Neurite Orientation Dispersion and Density Imaging (NODDI) Adds Biophysical Insight of White Matter Microstructural Injury in Neonatal Encephalopathy

Peter J Lally[1], Hui Zhang[2], Shreela S Pauliah[1], David L Price[3], Alan Bainbridge[3], Ernest B Cady[3], Seetha Shankaran[4], and Sudhin Thayyil[1]

[1]Perinatal Neurology and Neonatology, Imperial College London, London, United Kingdom, [2]Centre for Medical Image Computing, University College London, London, United Kingdom, [3]Medical Physics and Biongineering, University College London Hospitals NHS Trust, London, United Kingdom, [4]School of Medicine, Wayne State University, Detroit, Michigan, United States

Introduction: Descriptors of white matter (WM) diffusivity correlate with adverse neurological outcome in neonatal encephalopathy (NE) [1]. WM integrity measures derived from clinical diffusion tensor imaging (DTI) are difficult to interpret in terms of microstructural morphology. We aimed to examine changes in WM microstructure associated with NE, and relate these to tangible biophysical models by fitting to the neurite orientation dispersion and density imaging (NODDI) model [2].

Methods: We recruited with parental consent consecutive encephalopathic neonates (Thompson score ≥6) admitted to Calicut Medical College India over a period of 6 months. At age <3 weeks DTI (TR/TE=2800ms/94ms, 20 directions, b=0 s/mm^2 &1000 s/mm^2, 1.8x1.8x5mm^3) was performed at 1.5 Tesla (Siemens Avanto, Erlangen, Germany). Sarnat encephalopathy stage (none, mild, moderate or severe) was allocated at 3 days postnatal age. Image analysis used the FMRIB Software Library [3-4], incorporating tensor-based registration steps in DTI-TK [5] to generate a group-wise template. DTI data were fitted to the NODDI model in MATLAB, generating derived maps of orientation dispersion index (ODI) and neurite density index (NDI). These maps were compared between infants grouped by encephalopathy severity using tract-based spatial statistics (TBSS).

Results and Discussion: A total of 54 infants were recruited; 31 had usable TBSS data. The cohort mean fractional isotropy (FA) axial skeleton is shown in green (Figure 1a). Compared to normal/mild (n=22) the moderate/severe encephalopathy group (n=9) had significantly reduced WM FA (Figure 1b: red p<0.05; yellow p<0.01) and increased radial diffusivity (RD) (Figure 1c: red p<0.05; yellow p<0.01). This corresponded in the NODDI indices to a decrease in NDI (Figure 1d), but no change in ODI (Figure 1e), as supported with voxel-wise scatter plots of three key NODDI indices, colour coded with measures derived from DTI (Figure 2). These data suggest changes in FA and RD in the WM tracts of the moderate/severe neonates could be driven by a reduced density of neurites.

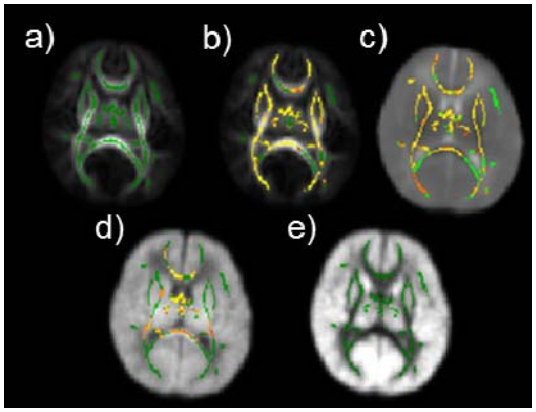

Figure 1a) Mean FA skeleton; b-e) are changes in indices from normal/mild to moderate/severe Sarnat encephalopathy grades: b) FA decreases; c) RD increases; d) NDI decreases; e) ODI is unchanged. Red and yellow voxels p<0.05 and p<0.01 respectively, green voxels p>0.05.

Conclusion: In this cohort, moderate/severe encephalopathy stages were associated with reduced FA and increased RD compared to normal/mild. Single-shell NODDI maps are noisy for individual subjects, but group-averaged maps confirm the presence of anatomically relevant information, indicating that changes may be caused by a lower neurite density in the affected WM. Analysis of single-shell DTI data with the NODDI model therefore yields additional indices which may reflect biophysical differences between the WM of different subject groups. An ongoing prospective study will compare these indices with those derived from multi-shell NODDI data.

References: [1] Tusor N et al. 2012 Pediatr Res 72(1):63-9. [2] Zhang et al. 2012 NeuroImage 61(4):1000-16 [3] Smith S et al. 2004 NeuroImage 23(S1):208-19. [4] Smith S et al. 2006 NeuroImage 31(4):1487-505. [5] Zhang H et al. 2006 Med Image Anal 10:764-85.

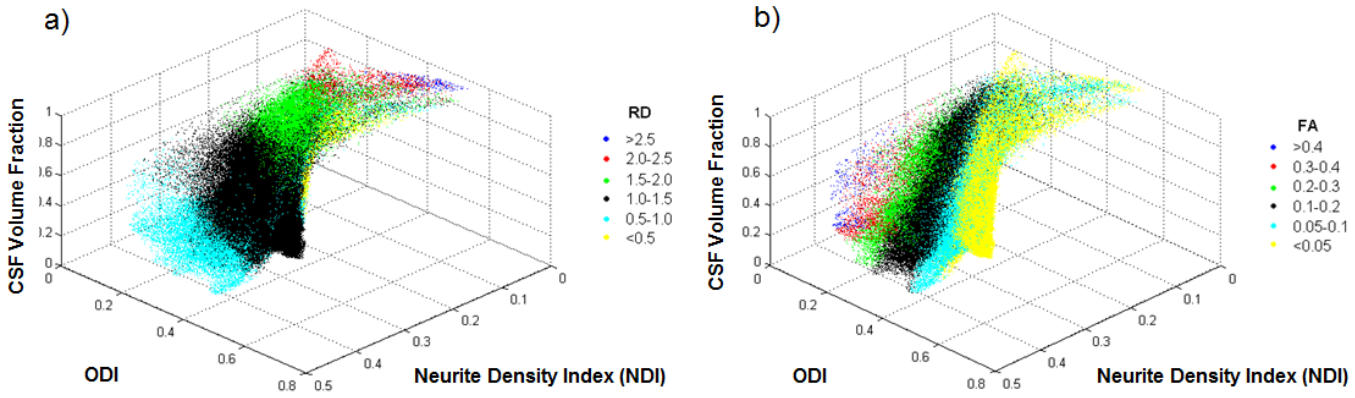

Figure 2 Voxel-wise scatter plots of DTI and NODDI values across the group-mean whole brain, colour coded for (a) RD and (b) FA. Increasing RD corresponds to a reduction in NDI with unchanged ODI. Decreasing FA also corresponds to a decrease in NDI, with a greater dependence on ODI. CSF: cerebrospinal fluid.