Simulated DTI data sets for the evaluation of voxel based analysis methods

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Introduction

Many diffusion tensor imaging (DTI) studies are starting to use voxel based analysis (VBA) to compare DTI data between healthy and diseased subjects. However, Jones et al. (2005, 2007) and Zhang et al. (2007) demonstrated that different VBA results can be obtained when different coregistration techniques, smoothing kernels, statistics, etc. were implemented during the VBA analysis of the same subject group (1-3). Since the location and extent of the underlying microstructural degradation was not known a priori in these studies, quantitative information regarding the accuracy, precision, or reliability of the obtained VBA results could not be provided. As such, these studies clearly demonstrate the need for a gold standard for validating different post-processing methods and their relative merits in VBA. To address the lack of ground truth knowledge regarding the underlying microstructural alterations, in this work, simulated DTI data sets are developed, which allows for modeling of anomalies in the diffusion properties of a predefined location and in a predefined number of voxels. In this context, an important requisite for the validity of the simulated DTI data sets is to model the induced pathology by simulating these diffusion properties accurately and realistically. To the best of our knowledge, this is the first framework that allows for constructing simulated DTI data sets with ground truth information of pathology. The simulated DTI data sets can be used to investigate the reliability, accuracy, and precision of a VBA or ROI analysis. In addition, the effect of the different parameters and post processing steps that are involved in the pipeline of a VBA analysis can be examined and even optimized, which could lead to a more reliable, standardized, and consistent post-processing of DT images for studying different pathologies.

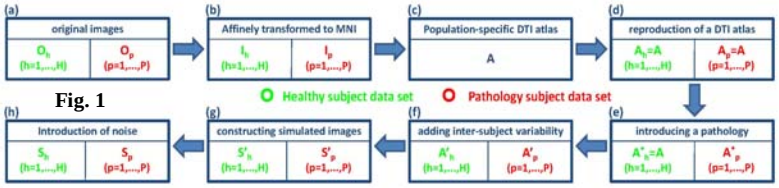

Fig. 1

Methods

Simulated DTI data sets are constructed that contain a ground truth pathology with a predefined location, extent, and level of tissue degradation. In Fig. 1, a general overview of the construction of these simulated DTI data sets is presented and can be summarized as follows: (a) *H* healthy subject and *P* pathologic DTI data sets are acquired on a 1.5 T scanner. (b) These DTI data sets are transformed to MNI space with an affine transformation. (c) A population specific atlas is constructed from these images in MNI space (4). (d) This atlas represents the fundamental data set of the ground truth method and is reproduced *N* (=*H*+*P*) times. (e) In half of these atlases, the diffusion properties are altered to introduce pathology in a predefined number of voxels. (f) Thereafter, the diffusion properties are modified to include inter-subject variability. (g) Next, all data sets are transformed to their individual space. To this end, non-affine deformation fields were calculated between the atlas space and the native space of the 40 original images by three different coregistration methods (basis functions, b-splines, viscuous fluid model). (h) Finally, a realistic amount of Rician noise is added to the data sets. To examine the effect of image alignment and tissue degradation on the sensitivity of the VBA results, 40 simulated data sets were generated with a specific level of noise and inter-subject variability Several levels of pathology (predefined increase of the transverse eigenvalues) were simulated in the splenium of the corpus callosum (size: 54 voxels in 4 consecutive axial slices) for 20 data sets. Two VBA analyses were performed demonstrating the subtle changes in outcome of regions with a significant FA difference between healthy and diseased subjects due to imperfections in coregistration: Analysis 1: The predefined deformation fields to transform the simulated data sets to native space were applied to invert the data back to atlas space. In doing so, perfect alignment is guaranteed taking into account the effects of data interpolation, allowing for the computation the effective levels of pathology (that is, prior to adding noise and inter-subject variability). Analysis 2: The data sets in native space (as in Analysis 1, but with noise and inter-subject variability added) are coregistered to the atlas using a non-rigid coregistration approach (5). For both analyses, the FA data were smoothed with a Gaussian kernel (3 mm FWHM) and a parametric t-test was used to compare the FA values between the healthy and the pathology data sets, followed by the Benjamini-Hochberg post-hoc correction for multiple comparisons. To quantify the VBA results, the sensitivity - calculated as the ratio of the number of true positives with the sum of the number of true positives and false negatives - is computed for both analyses and repeated 10 times.

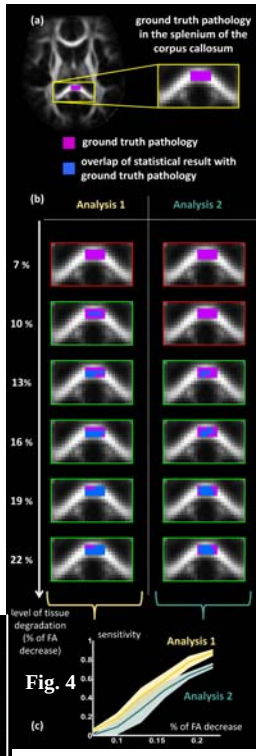

Fig. 4

Results

The correspondence of the simulated DTI data sets with realistic data sets is evaluated visually (Fig.2) and quantitatively (Fig.3). In Fig.2, the original (A) and the simulated (B) FA images are given a blue, and red color, respectively. After overlaying both images, corresponding voxels with similar FA values are colored purple. In Fig.3, different WM structures are delineated on the original and the simulated data sets, whereafter a percentage of overlap of these selected regions is calculated. In Fig. 4, the VBA results of Analysis 1 and Analysis 2 are displayed for different levels of tissue degradation, expressed as a percentage of effective FA change. One of the axial slices, in which the pathology was simulated, is shown in Fig. 4 (a). In Fig. 4 (b), the VBA results of the splenium are shown qualitatively for analyses 1 and 2 for different levels of simulated pathology and quantitatively in Fig.4 (c).

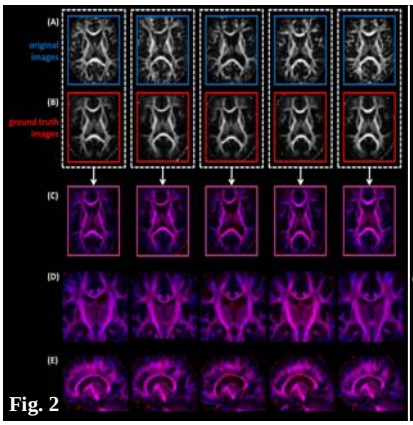

Fig. 2

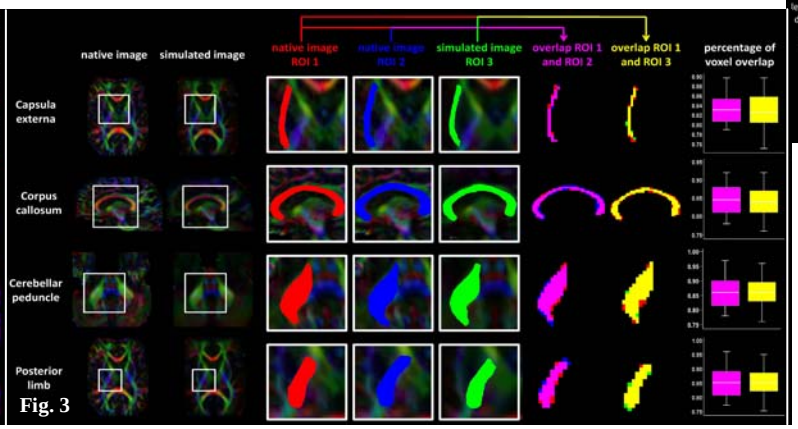

Fig. 3

Conclusion : In this work, simulated DTI data sets are constructed. These data sets can be employed in future studies to evaluate the numerous parameters that characterize a VBA pipeline and to quantitatively compare the accurateness, precision, and reproducibility of different VBA post-processing approaches.

Ref:[1]Jones etal,2005, NeuroIm; [2]Jones etal, 2007, ISMRM [3]Zhang etal., 2007, IEEETMI [4] VanHecke etal., 2008, NeuroIm [5] VanHecke etal., 2007, IEEETMI