Quantification Of White Matter Pathway Volume From Diffusion Tensor Tractography

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Introduction

Diffusion tensor tractography utilises directions of maximum diffusion to reconstruct white matter tracts in the human brain from which individual structures (pathways of interest) are segmented. Here we describe methods for determining white matter pathway volumes. In particular, we present a novel method that calculates partial volumes at reconstructed pathway boundaries and we show that this technique provides a more accurate estimate of volume than nearest neighbour approximations. The new method incorporates voxel-by-voxel computation of streamline densities (i.e. streamlines per unit volume) throughout the entire brain. In particular, streamlines are initiated at each image voxel and total numbers of streamlines passing through voxels are calculated. Specific pathways are then extracted and streamline density images calculated for these segmented pathways. By dividing the streamline density images obtained for the segmented pathways by the density image obtained across the entire brain a partial volume approximation at pathway boundaries is computed. This is referred to as density-based volume approximation.

Methods

Synthetic data generation: 2D symmetric second order tensors were computed at each 1.0mm^2 pixel of a 12×12 grid to generate synthetic pathways deviated around a hyperbolic singularity (see Fig 1a).

MRI data acquisition: One right-handed subject was scanned on a 1.5T General Electric Signa MRI system with maximum field gradient strength of 22mTm^{-1}. A diffusion tensor image (DTI) was acquired as described previously [1]. Whole brain coverage was achieved for near isotropic voxels (2.5mm×2.5mm×2.8mm). The DTI was then resampled to obtain 1.0mm^3 isotropic voxels.

Pathway segmentation: Pathways were segmented from the synthetic data by initiating streamline tractography [2,3] from three seed pixel regions within the 12×12 grid (see Fig 1b-d for pathway reconstructions and Fig 1e for seed voxel configurations). Resulting streamlines were coloured according to their orientation (left to right: red, anterior to posterior: green, inferior to superior: blue). Region of interest based pathway segmentation [4] was applied to the DTI data to extract the corpus-callosum. Streamline tractography was initiated at each image voxel and streamlines retained that pass through the mid-sagittal callosal section.

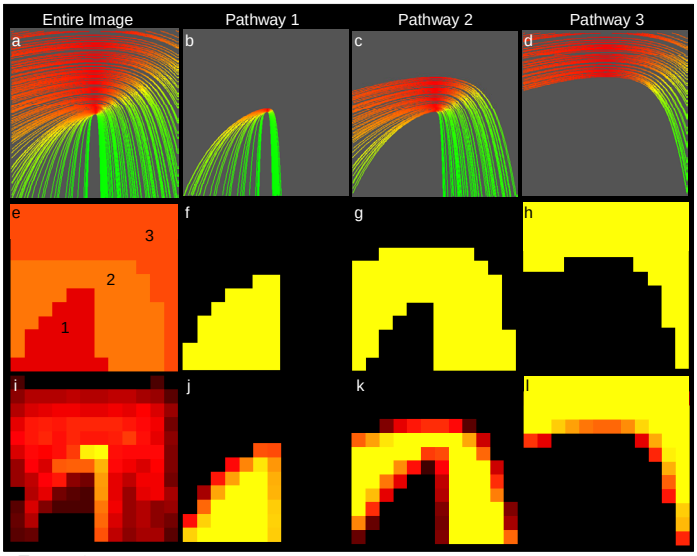

Figure 1

Pathway volume estimation

Nearest neighbour: For all vertices along each streamline the nearest voxel coordinate was determined and assigned a value of 1, all remaining voxels were assigned the value 0. Nearest neighbour pathway volumes for the segmented synthetic and DTI pathways were then integrated over each voxel in the entire image space (see Figs 1f-h).

Density-based: Streamline tractography was initiated from each image voxel and an image was computed of streamlines per unit voxel, S (see Figs 1i and 2a). Streamline density images were also computed for each pathway of interest, p (e.g. see Fig 2b). Density-based pathway volumes, d_p, were integrated over the entire image by,

$$d_p = \sum_{i \in I} \frac{P(i)}{S(i)}.$$

where $S(i)$ and $P(i)$ are the streamline densities at voxel, $i \in I$, over the entire image of seeded streamlines and the pathway of interest, respectively. The term $P(i)/S(i)$ computes the sub-voxel partial volume estimation at voxel, i (see Figs 1j-l and 2c for partial volume corrected images where voxel colours represent partial volume weightings between 0 (black) and 1 (yellow)).

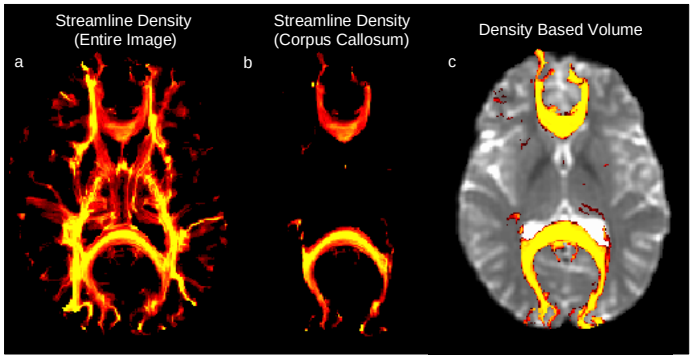

Figure 2

Precise numerical integration: In order to investigate the accuracy of nearest neighbour and density-based pathway area approximations in the 2D synthetic data each pathway area was numerically integrated by application of the trapezium rule. An estimate of computational error was calculated by the ratio of estimated area divided by numerically integrated area for the nearest neighbour and density-based techniques.

Table 1

Pathway	*Number of Streamlines (Seed Pixels)*	*Area (mm^2)*			*Area Error*	
		Nearest Neighbour (N)	*Density-based (D)*	*Numerical Integration (I)*	*N/I*	*D/I*
1	26	37	30.26	31.02	1.19	0.98
2	60	67	58.72	57.55	1.16	1.02
3	58	79	55.02	55.43	1.43	0.99
Total	144	183	144	144	1.27	1

Results

Total area calculated by the nearest neighbour technique for the three synthetic 2D pathways was 27% greater than the area of the 12×12 grid (see Table 1). This over-estimation of area was caused by overlapping pathway boundary pixels (see Figs 1f-h). Total pathway areas computed by the density-based technique were equivalent to the area of the 12×12 grid. Comparisons of nearest neighbour and density-based individual pathway areas with numerical integration reveal errors in the range of 8 to 43% for nearest neighbour and 1 to 3% for density-based approximations, with the nearest neighbour technique consistently over-estimating the area (see Table 1). Corpus-callosum volume computed by the nearest neighbour technique (172.73ml) was 1.9 times larger than the density-based approximation (90.97ml).

Discussion

We have shown that the partial volume approximation included in the density-based approach improves the accuracy of pathway volume quantification from synthetic 2D data, and that it is more accurate than the nearest neighbour technique. However, it is necessary to note that *streamline* density is a geometrical property dependent on the sampling and structure of the tensor field and should not be confused with *axonal* density. In addition, although the technique is highly accurate, it is limited by the quality of pathway segmentation and the fibre crossing problem in second order diffusion tensor fields. Nevertheless, by describing an accurate method for computation of white matter pathway volume we bring quantification to diffusion tensor tractography, and in addition, provide a new technique that will be applicable to analysis of tractography results determined from high angular resolution data. This method allows us, for the first time to accurately determine the volume of individual white matter structures of the brain in vivo and will be applicable to future investigations of white matter pathway volume in brain development, cerebral asymmetry, degeneration due to disease and normal ageing.

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Acknowledgements: This research was funded by Research Into Ageing.