Measurement of white matter maturation in the preterm brain using NODDI.

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

Purpose: Very preterm (VPT = <32 weeks completed gestation) infants are more likely to suffer from neurodevelopmental disabilities and recurrent health problems[1]. Adverse outcome is associated with white matter damage as revealed by diffusion-weighted imaging (DWI) and the diffusion tensor (DT) model[2]. However, a particular value of a DT parameter such as FA or MD can represent a range of microstructural conditions. Neurite Orientation, Dispersion and Density Imaging (NODDI)[2] uses a multi-compartment model, with multi-shell acquisition, to fit more specific parameters relating to geometric properties and neuronal packing. This separates some of the contributors to the DT parameters and enables local microstructure to be inferred. This has been performed in the infant brain at term[3] and this approach shows greater specificity than the DT model[2,3].

Using NODDI parameters, we investigated how microstructure changes in white matter regions of interest for VPT infants during the preterm period. The specificity of the parameters will aid in determining imaging biomarkers of cognitive health and facilitate earlier and more effective therapeutic intervention. To the authors' knowledge, this abstract represents the first time that the longitudinal changes in these parameters have been mapped in the preterm population.

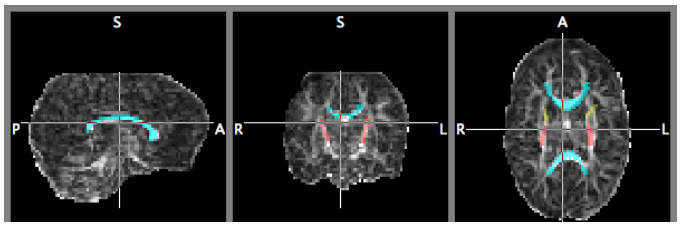

Figure 1: CC (blue), PLIC (red) and ALIC (yellow)

Methods: Eight VPT infants (26.3 ± 0.8 weeks gestational age (GA)) with normal cerebral ultrasound imaging were scanned soon after birth (32.4 ± 1.8 weeks GA) and at term equivalent age (44.2 ± 3.5 weeks GA). We acquired DWI in a 3T Philips MRI scanner with 6 volumes at b = 0s.mm^{-2}, 16 at b = 750 s.mm^{-2}, 32 at b = 2000 s.mm^{-2} (48 diffusion directions in total); resolution = 1.75x1.75x2.00 mm^3, TR = 9s and TE = 60ms, 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[4]. We fitted the diffusion tensor using non-linear least squares[5]. To identify the corpus callosum (CC), posterior and anterior limbs of internal capsule (PLIC/ALIC), we registered an FA atlas image[6] to each infant non-linearly[7] and propagated the labels with this transformation. These were adjusted manually. We fitted the NODDI model in the regions of interest and evaluated the three volume fractions: v_{ic} (intra-cellular), v_{ec}(extra-cellular) and v_{iso}(isotropic), 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.

Results & Discussion: We confirmed previously reported increases in FA during the preterm period (Fig 2.a). We observed significant increases in v_{ic} in all three regions, with similar rates of growth (Table 1). This suggests a global pattern of maturation in the white matter, perhaps due to reduced water content or axonal growth. The PLIC has higher values of v_{ic} compared to the CC and ALIC. This may represent increased myelination at term; myelin development on axons will be seen in the model as a reduction in v_{ec} – and hence an increase in v_{ic}.

Parameter ➔ Region ⬇	FA at: Preterm	Term	ODI at: Preterm	Term	V_{ic} at Preterm	Term
CC	.27±.02	.33±.03	.10±.02	.09±.02	.15±.02	.22±.04
PLIC	.37±.05	.50±.05	.10±.09	.09±.02	.21±.02	.32±.04
ALIC	.18±.04	.25±.03	.21±.05	.21±.05	.14±.02	.22±.04

Table 1: Average values of diffusion parameters ± standard deviation. Green signifies a significant increase. 'Preterm' signifies the scan taken shortly after birth, 'term' means at term-equivalent age.

The ODI showed no maturational trend in any of the areas (Fig. 2b). The ALIC has significantly higher ODI values compared to the other regions (Table 1, $p < 10^{-3}$ for each subject). The low ODI values in the CC and PLIC may reflect the parallel fibre bundles that are seen in histology. The ALIC's higher ODI may represent its lower maturity than the PLIC, but could also reflect partial volume effects caused by the smaller physical size of the ALIC. However, the CC has a higher FA than the ALIC but not a higher v_{ic} – using the NODDI parameters, we can infer that these differences are due to a higher degree of alignment rather than a higher fibre density. Thus the NODDI model distinguishes microstructural environments that are conflated using the FA measurement alone.

Conclusion: We have shown, for the first time, how NODDI parameters change in white matter regions of interest during 29-48 weeks EGA for the same infants. NODDI successfully disentangles microstructural contributions to the FA while still being performed within a clinically acceptable timeframe. By comparing microstructural parameters to cognitive tests undertaken during the first two years of life, we will determine more specific imaging biomarkers for future cognitive performance.

References: [1] Boardman *et al*, *Neuroimage*, vol. 52, 2010. [2] Zhang *et al*, *Neuroimage*, vol. 61, 2012. [3] Kunz *et al*, *ISMRM - Press*, vol. 21, 2013. [4] Jones *et al*, *NMR Biomed.*, vol. 23, 2010.[5] Alexander *et al*, *Neuroimage*, vol. 27, 2005.[6] Oishi *et al*, *Neuroimage*, vol. 56, 2011.[7] Modat *et al*, *Comput. Methods Programs Biomed.*, vol. 98, 2010.

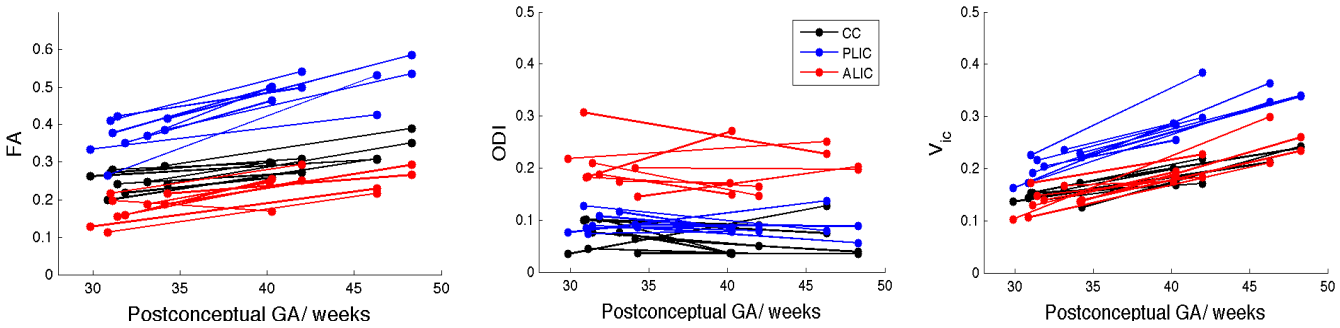

Figure 2 a, b, c: Diffusion model parameters against post-conceptual age. Lines join the values for preterm and term scans of the same infant.