multiple white matter regions in all these SH parameters (E for  $P_4$ , F for  $P_6$ , G for  $R_{\text{multi}}$  and H for 4<sup>th</sup> order SH coefficients) with the greatest changes identified with  $R_{\text{multi}}$ , indicating the increasing velocity observed in D were statistically significant during early postnatal white matter maturation.

### Discussion and Conclusions

In this study, we provided the evidence that HARDI enables detection of significant temporal changes during early brain development from multiple perspectives: 1) absolute diffusion power in high order SH, 2) relative weight of high order SH components compared to order 2 SH and 3) geometrical shapes of the diffusion profiles. Thus, our findings provide a new means which potentially can link the observed diffusion changes with the underlying white matter structures. To the best of our knowledge, our study is the first diffusion based early brain developmental study moving beyond the DTI regime.

### References

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