Voxel-wise histogram analysis of tractography streamline length for assessing brain injury

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Introduction: There is a growing interest in assessing white matter integrity *in vivo* using quantitative metrics derived from diffusion tractography. One of the most commonly used quantitative tractography metrics is the number of streamlines that define white matter tract of interest. Recently, Track Density Imaging (TDI) [1] has been proposed which may allow voxel-based analysis of streamline number in the entire brain to identify between-group differences in streamline density. However, every brain voxel may contain a number of different white matter tracts that contribute to the overall streamline number. This potentially renders the overall streamline number insensitive to changes in tracts with a low number of streamlines as they cross with tracts containing a larger number of streamlines. We propose to use an additional parameter, namely the streamline length, to identify the different populations of white matter tracts that occupy a voxel.

Methods: HARDI data (64 diffusion encoding gradients, b = 3000 s mm^{-2}, 2.5 mm isotropic resolution) were acquired using a 3T Siemens Tim Trio (Erlangen, Germany) for a healthy volunteer on two occasions to assess reproducibility, and on one occasion for a participant with severe traumatic brain injury (TBI).

The fibre orientation distribution was calculated using constrained spherical deconvolution [2]. Probabilistic diffusion tractography was performed in MRtrix (http://www.nitrc.org/projects/mrtrix). Every voxel of the entire brain volume was seeded with 50 probabilistic streamlines. All streamlines were then individually transformed to standard space, using a deformation obtained by non-linear registration of the individual FA image to FMRIB's FA template.

For every voxel, the distribution of streamline length of all streamlines traversing any given voxel was extracted. These distributions were calculated on a 2 mm grid in FMRIB58 space rather than a 1 mm grid to increase the signal to noise ratio.

The TBI participant had a known involvement of the genu of the corpus callosum, therefore a single corpus callosum voxel is shown here as an example. Figure 1 shows all streamlines traversing this voxel for the control and TBI participant. The histograms shown in Figure 1 summarize the distribution of streamline length within this voxel.

We assumed that the overall length distribution consisted of a mixture of an unknown number n of normal distributions, with a uniform distribution of outliers:

$$f(l) = \sum_{i=1}^{n} \left[p_i \frac{1}{\sqrt{2\pi\sigma_i^2}} \exp\left(\frac{-(l-\mu_i)^2}{2\sigma_i^2} \right) \right] + c$$

where $f(l)$ is the frequency f of length l. We used an Expectation Maximisation (EM) algorithm to obtain constant c and the mixing proportions p_i, means μ_i and variance σ_i^2 of each component. The Bayesian Information Criterion (BIC) was used to identify the optimum number n of normal distributions to describe the data.

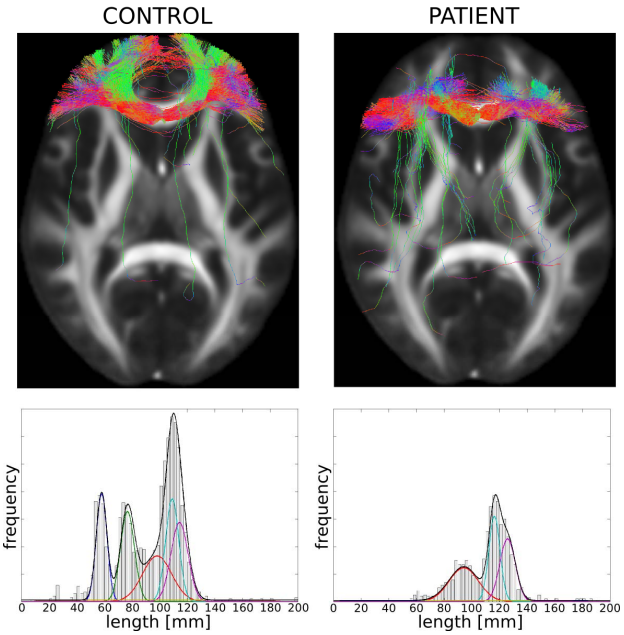

Figure 1: Top: streamlines traversing through a single voxel within the corpus callosum. Bottom: Distribution of the length of streamlines traversing a single corpus callosum voxel and fitted mixture of normal distributions.

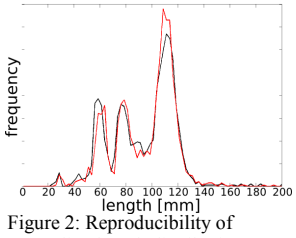

Figure 2: Reproducibility of streamline length distribution

Results: For the control participant, the length distribution within a single voxel in the genu of the corpus callosum was best described by a mixture of 5 normal distributions. Fit parameters are shown in Table 1 for both scans of the control participant, with the histograms displayed in Figure 2. Overall, voxel-wise streamline length histograms show good reproducibility over time.

The length distribution of the TBI participant was best described by a mixture of 3 normal distributions. Histogram plots for patient and control are shown in direct comparison in Figure 1. The histograms suggest a loss of short connections for the TBI participant in this area.

Discussion and Conclusion: The method described here is not restricted to the analysis of a single voxel or region of interest. Instead, it can be applied to all voxels within the brain, and voxel-wise comparisons between controls and patients can be performed in a fully automated fashion. The high reproducibility of length distributions within voxels indicate that this method will be suitable for serial studies.

References: [1] Calamante et al. 2010, Neuroimage 53(4):1233-1243; [2] Tournier et al. 2007, Neuroimage 35(4): 1459-1472

	μ_1 / σ_1 / p_1	μ_2 / σ_2 / p_2	μ_3 / σ_3 / p_3	μ_4 / σ_4 / p_4	μ_5 / σ_5 / p_5
Control scan 1	58.07 / 3.87 / 0.16	76.74 / 5.01 / 0.18	98.17 / 10.54 / 0.19	109.12 / 4.75 / 0.19	114.35 / 6.16 / 0.09
Control scan 2	59.45 / 4.27 / 0.16	77.72 / 4.28 / 0.18	101.44 / 11.10 / 0.20	108.76 / 4.14 / 0.20	113.14 / 6.34 / 0.08
Reproducibility [%]	±2.4 / ±10.1 / ±5.4	±1.3 / ±15.8 / ±0.2	±3.3 / ±5.1 / ±3.3	±0.3 / ±13.8 / ±2.5	±1.1 / ±2.9 / ±2.1
TBI	-	-	94.27 / 10.65 / 0.30	116.38 / 4.08 / 0.29	125.88 / 5.59 / 0.29