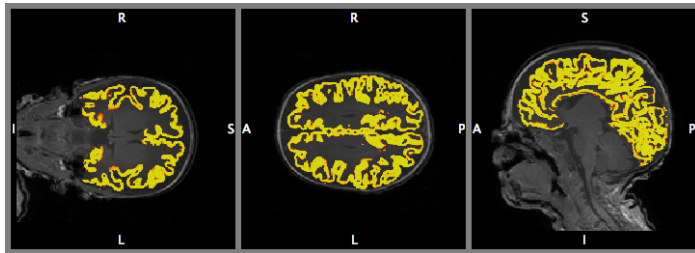


# Cortical maturation in the preterm period revealed using a multi-component diffusion-weighted MR model.

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**Target Audience:** Researchers or clinicians with an interest in diffusion imaging as applied to a preterm neonatal cohort.

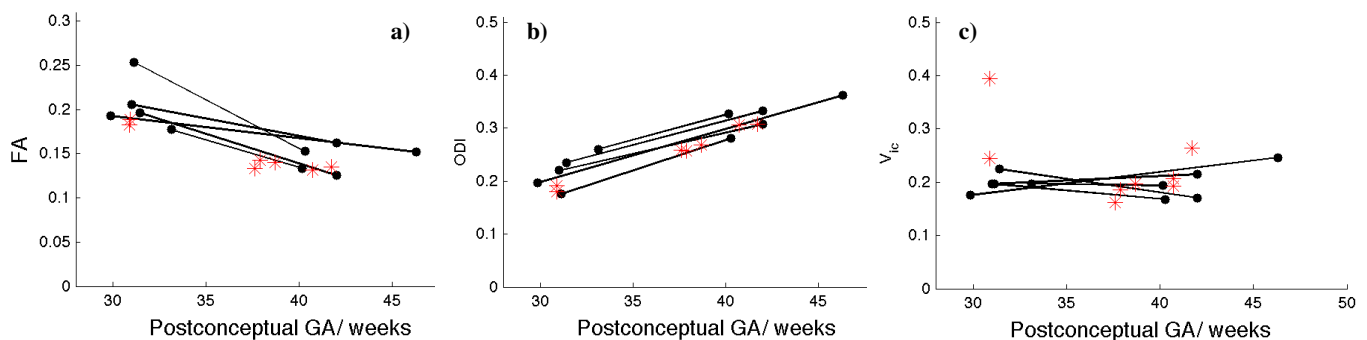
**Introduction/Purpose:** The human brain undergoes radical transformation late in gestation and cortical folding occurs largely during this period. In the cortex, radial glial cells act as scaffolding for neural migration, which has been imaged using the diffusion tensor model<sup>1</sup>. The cortical fractional anisotropy (FA) drops markedly during the preterm period as dendrites are elaborated and water diffuses more isotropically. However, FA is a summary measure and the same parameter value can represent a range of microstructure. Neurite Orientation, Dispersion and Density Imaging (NODDI)<sup>2</sup> uses a multi-compartment model, with multi-shell acquisition, to fit parameters relating to geometric properties and neuronal packing. Thus it disentangles contributions to the FA or other DT parameters and we gain greater insight into the microstructure. Very preterm infants (VPT = <32 weeks completed gestation) are vulnerable to crucial maturational processes being disrupted. By imaging cortical microstructure with the NODDI model, we aim to identify normal and abnormal patterns of growth so as to facilitate earlier and more targeted intervention.



**Figure 1:** A representative cortical segmentation of a 40-week infant.

**Methods:** 13 VPT infants ( $25.6 \pm 0.9$  weeks gestational age (GA)) with normal cerebral ultrasound imaging were scanned soon after birth ( $32.0 \pm 1.9$  weeks GA) and at term equivalent age ( $41.7 \pm 3.7$  weeks GA). We acquired DWI in a 3T Philips MRI scanner with 6 volumes at  $b = 0 \text{ mm}^2$ , 16 at  $b = 750 \text{ mm}^2$ , 32 at  $b = 2000 \text{ mm}^2$  (48 diffusion directions in total); resolution =  $1.75 \times 1.75 \times 2.00 \text{ mm}^3$ ,  $T_R = 9 \text{ s}$  and  $T_E = 60 \text{ ms}$ , with total duration 11m43s. We removed motion-corrupted volumes and eddy-current corrected the remaining data, rotating the b-vectors and modulating by the expansion/contraction of the transformation (Jones). We used the 'AdaPT'<sup>3</sup> algorithm to segment the cortical regions of the brain. We fitted the NODDI model in the cortex and evaluated the three volume

fractions:  $v_{ic}$  (intra-cellular),  $v_{ec}$  (extra-cellular) and  $v_{iso}$  (isotropic, representing CSF), each of which has its own signal equation. The intra-cellular signal depends on the orientation dispersion index (ODI) – a summary measure of how dispersed the local structure is.



**Figure 2 a, b, c:** Parameter values against gestational age. Black lines join data points from the same infant. Red crosses represent infants with one time-point only.

**Results/discussion:** We segmented the cortex (Figure 1) and reproduced previously-reported decreases in FA (Figure 2a). The ODI increased significantly (Figure 2b) which we interpret as being due to the addition of basal dendrites and disappearance of radial glia, known in histology and suggested as a factor in diffusion imaging by McKinstry<sup>1</sup>. The  $v_{ic}$  shows no trend during this period (Figure 2c). Although there is histological evidence for increasing dendritic density<sup>3</sup> this will not necessarily manifest itself as a change in  $v_{ic}$ . In the NODDI model,  $v_{ic}$  represents the fraction of the voxel that has directional diffusion over a distribution determined by the ODI parameter. Because the ODI is increasing, the model may not be able to distinguish highly-dispersed intra-axonal space from the hindered diffusion in the extra-axonal space. However, the NODDI parameters have highlighted that the decreases in FA arise largely from increased dispersion in the water's diffusion. This stands in contrast to white matter regions, where the orientation is unchanging and the  $v_{ic}$  increasing in this time period.

**Conclusion:** The formation of neuronal connections is vital in development. We have shown that the decrease in cortical FA reflects an increase in orientation dispersion, while other microstructural parameters remain constant. By linking disrupted cortical maturation to measures of cognitive outcome over the first two years of life, we will be able to develop specific measures of cognitive outcome for clinicians to use to aid this at-risk population.

**References:** [1] McKinstry *et al*, *Cereb. Cortex*, vol. 12, 2002. [2] Zhang *et al*, *Neuroimage*, vol. 61, 2012. [3] Cardoso *et al*, *Neuroimage*, vol. 65, 2013. [4] Sizonenko *et al*, *Cereb. Cortex*, vol. 17, 2007.