Uncertainty and Reproducibility of Quantitative DTI and Fiber Tracking of the Human Brain

Klein, J.[1,], Schlüter, M.[1], Rexilius, J. [1], Konrad, O. [1], Erhard, P.[2], Stieltjes, B.[3], Althaus, M. [1], Dreher, W.[2], Leibfritz, D.[2], Hahn, H.K.[1] & Peitgen, H.-O.[1]

[1] MeVis Research, Bremen, Germany, [2]FB 2 (Chemistry) and Center for Advanced Imaging (CAI), Bremen, Germany, [3]Dept. of Radiology, German Cancer Research Center, Heidelberg, Germany

Introduction. Diffusion tensor imaging (DTI) techniques like fiber tracking (FT) or quantification of DTI related parameters have the potential to identify major white matter tracts afflicted by an individual pathology or tracts at risk for a given surgical approach. However, the reliability and reproducibility of these techniques are known to be limited by the quality of acquired data, the underlying models and algorithms, and by the methods for reporting and displaying the results.
We show how different image resolutions of the acquired data influence the quantification and fiber tracking process, derive a relationship between the diffusion anisotropy (DA) and the orientation uncertainty (OU) by considering image noise, and present methods to assess and visualize the uncertainty of fiber reconstructions.
As a consequence, we are able to develop and evaluate robust preprocessing, fiber tracking, and quantification algorithms which take partial volume effects into account and which are able to compute DTI parameters along fiber bundles automatically.
Our optimized color-coding scheme for DTI data as well as our fiber clustering algorithm address the problem of presenting the results to the clinicians in such a way that uncertainties in the interpretation are reduced and the perception of the visualization is enhanced.

Methods. We acquired echo planar diffusion tensor data from both 1.5T and 3.0T scanners. For examining resolution-dependent differences, the data was acquired at several image resolutions. Using a deflection-based fiber tracking algorithm [8], we reconstructed parts of the cingulum as well as parts of the pyramidal tract for all DTI data sets [3]. A method which is capable of an automatic quantification of MR DTI parameters along arbitrarily oriented fiber bundles [5] is used for measur-

ing the average fractional anisotropy (FA) along the fiber bundles. Moreover, we propose to determine the volume of the sheath that encloses the single fiber tracts.
By considering image noise, we derived a local relationship between DA and OU [8]. Because of this relation, a decrease of the DA implies an increase of the OU. With this observation a white matter lesion model on diffusion tensor data can be developed, where fiber bundle disturbance of arbitrary strength can be simulated at arbitrary locations. Thus, it is possible to assess existing and forthcoming FT algorithms with respect to the robust fiber bundle reconstruction in the presence of white matter lesions.
Moreover, we developed a method to assess and visualize the uncertainty of fiber reconstructions based on variational complex Gaussian noise, which provides an alternative to the bootstrap method (cf. Fig. 1 left). We compare fiber tracking results with and without variational noise as well as with artificially decreased image resolution and signal-to-noise [1,2].
For quantification of DTI parameters, we introduced a method which assumes a probabilistic mixture model inside a region of interest (ROI) including the two pure tissue classes fiber and background. Since the voxel size is not negligible compared to the extension of the quantified fiber bundle, partial volume effects have to be considered. Therefore, we added a mixture or partial volume class to our model [6,9,10]. Our automatic quantification along bundles allows for a robust and reliable measurement of DTI parameters as outliers only have a very small influence in the results [5].
For visualization, we introduce a new color coding paradigm for DTI based fiber bundle orientation [7]. The color coding is defined with respect to an arbitrary projection plane, which can be automatically adjusted in order to minimize the local ambiguity of the encoding. Finally, our grid-based spectral fiber clustering groups anatomically or geometrically related fibers in order to improve the perception of tracking results (cf. Fig. 1 center) [4].

Results. Our experiments confirm that DTI parameters like average FA, the volume of the sheath around fibers, or the number of fibers depend on the image resolution, but the amount of change also depends on the kind of fiber bundle. While the average FA value increases remarkably for the cingulum when increasing the resolution, the FA value for the pyramidal tract only slightly increases. This may be explained by the fact that the tensor field is more sensitive in areas where different fiber structures are close to each other as in the case of the cingulum. The volume of the sheath, however, differs more for the pyramidal tract. This may be explained by partial volume effects where bundles in isotropic surroundings are assessed too large whereas fibers in inhomogeneous areas are not tracked at borders.

Our proposed lesion phantom based on the relationship between OU and DA is employed to improve our deflection based FT algorithm. We applied it to synthetic fiber bundles as well as to real DTI data and demonstrated the robustness of the modified FT algorithm.

Using our variational complex Gaussian noise, the uncertainty due to image noise can be measured and visualized. We found a high robustness to a decreased signal-to-noise ratio, but still, the effects of image quality on the tracking result will depend on the employed fiber tracking algorithm and must be handled with care, especially when being used for neurosurgical planning or resection guidance.

Furthermore, we showed that the results of our quantification are largely independent of the ROI extension, which facilitates reproducible quantification of white matter infiltration [10]. The automatic quantification along fiber bundles drastically reduces the manual effort and hence the time for quantifying, e.g., the FA along a complete bundle.

An excellent differentiation of fiber orientations is achieved by our color coding so that it directly improves in vivo brain navigation with potential application to therapy planning. Moreover, our fiber clustering automatically determines the number of clusters depending on the desired granularity and constitutes the basis for an enhanced perception and interaction.

Finally, we demonstrated that the introduced methods not only allow for an early, direct, and sensitive detection of white matter infiltration (cf. Fig. 1 right), but may also be employed for monitoring the therapy of ALS or MS patients, which emphasizes the clinical relevance of our results [6,9,10].

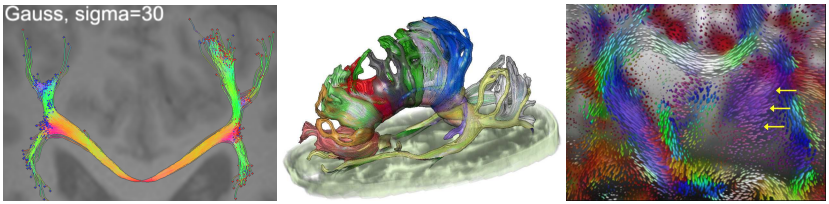

Figure 1. Left: Complex Gaussian noise used to visualize the uncertainty due to noise [2]. Center: Fiber clustering is used to improve perception and interaction [4]. Right: Colored glyph based rendering of structural changes induced by a Glioblastoma [9].

Discussion. There are several reasons that have prevented DTI to become a widespread clinical diagnostic modality so far. Among these, reproducibility as well as the inherent uncertainty in the data and in the results are the most important factors. Until now, we introduced some initial techniques for quantifying and visualizing the uncertainty of the DTI data, for developing and evaluating robust fiber

tracking and quantification algorithms, and for presenting the results to the clinicians such that they are easy to use and ambiguities are reduced. In the near future, we would like to identify risk structures based on the reconstructed fiber bundles in order to further reduce the risk of specific interventions and increase patient safety. Uncertainties, which cannot be reduced, may be visualized as confidence margins.

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Correspondence. Jan Klein, MeVis Research, Email: klein@mevis.de