

PROBABILISTIC TRACTOGRAPHY DRIVEN WHITE MATTER WIDTH MEASUREMENT

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Introduction Brain atrophy is a common feature of many neurological conditions such as Alzheimer's disease (AD). The quantitative evaluation and characterisation of atrophy can form potentially useful biomarkers for assessing the evolution of such conditions. Most present literature on the measurement of atrophy aims to measure the whole brain, global grey and/or white matter, specific lobes, or specific grey matter structures such as the hippocampus. However, the resulting atrophy caused by such conditions also affects the white matter (WM) tracts of the brain via degenerative processes, and so a measurement of WM structures may be a useful imaging biomarker. If specific tract systems are more prone to atrophy than others then there is the potential that tract-specific atrophy measurements may be more sensitive than less targeted methods. With this aim in mind, this work presents a novel method for quantifying the width of WM tracts which may be used to differentiate between healthy and AD subjects.

Methods High angular resolution diffusion-weighted imaging was performed on subjects using a reversed k-space distortion corrected protocol [1]. Acquisition: 3 T Philips Achieva scanner; 8 element SENSE head coil; SENSE factor 2.5; phase-encoding in L-R orientation; SE-EPI with $TE = 54$ ms, $TR = 11884$ ms, $G = 62$ mTm⁻¹, 112×112 matrix, reconstructed resolution 1.875×1.875 mm², slice thickness 2.1 mm, 60 slices, $b = 1200$ smm⁻² ($\Delta, \delta = 28.5, 13.5$ ms), and $1 b = 0$ image. After processing the acquired data using q-ball and model-based residual bootstrapping [2,3], to determine multiple fibre orientations in every voxel, the *PICo* multi-fibre probabilistic tractography method [4,5] was used to extract the tracts of interest. The uncinate fasciculus (UF) was extracted from both hemispheres of 10 datasets from young controls. A threshold value of 10 %, was identified as optimum for the UF and the binarised tract was then up-sampled by a factor of 3 and subsequently smoothed using a box kernel of size $3 \times 3 \times 3$. Tract skeletonisation was performed using an electric field model in which the repulsive force associated with charges placed on the surface of the tract is used to define a vector field [6]. In turn, topological characteristics of this vector field, such as critical points and low divergence points were used to generate the curve-skeletons of the extracted tracts (Fig 1: A). Using the generated curve-skeletons, the widths of the tracts were computed as a function of position along the curve-skeletons (Fig 1: B). Here, we present the mean geodesic distance for each point on the skeleton, which is the distance from the surface to the skeleton along the geodesic and was calculated by tracking from every boundary voxel through the electro-static vector field until we reach a skeleton voxel.

Results Seven of the subjects demonstrated right hemisphere lateralization, where the right UF had a higher mean width score than the left but there was no statistically significant lateralization at the group level (paired t-test $p = 0.21$). Figure 2 illustrates the normalized histogram plot of width values of the Left (Blue) and the Right (Red) UF of the entire group, from which it can be seen that there is a shift towards higher width values in the Right UFs' histogram. This evidence of possible right hemisphere lateralization is comparable to published *in vitro* work [7], which found right hemisphere lateralization in the UF in 80% of their subjects.

Discussion & Conclusions This work introduces a novel approach to quantify the width of the WM structures in the brain. Our results are consistent with *in vitro* measurements of the UF [7]. However, previous diffusion MRI measurements of the same tract have observed lateralisation to the left hemisphere [8]. The cause of this discrepancy is unclear at this time. The proposed method may be used to quantify tract-specific white matter atrophy that results from conditions such as AD, and may be used to differentiate width variations between normal and patient groups or in the analysis of longitudinal studies to assess the performance of a given treatment regime on the rate of atrophy.

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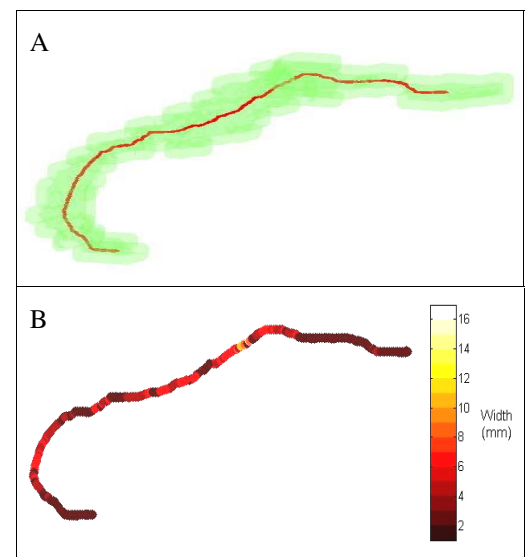


Figure 1: A) The isosurface representation of the tract (green) overlaid with its skeleton (red). B) Tract skeleton colour-coded by width values.

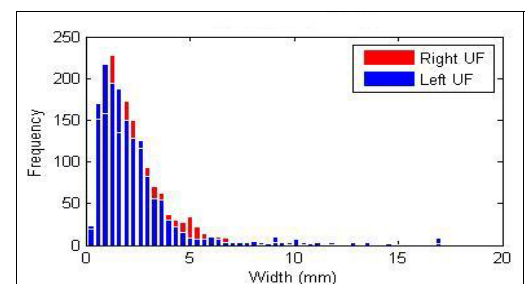


Figure 2: Normalized histogram plot of the width values of the Left and Right UF tracts of all the subjects.