Choices in processing steps for diffusion MRI analyses: Does it really matter?

Szabolcs David[1], Chantal M. W. Tax[1], Max A. Viergever[1], Anneriet Heemskerk[1], and Alexander Leemans[1]
[1]*Image Sciences Institute, University Medical Center Utrecht, Utrecht, Utrecht, Netherlands*

Target audience: Researchers with an interest in diffusion MRI tractography

Introduction: With advanced diffusion-weighted (DW) MRI methods becoming more popular to investigate white matter properties in clinical and biomedical applications, a lot of efforts are being made to optimize the pipeline to analyse the data [1]. Different steps and settings during processing procedures (e.g. corrections to subject motion, eddy current induced distortions and EPI deformations, spatial normalization, and tensor estimation methods) can influence the resulting outcome and may complicate interpretation and statistical inferences [2, 3]. The purpose of this work was to investigate whether the choice of (a) interpolation strategy (linear vs. cubic spline) during subject motion / eddy current distortion correction and (b) the tensor estimation procedure (robust vs. ordinary linear least squares – OLLS) would *significantly* affect the outcome, which in this work was confined to an example of a tractography based analysis of the uncinate fasciculus.

Methods: Acquisition: Ten healthy volunteers were scanned on a 3T MR system with a diffusion MRI scan protocol consisting of: 60 DW images with b-value of 1200 s/mm^2; 6 non-DW images; isotropic voxel size of 2.4 mm (more details are provided in [4]). Processing: All datasets were processed with ExploreDTI [5] using four different pipelines: linear and cubic spline interpolation during correction for subject motion and eddy current distortions [6] in combination with two diffusion tensor estimation methods: REKINDLE [7] and the OLLS approach [8]). Analysis: An automated atlas based fiber tractography based on the framework presented in [9] was used to reconstruct the right uncinate fasciculus (R-UNC). Details of the ROI protocol to extract the R-UNC are described in [10]. Statistical evaluation: Fractional anisotropy (FA), volume, and mean diffusivity (MD) of the R-UNC tracts are compared between the four processing pipelines using paired t-tests. Combinations in which both the tensor estimation and the interpolation approach are different were not examined.

Results: Fig. 1 illustrates the differences in trajectories of the R-UNC between the four different processing pipelines for a representative subject. Generally, small differences are observed in the length and the overall configuration of the tract pathways. Fig. 2 shows the spatial heterogeneity of the FA difference between REKINDLE and OLLS for the linear interpolation strategy. We found, however, *significant* differences in FA values between the tensor estimation methods for a given interpolation approach and between the two interpolation approaches for a given tensor estimation method (Fig. 3 A). As shown in Fig. 3 B, predominantly the interpolation method affected the MD estimates. There was only a minor effect of estimation method on the volume of the tract (Fig. 3 C).

Discussion and Conclusion:

In this work, we have shown that the influence of tensor estimation and interpolation methods on a typical diffusion analysis is significant. Both the interpolation method and the tensor estimation method result in small local, yet significant differences in the diffusion metrics. Comparisons of data from different processing pipelines should be interpreted with care. Considering the interaction of the processing parameters there is *no significant difference* in the effect size of tensor estimation and interpolation strategy in the case of FA. For MD the outcome is more affected by the interpolation method, while volume is more sensitive to the choice of tensor fitting algorithms.

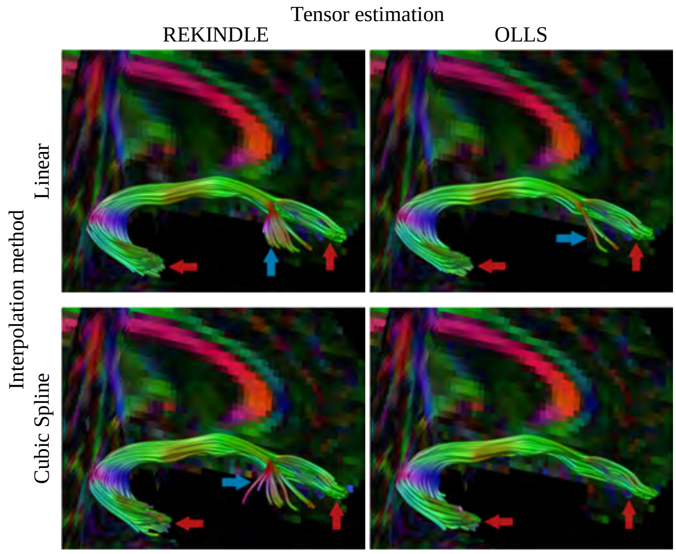

Fig. 1: *Tracts representing the right uncinate fasciculus reconstructed with four different preprocessing strategies from the same subject. Arrows indicate differences in architectural configurations.*

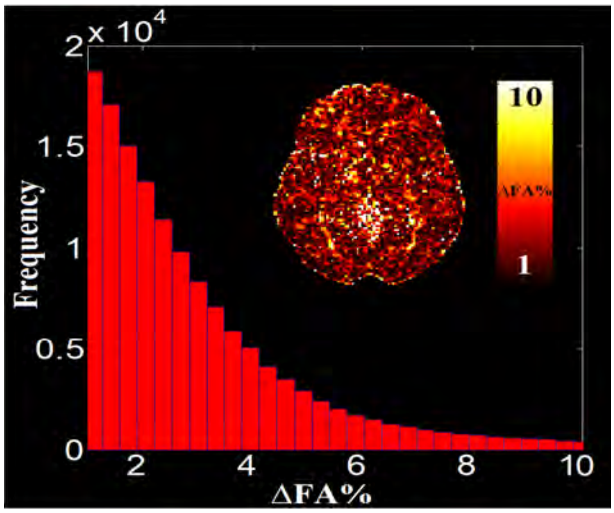

Fig. 2: *Voxel wise difference in FA between OLLS and REKINDLE for a representative subject. Image scale and histogram X axis indicate FA differences between 1% and 10% value.*

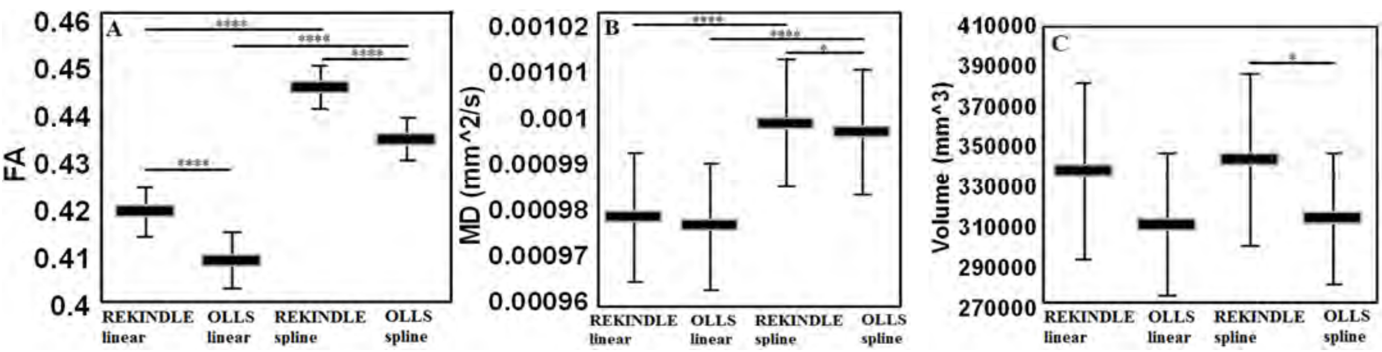

Fig. 3: *Average and standard error of the mean FA (A), MD (B) and volume (C) of all ten R-UNCs. Significant differences can be found between all the FA and some of the MD values; however volumetric difference only occurs between REKINDLE and OLLS with cubic spline interpolation. Data sets that are significant at different levels: * p<0.05, ** p<0.01, *** p<0.001, **** p<0.0001.*

References:

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