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# Probabilistic Neighbourhood Tractography in the Preterm Neonatal Brain

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## Authors:

Devasuda Anblagan<sup>1</sup>, Mark Bastin<sup>1</sup>, Lucy Kershaw<sup>1</sup>, Susana Maniega<sup>1</sup>, Jonathan Clayden<sup>2</sup>, Chinthika Piyasena<sup>1</sup>, Graham Wilkinson<sup>1</sup>, Neil Roberts<sup>1</sup>, Scott Semple<sup>1</sup>, Jane Norman<sup>1</sup>, James Boardman<sup>1</sup>

## Institutions:

<sup>1</sup>University of Edinburgh, Edinburgh, United Kingdom, <sup>2</sup>University College London, London, United Kingdom

## Introduction:

Preterm birth is a leading cause of cognitive impairment in childhood and is associated with alterations in brain development. Diffusion MRI (dMRI) and tractography may provide insights into the cerebral changes that accompany preterm birth by supplying biomarkers of white matter microstructure in tract or fasciculi-of-interest (FOI).<sup>1</sup> This pilot work describes the first application of an automatic single seed point tractography-based segmentation method, probabilistic neighborhood tractography (PNT),<sup>2,3</sup> to study the developing brain.

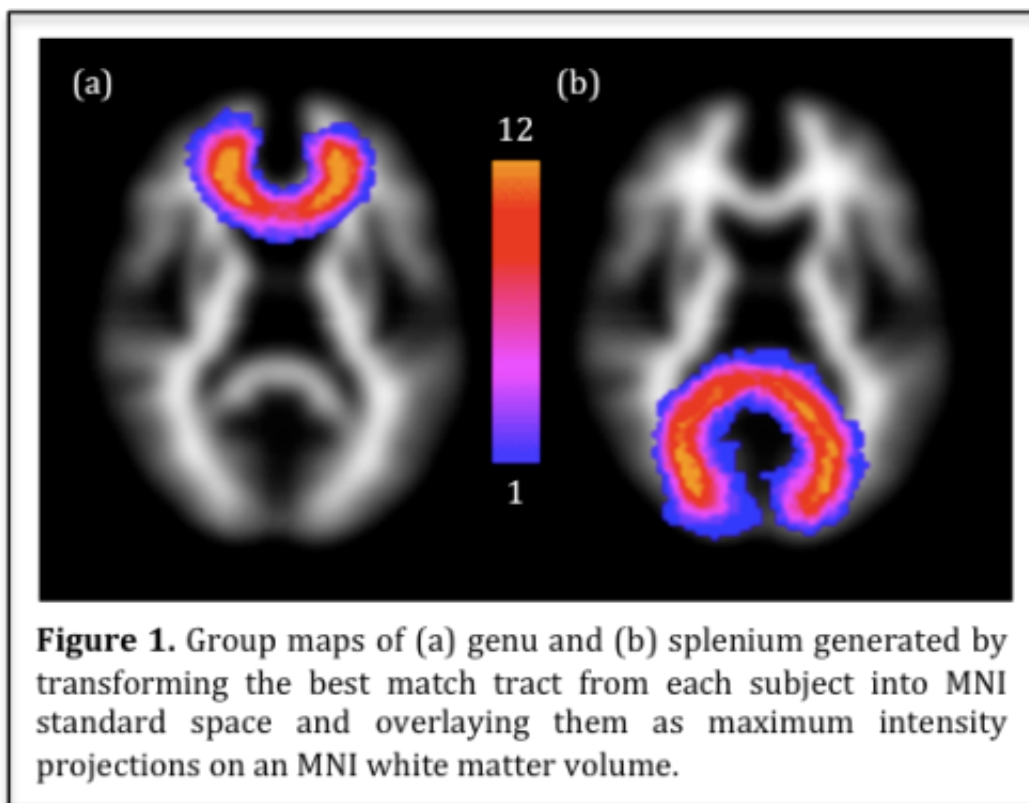
## Methods:

Twelve preterm infants born at a mean postmenstrual age (PMA) of  $28 \pm 2$  weeks underwent a high resolution axial dMRI protocol at term equivalent age (mean PMA  $40 \pm 2$  weeks) without sedation, with informed parental consent. The dMRI protocol was acquired using a MAGNETOM Verio 3 T clinical scanner (Siemens AG, Germany), and consisted of 11 T2- and 64 diffusion-weighted ( $b = 750 \text{ s/mm}^2$ ) single-shot spin-echo EPI volumes acquired with 2 mm isotropic voxels ( $256 \times 256 \text{ mm}$  field-of-view, 50 contiguous interleaved slices with 2 mm thickness). Eight FOI were identified using PNT from the dMRI data (<http://www.tractor-mri.org.uk>).<sup>3</sup> Tracts assessed were the genu and splenium of corpus callosum, cingulum cingulate gyri (CCG), corticospinal tract (CST), and inferior longitudinal (ILF) fasciculi. Using a neighborhood of seed voxels, the seed point that produced the best matching tract to the reference (MNI standard space) was determined using tract shape models determined from a group of normal volunteers aged 25–65 years. To reduce false positives and reduce noise-related fall-off in connection probability with distance from the seed point, pruning of streamlines that did not resemble the median path of the best match tract was employed.<sup>3</sup> Then, all best match tracts were visually assessed by an experienced rater and any subject with aberrant or truncated pathways that were not anatomically plausible representations of the FOI were excluded from further analysis. For anatomically acceptable tracts, the resulting tractography masks were applied to each subject's mean diffusivity ( $\langle D \rangle$ ), fractional anisotropy (FA), axial ( $\lambda_{Ax}$ ) and radial ( $\lambda_{Rad}$ ) diffusivity volumes to provide tract-averaged measures of these biomarkers for the eight FOI. A model-based goodness-of-fit measure ( $R$ ) was also calculated for each tract in each subject.<sup>2,4</sup> This measure of topological similarity generally has a negative value, and the more negative it is, the less good is the fit between the reference and best matching tract.

## Results:

Figure 1 shows the tract segmentation across all 12 subjects for genu and splenium, indicating the close spatial correspondence of the segmented pathways for these two tracts. Visual assessment of the individual segmented tracts indicated that PNT provided anatomically acceptable representations of the FOI for the vast majority of pathways (92% over all subjects and tracts), with a minimum of 75% for right CCG. Values of  $\langle D \rangle$  ranged from  $1139 \pm 70$  for right CST to  $1707 \pm 209 \mu\text{m}^2/\text{s}$  for left ILF, while FA ranged from  $0.19 \pm 0.02$  in left ILF to  $0.31 \pm 0.03$  in splenium. Values of  $\lambda_{Ax}$  varied from  $1512 \pm 76$  for right CST to  $2061 \pm 161 \mu\text{m}^2/\text{s}$  for splenium, while  $\lambda_{Rad}$  ranged from  $952 \pm 87$  for right

CST to  $1532 \pm 200 \mu\text{m}^2/\text{s}$  for left ILF. Finally median ( $\pm$  IQR/2) values of  $R$  ranged from  $-3.68 \pm 0.79$  for genu to  $-47.26 \pm 7.45$  for left CST and are generally lower, i.e. showing less topological similarity to the reference tract, than those seen in the adult brain.<sup>4</sup>



	Acceptable Tracts (%)	$\langle D \rangle$ ( $\mu\text{m}^2/\text{s}$ )	FA	$\lambda_{Ax}$ ( $\mu\text{m}^2/\text{s}$ )	$\lambda_{Rad}$ ( $\mu\text{m}^2/\text{s}$ )	$R$
Genu	100	$1521 \pm 80$	$0.27 \pm 0.05$	$1973 \pm 74$	$1296 \pm 105$	$-3.68 \pm 0.79$
Splenium	100	$1543 \pm 128$	$0.31 \pm 0.03$	$2061 \pm 161$	$1284 \pm 117$	$-22.18 \pm 4.77$
Left CCG	92	$1466 \pm 236$	$0.21 \pm 0.03$	$1779 \pm 257$	$1310 \pm 227$	$-11.49 \pm 6.21$
Right CCG	75	$1359 \pm 56$	$0.20 \pm 0.02$	$1643 \pm 74$	$1216 \pm 50$	$-25.54 \pm 11.29$
Left CST	92	$1187 \pm 73$	$0.29 \pm 0.03$	$1562 \pm 85$	$999 \pm 75$	$-47.26 \pm 7.45$
Right CST	92	$1139 \pm 70$	$0.30 \pm 0.05$	$1512 \pm 76$	$952 \pm 87$	$-30.85 \pm 6.34$
Left ILF	83	$1707 \pm 209$	$0.19 \pm 0.02$	$2058 \pm 229$	$1532 \pm 200$	$-11.90 \pm 2.37$
Right ILF	103	$1559 \pm 273$	$0.22 \pm 0.03$	$1924 \pm 290$	$1376 \pm 267$	$-21.00 \pm 5.29$

**Table 1:** Mean ( $\pm$  SD) values for tract-averaged  $\langle D \rangle$ , FA,  $\lambda_{Ax}$  and  $\lambda_{Rad}$  for the eight fasciculi-of-interest. Also shown are median ( $\pm$  IQR/2) values for the absolute goodness-of-fit of the best match tract to the reference ( $R$ ) and the number of tracts that were considered anatomically plausible representations of each fasciculus.

### Conclusions:

We have shown that quantitative measurements of dMRI biomarkers can be made in a number of FOI in preterm brain from dMRI data using single seed point PNT. These values demonstrate the increased diffusivities and reduced FA indicative of white matter development at neonatal stage compared with the adult brain.

### Lifespan Development:

Normal Brain Development: Fetus to Adolescence

[1] Thompson, D.K. (2011), 'Characterization of the corpus callosum in very preterm and full-term

infants utilizing MRI', *Neuroimage*; vol. 55, no. 2, pp. 479-490. [2] Clayden, J.D. (2007), 'A probabilistic model-based approach to consistent white matter tract segmentation', *IEEE Trans Med Imaging*, vol. 26, pp. 1555-61. [3] Clayden, J.D. (2011), 'TractoR: Magnetic resonance imaging and tractography with R', *Journal of Statistical Software*; vol. 44, pp. 1-18. [4] Bastin, M.E. (2010), 'Quantifying the Effects of Normal Ageing on White Matter Structure using Unsupervised Tract Shape Modelling', *Neuroimage*; vol. 51, no. 2, pp. 511-10.

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