METHODOLOGY FOR THE ESTIMATION OF THE EXTENSION OF A WHITE MATTER TRACT INTO AND THROUGH ASSOCIATED GREY MATTER

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Introduction: The definition of white matter (WM) tracts using diffusion tractography is now an established post-processing technique, which has provided much information on the integrity of the tracts in a variety of diseases (1). The basic principles are that in tissue water diffuses much more easily parallel to the tracts than perpendicular to them. Thus, by sensitising the MR sequence to measure the diffusion coefficient in a sufficiently high number of directions, white matter tracts can be estimated by following the direction of principal diffusivity as determined from diffusion tensor (DT) (2), or more complex (3) models.

Diseases such as multiple sclerosis (MS) have for many years been considered primarily diseases of the WM, however it is clear from histological and MR studies that the grey matter (GM) is also affected (4). It is known that a WM tract acts as a pathway carrying information between areas of GM, which are therefore connected to the tract. Much work has shown abnormalities in the diffusion properties of WM (1) and GM (5) in MS, but not the spatio-temporal relationship between these changes. One problem is defining which areas of the GM are associated with a specific WM tract. This work proposes a methodology for extending WM tract data to encompass an area of GM which is likely to be associated with it, rather than relying on pre-defined anatomical knowledge.

Method: Depending on the tractography method and associated parameters used many calculated WM tracts will abut or extend slightly into GM, however due to the reduced fractional anisotropy of GM and other commonly used tractography criteria the tract will not extend through the full width of the GM. This method extends the tract through the GM by defining two points: a starting point (sp) being a voxel on the boundary of the tract in GM or on the GM/WM boundary and an end-point (ep) found on the outer edge of the GM, that is the boundary with the CSF surrounding the brain. For each sp, the ep is chosen by satisfying two criteria: 1) The line connecting sp and ep must be the shortest possible; 2) The line connecting sp and ep must not pass through WM or non-brain tissue voxels. The voxels that lie on the straight line between these two points are then classified as part of the tract. This process was performed in a 3-dimensional manner, with the nearest possible ep being assessed in any direction and in a 2-dimensional manner in three orthogonal planes and the results combined to produce a final mask of the tract. Finally the extended tract was dilated and subsequently eroded by 2 voxels, in 3 dimensions to fill in any small gaps in the GM portion of the tract and then masked using the T_1-weighted GM segment and the original tract to remove any non-brain and non-tract WM voxels. The final tract can then be used to estimate the GM which is likely to be associated with the specific WM tract.

We applied this method to the cortico-spinal tracts (CST) obtained using a DT dataset, obtained by averaging the DT from 15 healthy control subjects (6 male, average(±SD) age 40±14 years) in standard space, according to (6). The sequence was a spin-echo EPI sequence (TR/TE= 26.1s/81ms, 1 NEX, 22 cm FOV, 128x128 matrix, 16 diffusion gradient directions, 2.3 mm slice thickness). We used the tractography algorithm from the Camino package (www.camino.org) (7), with seed regions of 60 voxels over 2 axial slices in the posterior limb of the internal capsule. A sagittal-axial exclusion mask was also applied to avoid spillage of the tract in unwanted areas such as the contra-lateral side of the brain. Segmentation of a corresponding 15 subject averaged T_1–weighted dataset (IR-FSPGR, TI/TR/TE=450/143/5.1 ms, FA=20°, matrix 256x256, 310 mm FOV, 1.2 mm slice thickness) in standard space into WM and GM was obtained using SPM5 (www.fil.ion.ucl.ac.uk/spm/) and applying the maximum likelihood algorithm with a lower probability threshold of 0.4. The results of the extended tracts can be easily reported in native space for each subject by applying the inverse transformation obtained from the registration step.

Results: Figure 1 shows a tract extended with a) the 3D method and b) the multi-planar 2D method. The extended tract is shown in red superimposed on a mask of the GM with the original tract shown in blue on top of the extended tract. As can be seen there are differences between the two methods. The 3D method appears to include less GM tissue. This is probably due to the topography of the GM. The thickness of the sulci is unlikely to be equal in all directions meaning that the minimum 3D distance to the ep from many voxels will be determined by this thickness. This will limit the amount of tissue included in the tract extension, whereas this effect is reduced by extending the tract in 3 orthogonal directions and combining the results.

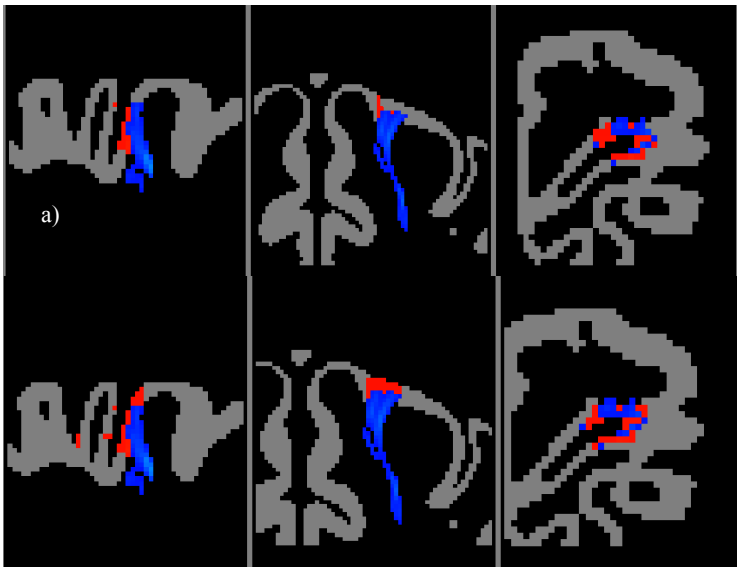

Figure 1: a) and b) from left to right sagittal, coronal and axial views of the original tract (blue) and extended voxels (red) overlaid on the GM segment (grey)

Discussion: There is no in vivo method for determining which specific GM areas are associated with a given WM tract. This method simply extends the tract across the width of the GM based on geometrical means, rather that diffusion based criteria. Another option for achieving this result is using the principal diffusion direction of the GM voxels and extending the tract on this basis, however the low FA in GM and the increased uncertainty in the principal diffusion direction mean that this is unlikely to give a robust result. This method provides a reproducible and simple method for estimating the area of GM which is likely to be connected to a specific WM tract.

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References: 1) Ciccarelli et al. Lancet Neurology 2008;7:715 2) Basser & Pierpaoli JMR Series B 1996;111:209 3) Assaf et al. MRM 2000; 44:713 4) Chard & Miller JNS 2009; 282:5 5) Rovaris et al. Neuroimage 2005; 24:1139 6) Wheeler-Kingshott et al. 17th Meeting ISMRM 2009; 3590 7) Cook et al. 14th Meeting ISMRM 2006; 2759