

Automated vs. Conventional Tractography in Multiple Sclerosis: Variability and Correlation with Disability

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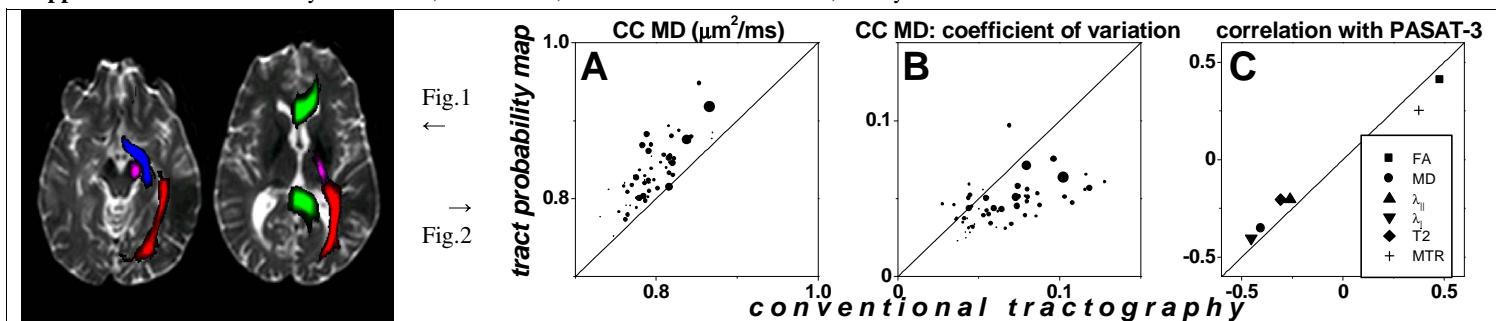
Introduction: Diffusion tensor imaging (DTI) tractography enables interrogation of white matter tracts that subserve different functions. However, with many of the commonly used tractography algorithms, tract reconstruction is laborious, time consuming, and often highly variable from scan to scan. Variability in reconstructed tract volume is particularly problematic, but even variability in tract-specific MRI indices, which is considerably smaller, can limit sensitivity for detecting changes over time that may cause or correlate with disability.^{1, 2} Rapid, automated, reproducible methods will be very helpful in making tractography clinically useful. Although atlas-based approaches and nonlinear registration techniques may provide the best solution,³ such methods are often slow and at best semi-automatic. Recently, we introduced a method for creating tract probability maps, based on linear registration, and we evaluated its use in healthy brains.⁴ Similar methods have been proposed in disease,⁵ but difficulty in registering lesioned and atrophic brains to healthy ones may limit their usefulness. Here, we compare the performance of the tract probability map method to conventional tractography in four major white matter tracts in multiple sclerosis (MS), focusing on systematic differences in MRI indices, variability in scan-rescan experiments, and correlations with clinical disability.

Methods: We studied 90 people with MS, scanned between 1 and 8 times over a 4 year period, and 29 healthy controls. As previously described,^{1, 2} we collected DTI (2.2 mm isotropic voxels), double echo proton density/T2-weighted turbo spin echo, and magnetization transfer data on a 3 Tesla Philips Intera scanner. DTI maps (mean [MD], parallel [$\lambda_{||}$], and perpendicular [λ_{\perp}] diffusivity, and fractional anisotropy [FA]) were created along with coregistered T2 relaxation time and magnetization transfer ratio maps (MTR). Using the fiber assignment by continuous tractography method,⁶ we reconstructed the courses of the corpus callosum (CC), corticospinal tracts (CST), optic radiations (OR), and optic tracts (OT) and saved the results as binary masks. Via a 12-parameter affine transformation model in FLIRT,⁷ we coregistered the $b=0$ maps for every healthy control to a “reference” control scan and transformed the tract masks accordingly. As an estimate of the probability that a tract traverses a given voxel, we calculated the voxel-wise average of the transformed masks. Next, we derived the MRI index maps for every MS scan and coregistered the results to the reference via the same transformation matrix. To account for gross errors, usually related to brain atrophy, that result in registration of cerebrospinal fluid (CSF) or gray matter in the MS scans to white matter in the reference scan, we eliminated from consideration all voxels with FA<0.25. Finally, we averaged the MRI indices within the surviving voxels for each tract, weighted by the voxel-specific value of the tract probability map. To compare results from the tract probability mask method with conventional tractography, we averaged across and appropriately weighted data from multiple scans of each participant.⁸ We also calculated the coefficient of variation (CV) of MRI indices across scans for both methods. As an empirical measure of the usefulness of the results, we calculated correlations between MRI indices and a clinical score appropriate to the tract in question – the paced auditory serial addition test (PASAT-3) for the CC, 1.25% contrast letter acuity for the OR and OT, and the expanded disability status scale (EDSS) for the CST. We have reported significant correlations of these disability scores with these tracts, conventionally reconstructed, in the past.

Results: Fig. 1 shows left-sided tract probability maps superimposed on axial slices of the $b=0$ map from a person with relapsing remitting MS and moderate brain atrophy. Tracts that abut CSF spaces, such as the CC (green), OR (red), and OT (blue) are in places subject to substantial partial volume averaging with CSF, whereas other tracts, such as the CST (violet), are less susceptible. Results for the CC are shown in Fig. 2. Fig. 2A shows that CC-specific MD is systematically higher using tract probability maps compared to conventional tractography, though the results are highly correlated (the size of the data points is proportional to the number of observations per person). On the other hand, Fig. 2B shows that the CV across multiple scans of the same person is systematically higher for conventional tractography. Finally, Fig. 2C shows that correlation coefficients relating CC-specific MRI indices to PASAT-3 scores are similar for the two methods; all correlation coefficients had $p<0.01$ and were adjusted for age and sex. Not shown: For all examined tracts, variability was lower for the tract probability method. With respect to median MRI indices, the CST demonstrated the same systematic differences as the CC, whereas results in the OR were similar for the two methods; for both tracts, correlations with disability scores were similar across methods. For the OT, however, median MRI indices were poorly correlated for the two methods, and correlations with disability were absent for the tract probability method. Differences in MRI indices by method were similar in the MS and control groups.

Discussion: Tract probability mapping is a rapid, totally automated method for extracting tract-specific data from MRI scans that can easily be exported to the clinic. Our results demonstrate that the method is less variable than conventional tractography but that its applicability should be evaluated on a tract-by-tract basis. Due to inclusion of non-tract structures such as CSF, failure is expected for small tracts such as the OT. However, even when results are systematically different from those derived from conventional tractography, such as in the CC and CST, the correlation with disability is unaffected. Thus, when carefully evaluated and interpreted, the method can be extremely useful in brain-altering diseases such as MS.

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