Quantitative fiber bundle-driven analysis of diffusion MRI data

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Target audience – Scientists who want to perform a fully automatic, quantitative analysis of the diffusivities along selected white matter fiber bundles.

Introduction – Analysis of DTI data in multi-subject imaging studies is usually performed by analyzing diffusivity measures (e.g. Fractional Anisotropy (FA), etc.) with Voxel Based Morphometry (VBM) [1] or Tract Based Spatial Statistics (TBSS) [2]. In recent years, various techniques for the quantitative tractography-based analysis of fiber bundles have evolved [3, 4]. While these new methods facilitate a selective analysis of white matter bundles, they are hard to automate and often restricted to bundles with tubular shape [4]. In this contribution, we present a new automatic method for the quantitative analysis of DTI data that extends a previously presented approach [5]. It utilizes atlas-guided fiber clustering to extract fiber bundles for the analysis. The method prevents the occurrence of interpolation effects [6] at the boundaries of white matter structures that are a result of the spatial normalization. To demonstrate the practicability of this new technique, an initial study was conducted to analyze hemispheric differences in the brain diffusivity of healthy volunteers.

Workflow of the quantitative analysis – The presented quantitative analysis technique is based on the notion to employ fiber bundles in order to prevent adverse interpolation effects that can occur at structure boundaries (e.g. intersection between gray and white matter or different white matter bundles). A processing overview is given in Fig. 1. Instead of modifying the quantitative values during the spatial normalization, the values are projected onto the fiber tracts and the normalization is applied only to the tracts. Since fiber tracts are defined by a set of points in 3D space, the spatial normalization is merely a coordinate transformation that changes the course of the tract, whilst the projected values are preserved. After the normalization, fiber bundles are extracted using an atlas-guided clustering approach [7]. As a result, we obtain the fiber bundles for each individual data set in the normalized space, whilst the quantitative values are still projected onto the tracts. Then, quantitative values are gridded for the voxel-wise quantitative analysis. Since the gridding is performed independently for each fiber bundle, contributions of voxels that do not belong to the particular bundles are suppressed and interpolation of quantitative values from different bundles is prevented. Finally, statistical analysis is performed voxel-wise for each bundle.

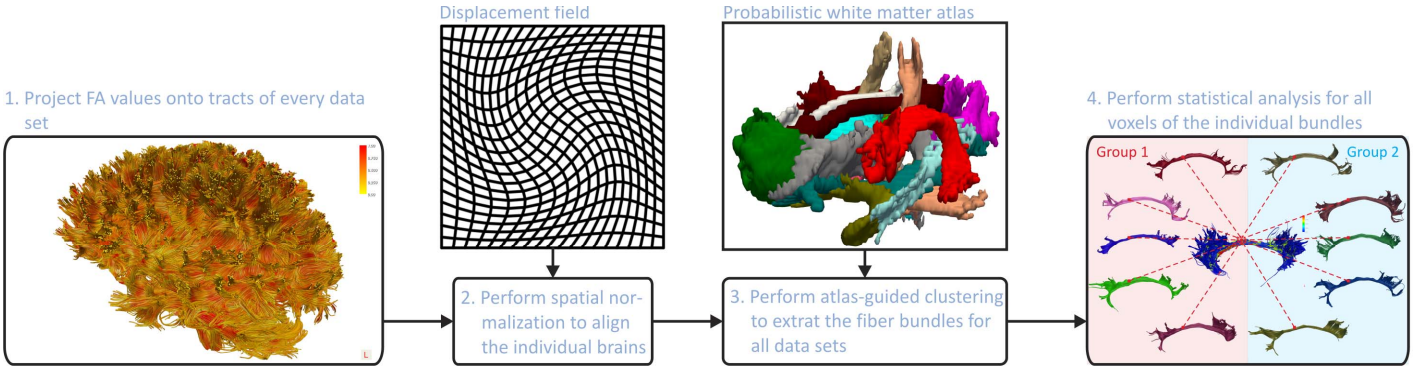

Fig. 1 – Workflow of the quantitative fiber bundle-based analysis. After data acquisition and pre-processing, individual quantitative values are projected onto the tracts of each data set (1). Non-linear, spatial normalization is performed and fiber tracts are transferred into the normalized space (2). Fiber bundles of interest are extracted with an atlas-guided fiber clustering approach (3). The statistical analysis is finally performed for every fiber bundle in every voxel that is occupied by the particular fiber bundle (4).

Materials and Methods – In order to demonstrate the feasibility of the proposed technique, DTI data sets of 46 healthy volunteers were acquired on a clinical 3 T whole body MR-Scanner (Magnetom Tim Trio, Siemens Healthcare, Erlangen, Germany), using a conventional EPI sequence [8]. A 12 channel head coil was employed and the following parameters were used: T_E=91 ms, T_R=6800 ms, α = 90°, iPAT=2, matrix of 96×96, 55 slices with a thickness of 2.5 mm, resulting in a voxel size of 2.5×2.5×2.5 mm^3. Five b_0 images without diffusion weighting as well as 70 diffusion weighted images sampled with different gradient directions at b=1000 s/mm^2 were acquired. In-plane interpolation was performed on the MR-scanner, resulting in a voxel size of 1.25×1.25×2.5 mm^3. The Diffusion Toolkit [9] was used to perform whole brain fiber tractography. Tracts having a length less than 30 mm were removed from the data set. All 46 data sets were flipped from left to right to achieve a superimposition between the bundles of both hemispheres. The resulting two groups of subjects (46 original and 46 flipped) were used to perform the quantitative analysis (see above). FA-Values were projected onto the fiber tracts. Non-linear co-registration was performed with the ANTs framework [10] for all 92 data sets using the FA. All data was transferred into the template space and an atlas-guided clustering [7] was used to extract the fiber bundles. A voxel-wise quantitative analysis of the FA was conducted for all bundles. Different statistical tests (permutation tests with 1000 permutations [11] and two-sample t-tests) were investigated. To correct for multiple comparisons the Šidák correction and the False Discovery Rate (FDR) [12] were tested with significance level $p < 0.01$. Only clusters with cluster size > 30 were considered valid clusters.

Results – The quantitative analysis was successfully performed for all fiber bundles. Hemispheric differences were observed in various bundles (e.g. anterior part of the cingulum bundle (CB), uncinate fasciculus, etc.). After application of the correction method, results are still significant. The observed differences in FA between the bundles are in accordance with the literature [13]. Results of the hemispheric differences in the CB are shown in Fig. 2.

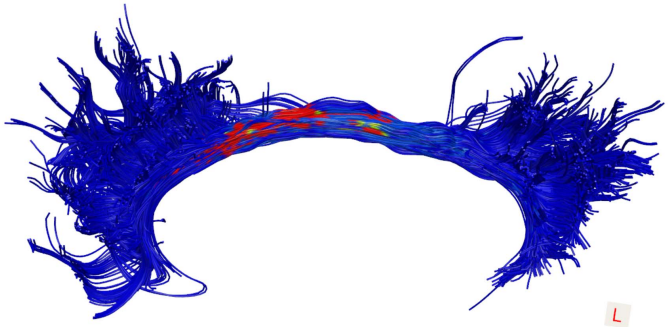

Fig. 2 – Results for the hemispheric differences in the cingulum bundle using the FDR. No statistically differences were found in the blue parts of the bundle. Significant differences are shown in green (before correction) and in red (after correction).

Discussion & Conclusion – With this contribution we presented a new fully automatic method for the quantitative analysis of DTI data sets that uses an atlas-guided clustering approach to extract the fiber bundles and to enhance the analysis. Even though the processing steps are more complex compared to VBM or TBSS, the use of fiber bundles prevents the occurrence of adverse interpolation effects at the boundaries of white matter structures.

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