Diffusion Kurtosis Imaging based Tractography

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Target audience: researchers interested in diffusion weighted imaging and in particular tractography methods; clinicians interested in evaluating a novel tractography method compatible with clinically suitable scanning times.

Purpose: Tractography is a non-invasive technique that allows visualization of white matter pathways *in vivo* from diffusion weighted (DW) MRI images[1]. The simplest tractography algorithms are based on the diffusion tensor (DT) estimated from diffusion tensor imaging (DTI). DTI's main limitation is to only allow the estimation of one diffusion direction per image voxel, failing to map regions with complex white matter geometries such as crossing, bending or highly angulated fibres. To overcome this limitation, tractography algorithms based on new DW models such as diffusion spectrum imaging (DSI) were developed and are able to resolve crossing fibres in neural tissues, at the expense, however, of very long scan times[2]. On the other hand, techniques based on q-ball imaging data[3] are able to estimate multiple fibre directions in each voxel requiring much less data (shorter scanning times). Nevertheless, since they are based on single shell acquisitions (single DW value), they do not take into account the non-Gaussianity behaviour of water diffusion in biological tissues. Diffusion kurtosis imaging (DKI) extends the DTI model, allowing quantification of the non-Gaussianity of water diffusion using the kurtosis tensor (KT) which can be estimated from data acquired within clinical scanning times. In a previous study, Lazar et al. used DKI to estimate the fibre orientation distribution function (ODF) which could be used to predict two to three crossing fibres per voxel[4]. More recently, Neto Henriques et al. showed that the KT's 3D geometry by itself could be more sensitive to crossing fibres than the ODF proposed by Lazar et al.[5] In this study, two DKI-based tractography algorithms are proposed and tested on DT and KT obtained from simulated and real brain MRI data: the first algorithm is constructed based on the ODF estimations suggested by Lazar et al.[4] (LDKI), while the second is based on the observations by Neto Henriques et al.[5] (NDKI).

Methods: 1. Simulations - Line crossings with intersection angles of 90° and 45^0 were manually defined over matrices of 7×6 voxels to simulate diffusion DW images of two different crossing fibre geometries (Fig.1. A and B). For each voxel of the matrices, DT and DK were estimated based on the multi-compartment models suggested by Neto Henriques et al.[5], which assumes that tissue elements can be represented by anisotropic intra and extra-cellular compartments. According to previous reports[6], the axial and radial diffusivities for the intra-cellular compartment were set to $0.99×10^{-3}$ and 0 mm^{2}s^{-2}, while the axial and radial diffusivities for the extra-cellular compartment were set to $2.26×10^{-3}$ and $0.87×10^{-3}$ mm^{2}s^{-2}. Since the intra and extra-cellular volume fraction of each population of fibres was always set to 0.25, an additional compartment with isotropic diffusivity of $2.26×10^{-3}$ mm^{2}s^{-2} was added to model the diffusion properties of the volume not occupied by the intra or extra-cellular compartments.

Fig.1 Tractography maps reconstructed from simulated diffusion weighted images. Top panels, represent the ground truth of simulated fibres crossing at 90° (panel A) and 45° (panel B). Panels C and D are the tractography reconstructions obtain by LDKI, while panel C and D are the reconstructions obtain by NDKI.

2. MRI experiment – DW images were acquired on 6 healthy adults (4 males and 2 females aged between 25 and 32 years) on a 3T Siemens Trio and using a twice refocused spin echo sequence (TR/TE=9600/111ms). All brain DW images were acquired with a voxel resolution of 2×2×2mm^{3}along 30 equally spaced gradient directions and 5 b-values (500, 1000, 1500, 2000, and 2500 s.mm^{-2}). Additionally, for each participant, 26 acquisitions with no diffusion sensitizing gradients were also obtained (b-value=0). According to previous optimized processing methods for DKI[7], data was smoothed with a Gaussian kernel with FWHM=2.5mm and estimates of DT and KT were obtained using a linear DKI fit approach.

3. Tractography algorithms – After computing DT and KT, ODF were estimated according to the method proposed by Lazar et al.[5]. Fibre directions were extracted from the ODF estimates (for LDKI) and directly from the KT (for NDKI) using two home built MATLAB functions. For both LDKI and NDKI, tractography was performed using an adapted version of a DTI streamline algorithm[8], allowing the reconstruction of tracts from multiple fibre directions estimated per voxel. Tract reconstructions were initialized in all white matter voxels for all fibre direction estimates and propagated through voxels following these fibre directions with smaller angle deviation; tracking was finished when reaching a voxel with fractional anisotropy[9] lower than 0.2 or where the angle deviation exceeded 60°. The reproduced tracts were visually inspected using a MATLAB built toolbox, the DKIu[5] (for visualization of simulated data) and TrackVis (for visualization of real brain data)[2]

Results and Discussion: Both DKI-tractography algorithms accurately resolved simulated fibre crossings at 90° (Fig 1. C and E). However, fibres crossing at 45° are only resolved by NDKI (Fig 1. E and F). NDKI's improved ability to resolve crossing fibres is also supported by the tractography maps obtain from real data. For example, Fig. 2 shows that NDKI resolved a large number of corpus callosum fibres crossing with the corticospinal tracts (Fig. 2 shows the example of a representative subject – consistent upon visual inspection with the results for the remaining 5 subjects).

Conclusion: DKI shows potential to provide robust tractography techniques from acquisition schemes that could be used in clinical applications. Further studies are necessary to compare the DKI-based algorithms with other tractography methods based on DSI or Q-ball imaging. Further tests should also be performed to investigate the minimum requirements (in terms of number of diffusion directions and b-values) for the presented DKI tractography methods so as to maximize their usability in clinical practice.
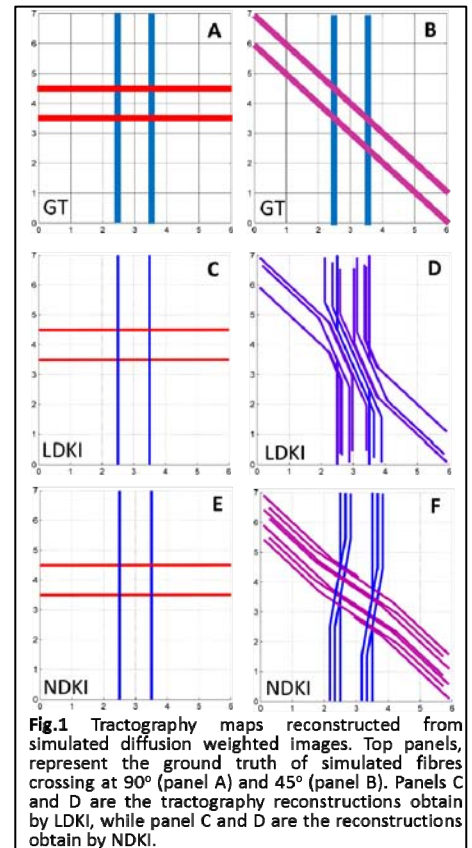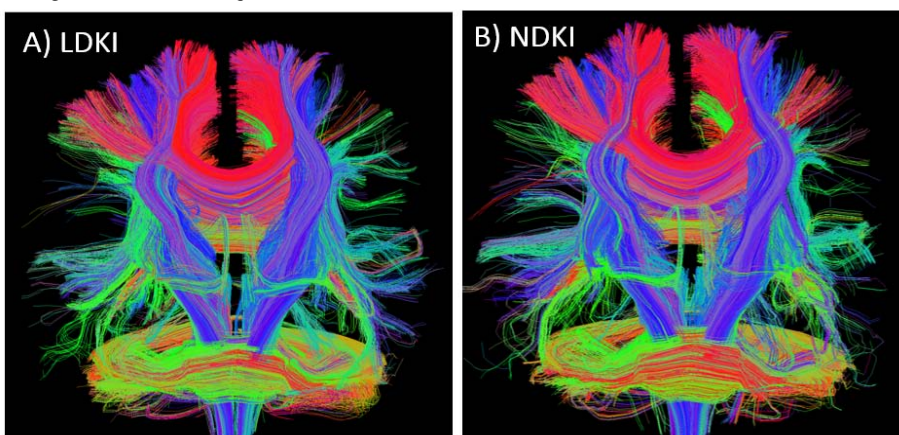
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Fig.2 Coronal view of the tractography obtained from real data using LDKI (panel A) and NDKI (panel B)