Quantitative Validation of White Matter Fiber Tractography by use of an Anatomically Realistic Synthetic Diffusion Tensor Phantom

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Introduction

Diffusion Tensor (DT) Imaging can disclose the 3D organization of fibrous tissue. Although Diffusion Tensor Tractography (DTT) is a very promising non-invasive method for reconstructing the white matter axonal pathways, its current clinical use is limited due to the lack of a golden standard to validate this technique. Therefore we propose a framework to construct a noise-free synthetic diffusion tensor dataset, originating from a known fiber distribution that resembles the true white matter anatomy as accurate as possible (including slender as well as thicker, crossing and "kissing" fasciculi with realistic curvature and torsion parameters).

These ground-truth fibers are obtained by performing Density Regularized Fiber Tracking (DRFT, [1]) on *in vivo* data. The environmental architectural information proffered by the DRFT results, together with the pointwise measured FA (Fractional Anisotropy) and Mean-ADC (Apparent Diffusion Coefficient), were modeled into an anatomically realistic noise-free synthetic DT dataset, which eventually was used to optimize and quantitatively validate several existing tractography algorithms.

Theory: how to build the phantom?

The best way to acquire anatomically realistic ground-truth fibers is to perform tractography on an in vivo diffusion tensor dataset. However, since we want to build a noise-free phantom, without spurious fibers, a few precautions are necessary. In a first step, the DWIs (Diffusion Weighted Images) were realigned and smoothed with a 3D scalar partial-differential-equation filter (aka nonlinear anisotropic diffusion filter) [2]. Secondly, an altered version of the RESTORE method [3] was used to robustly estimate the diffusion tensors: first the original *non-smoothed* DWIs were used to identify outliers in the data, then these outliers were rejected during the final tensor fitting of the *smoothed* DWIs. The RESTORE technique is also considered to remove the need for cardiac gating.

In a third step, we seeded the whole brain white matter with 5000 starting points from which DRFT was initiated. In order to be able to include crossing fiber bundles in the phantom, we used tensor deflection, a technique that can traverse such regions [4]. The final set of ground-truth fibers was then found by discarding all tracts shorter than 2 cm and smoothing the remaining ones by cubic spline fitting.

In a fourth step, we built the corresponding DT dataset. For this purpose we extended the work done by A. Leemans [5]: in stead of using fixed parameters for each fiber and for each point along these fibers, we use the pointwise environmental architectural information provided by the DRFT results. *DRFT is performed by simultaneously tracking of typically 27 temporary tracts with any line propagation method. After each step, the mean distance (m_d) of these tracts to their center of mass and its standard deviation (σ_d) is calculated and a decision is made whether or not to discontinue any of the temporary tracts [1].* To give the ground-truth fibers a certain spatial extent in the phantom, a cylindrical tube is built around them. This tube has a saturated Gaussian profile with a width proportional to m_d *x f(# temporary tracts at that point)*. *f* is a sigmoidal function that puts less weight to less probable sections (i.e. segments surrounded with a low number of temporary tracts). The steepness of the profile is inversely proportional to σ_d. Each point also gets an actually measured FA and Mean-ADC value.

In a fifth and last step we made noisy realizations of the above phantom, by first backwards calculating the DWIs corresponding with the noise-free synthetic DT dataset, then adding Rician distributed noise to these DWIs and recalculate the tensors again.

Material and methods: how to use the phantom for optimization and validation purposes?

We can now apply different tractography algorithms on the synthetic DT phantom and subsequently compare the reconstructed fibers with the ground-truth ones. Therefore we used following similarity measure: $S = R_{CS}\exp(-MED)$, with R_{CS} the corresponding segment ratio and *MED* the Mean Euclidian Distance [5]. In the calculation of *MED* however, an extra term (*f,* see above) makes sure that less probable ground-truth fibers get less weight.

The described framework was used to optimize internal and operator dependant parameters of the tracking algorithms mentioned in Fig. 3. These optimized algorithms were then applied on a range of noisy realizations of the phantom (Fig. 3).

The initial in vivo dataset was acquired on a Siemens Trio (10 b0 volumes, 60 diffusion sensitizing gradient orientations, b-value = 1000 [s mm^{-2}], 128 x 128 x 60 matrix of isotropic voxels (2.0 mm)^3).

Results

A good correspondence is found between the color coded synthetic FA images (Fig. 1.a and 2.a) and the original in vivo ones (Fig. 1.b and 2.b), even in regions with crossing fibers. In Fig. 3 we see that some techniques degrade faster with larger noise levels than others, but the best ones remain quite robust until an SNR of ±45. In order to select the best tracking method, other parameters, such as computation time (see values between brackets in the legend of Fig. 3), can be important.

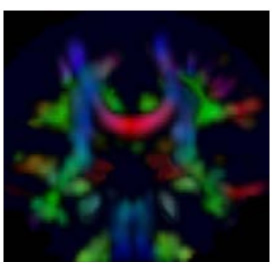

Fig. 1.a: Phantom

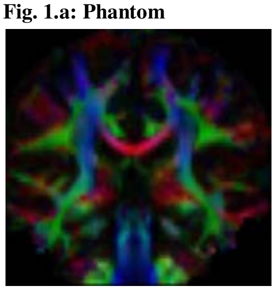

Fig. 1.b: In vivo

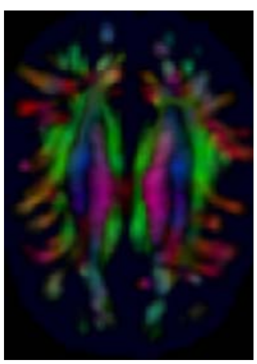

Fig. 2.a: Phantom

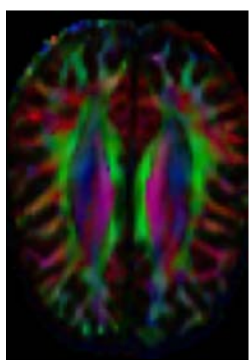

Fig. 2.b: In vivo

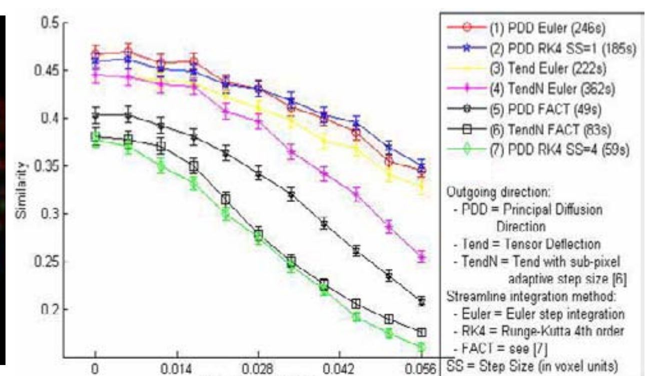

Fig.3

Discussion and Conclusion

With an anatomically realistic DT dataset we can quantitatively predict how a (new) DTT algorithm will perform on real in vivo data. In previous work, several authors already used synthetic datasets, but always with very ad hoc and far less elaborated underlying fiber distributions. By using in vivo Tensor Deflection DRFT results we were able to model the most important in vivo occurring bundle geometries into a noise-free DT dataset. Noise and MRI acquisition artifacts (such as physiologic movement and susceptibility artifacts) can be incorporated in the synthetic DWIs during the last step of building the phantom.

References: [1] Delputte et al., Proc ISMRM 2005, p. 1309; [2] Chen et al., MRM 2005, 54: 393-407; [3] Chang et al., MRM 2005, 53:1088-1095; [4] Lazar et al., HBM 2003, 18:306-321; [5] Leemans et al., MRM 2005, 53: 944-953; [6] Chou et al. Proc ISMRM 2005, p. 1308; [7] Mori et al., Ann Neurol 1999, 45:265-269