A Monte-Carlo approach for estimating white matter density in HARDI diffusion data

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Introduction: Diffusion weighted MRI (DWI) has been widely used to study human brain structure and disease processes. Due to its simplicity and the presence of semi-quantitative measures (such as fractional anisotropy (FA)), the diffusion tensor (DT) model has become the de facto standard for analysis of DWI data. However the DT model is limited by its inability to resolve crossing fiber populations and thus cannot be trusted in the third of white matter voxels with more than a single fiber population [1]. More recently, the use of higher order models such as the constrained spherical deconvolution (CSD) [2] using high angular resolution diffusion imaging (HARDI) have overcome some of these limitations. In this abstract we use test the influence of the number of averages and cutoff values on Whole-brain Track-Density (visitation) maps [3], generated by Monte Carlo methods using repeated probabilistic tracking. Furthermore, we test the applicability of VBM analysis on visitation maps.

Methods: Twelve normal elderly subjects (NC) from the Australian imaging biomarkers and lifestyle study (AIBL) were recruited for the analysis. High resolution structural (T1-weighted MPRAGE, 1x1x1.2 mm) and HARDI diffusion data were acquired for each of the subjects. The HARDI scans were acquired with an EPI sequence (60 diffusion encoding directions, b-value = 3000 s mm^{-1}, 2.3 mm isotropic) on a Siemens Trio scanner (Siemens, Erlangan, Germany). The T1-weighted scans were co-registered to the b0 image of the diffusion scan using an affine registration [4] and skull-stripped using the brain extraction tool [5]. Following this, probabilistic tractography was performed with the MRtrix software (http://www.brain.org.au/software) by seeding once at each voxel of the co-registered skull stripped mask.. Visitation maps were generated from the tractograms by counting the number of tracks that pass through each voxel. To test the stability of the visitation maps, the above procedure was repeated a hundred times and two average maps were generated by averaging N randomly picked visitation maps. The error between the two average images was computed using $Err = |I_1 - I_2| / ((I_1 + I_2)/2)$. The procedure was again repeated to test the influence of the cut-off parameter (default 0.10). The cutoff parameter stops the tracking when the amplitude of the fiber orientation distribution along the direction of tracking falls below the specified value. Visitation maps corresponding to the best choice of parameters were generated for each subject to assess if the visitation maps could be used in voxel based morphometry (VBM) studies,. These visitation maps were then used to generate a population specific atlas [6]. Each of the cases was registered to the atlas using a block matching linear registration [3] and the diffeomorphic demons non-linear registration algorithms [7]. The maps were normalized by dividing each voxel by the mean of a ROI drawn bilaterally on the mid cerebellar peduncles. The subjects were randomly split into two groups and a VBM study was conducted by comparing the two groups with a two sample t-test using the SPM8 toolbox. A Shapiro-Wilk test was performed at every voxel on the residual images to test the assumption of normality.

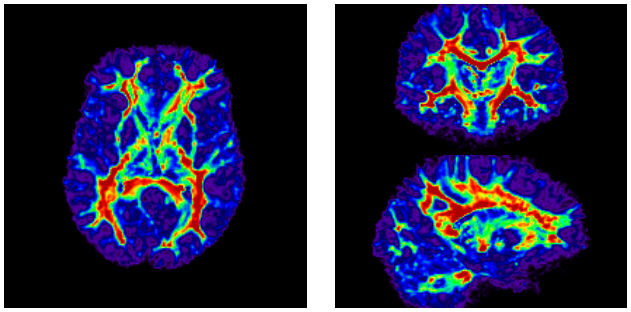
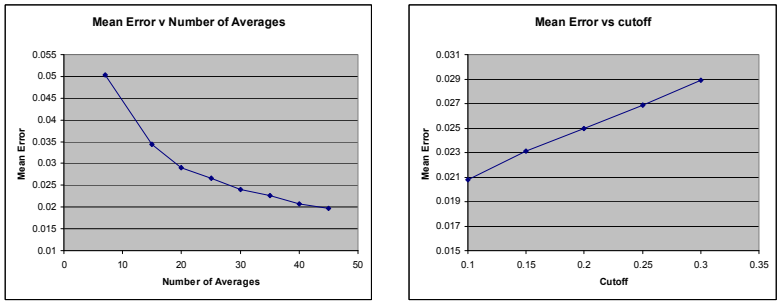


Figure 1. An example of the visitation map for an NC subject.



(a)

(b)

Figure 2. Mean Error as a function of the number of averages (a) and cutoff (b). Note 40 averages were used for the cutoff test.

Results: An example of the visitation map for a NC subject is presented in Figure 1. Qualitatively, the visitation maps show the main fiber bundles in the brain. The error metric as a function of the number of averages and as a function of the cutoff is presented in Figure 2. The best choice of parameters was deemed to be 40 averages (best trade-off between time and error) with a cutoff of 0.1. The results of the Shapiro-Wilk test are presented in Figure 3. These show that although the residuals are not normally distributed everywhere, they follow a normal distribution in the main fiber tracks. Furthermore, the proportion of non-Gaussian residuals was 0.035.

Discussion: We have presented a Monte Carlo method for estimating fiber density using HARDI data, namely Whole-brain Track-Density or visitation maps. We investigated the stability of the maps by using different number of averages and different cutoff values. Furthermore, unlike FA maps [8] the residuals of the visitation maps were normally distributed and hence suitable for VBM analysis. This result also indicates that the visitation maps can be used as a quantitative index for HARDI data. Current work is focused on the influence and impact of differing seeding and tracking techniques as well as the exploration of other automated normalization procedures. Furthermore we plan to compare the current results with that obtained using other diffusion measure.

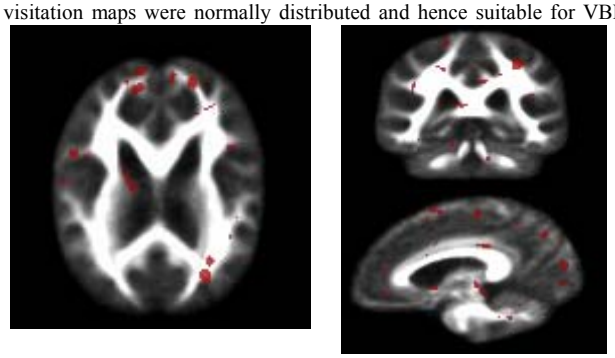


Figure 3. Results of the Shapiro-Wilk test overlaid on the population atlas. Red patches illustrate voxels where the residuals are not normally distributed.

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