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Optimal Diffusion Kurtosis Imaging for Clinical Use – Fewer diffusion weightings or diffusion directions?

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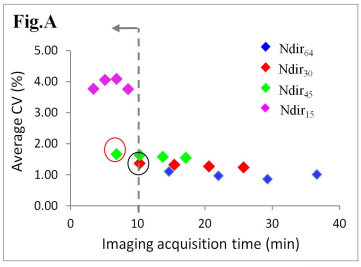
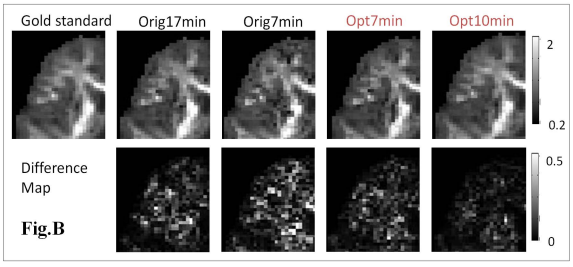
Introduction: Diffusion kurtosis imaging (DKI) measures the non-Gaussian diffusion distribution[1] and has gained much interest lately as a tool that can reveal significantly more tissue microstructure information over and above that can be achieved from Diffusion tensor imaging (DTI)[2]. However clinical application of DKI faces a major challenge, as it involves a long acquisition time from a requirement for additional measurements than standard DTI measurements to fit a more complex model (21 model parameters, compared to as little as 6 in DTI). A typical DKI acquisition requires data from many non-zero b-values and at least 30 directions and may take as long as 17 minutes or more. Shorter acquisitions with fewer b-values and directions have been suggested such as the use of 30 diffusion directions with two non-zero b-values (1000 & 2000 s/mm^2, referred to as Orig7min scheme). However, little is known regarding the variability in estimated DKI parameters using the shorter duration acquisition. In this study, we study the effect of b-values and diffusion directions to estimated DKI parameters with the goal of finding optimal DKI imaging schemes within a clinically feasible image acquisition time (< 10min), and to understand the estimation variability in using these optimal DKI schemes.

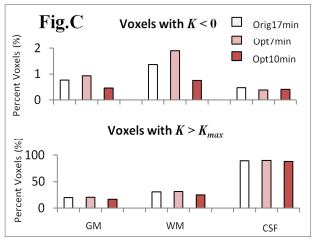
Methods: Imaging and reconstruction: DKI data was collect on a healthy male volunteer on a 3T Siemens Trio scanner with parallel imaging (factor 2). A total of four DKI datasets each were acquired with eight b_0 volumes and 64 diffusion directions, measured at five non-zero b-values (500, 1000, 1500, 2000, 2500 s/mm^2. TE/TR = 101ms/5500ms. 40 axial slices were acquired with an isotropic resolution of 2.7mm. A 3D T1MPRAGE images were also acquired for anatomy. Diffusion weighted data were preprocessed with co-registration to the b_0 volume and Gaussian smoothing (kernel of 3mm) in SPM8. DKI reconstruction used the constrained linear least squares method[4], where three constraint were used to reduce erroneous fitting (constraint#1: $D \geq 0$; constraint#2: $K \geq 0$; constraint#3 $K \leq K_{max} = 3/(D \cdot b_{max})$, where D is diffusion coefficient and K is diffusion kurtosis along any diffusion direction). DKI parameters (MK, K_a, K_r) were generated using elliptical integration[4]. Reconstruction was performed on the average of the four complete DKI dataset, and served as the gold standard. Data was then further parsed to obtain different combinations of b-value and diffusion direction subsets to construct various imaging schemes: two to five b-values ($Nbval_2$ to $Nbval_5$) and 15, 30, 45, 64 diffusion directions ($Ndir_{15}$ to $Ndir_{64}$). Data analysis: *ROI analysis*, 4 regions: corpus callosum genu, internal capsule, thalamus and basal ganglia were used to measure regional DKI parameter. In order to reduce bias due to the sampling of the unit sphere vs. the underlying tensor direction, eight subsets of maximally different diffusion directions were selected from each of the four full DKI dataset, resulting in 32 data points for each ROI. *Whole brain analysis*, white matter (WM), grey matter (GM) and CSF were considered separately based on segmentation of the T1MPRAGE image. Estimation accuracy was assessed based on the bias compared to the gold standard value for each parameter. Estimation variability was assessed based on coefficient of variation (CV) from 32 data points in ROI analysis, and from 4 repetitions in the whole brain analysis. To assess the susceptibility of different imaging schemes to erroneous fittings, unconstraint linear least squares fitting was used and voxels that violated specific constraint were counted within each brain mask.

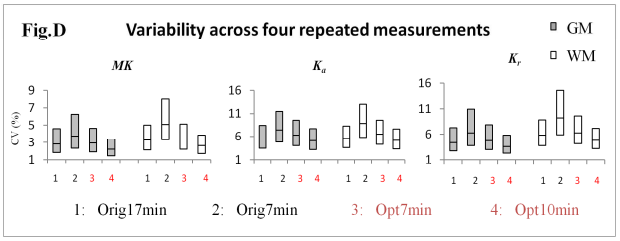
Results: 1) Effect of number of b-values and diffusion directions. **Figure A** shows an example of the estimation variability in genu averaged for all DKI parameters (MK, K_r, K_a) with different number of diffusion directions ($Ndir_{15}$, $Ndir_{30}$, $Ndir_{45}$, $Ndir_{64}$) and b-values (Left to right: $Nbval_2$, $Nbval_3$, $Nbval_4$, $Nbval_5$). The average CV was plotted against an estimate of image acquisition time based on diffusion weighted volumes required for the particular scheme. The CV reduced with increased number of diffusion directions and significant improvement in the estimates was observed going from $Ndir_{15}$ to $Ndir_{30}$. Increased number of b-values did not contribute much to reduction of estimation variability. Two optimal imaging schemes were determined that had an acquisition time of less than 10 min and used two b-values (b = 1000, 2500 s/mm^2). One of them required 30 diffusion directions (~7min, Opt7min scheme, circled in red) and the other required 45 diffusion directions (~10min, Opt10min scheme, circled in black).

2) Performance of different imaging schemes. These two optimal imaging schemes were compared to the Orig17min (5 non-zero b-values and 30 diffusion directions[1]) and Orig7min schemes, as well as the gold standard, to assess their performance. **Fig. B** shows the K_r map from the different imaging schemes from the 1st DKI dataset. A difference map showing absolute K_r difference from the gold standard is also shown. The Orig7min scheme has the noisiest K_r map and highest difference compared to the gold standard. The Opt7min scheme performed similarly as the Orig17min scheme. The Opt10min scheme showed the smoothest K_r map and least difference from the gold standard. **Fig. C** shows the distribution of voxel-wise CV from four repeated DKI datasets within GM and WM for different imaging schemes (box indicates median, 25th and 75th percentile CV). For both GM and WM, the estimation variability is the highest using the Orig7min scheme. The Opt7min scheme showed slight higher CV than the Orig17min scheme. The Opt10min scheme demonstrated the lowest variability across repeated measurements, as well as spatial variability indicated by the small inter-quantile distance (shorter boxes). **Fig. D** shows constraint violations for the imaging schemes with a b_{max} of 2500 s/mm^2 (Orig17min, Opt7min and Opt10min). Diffusion coefficient violation ($D < 0$) was only observed in less than 0.5% of brain voxels for all schemes. The Opt10min scheme had the lowest constraint violations in all conditions. The Opt7min scheme has higher chance of estimating voxels with negative kurtosis values ($K < 0$) than the Orig17min scheme.









Conclusion: Overall more reliable DKI estimation appears to be dependent on more diffusion directions than more diffusion weightings. The optimal imaging scheme with 2 b-values and 45 diffusion directions (~10min) provides lower estimation variability and less erroneous fitting than the commonly used 17min scheme with 5 b-values and 30 diffusion directions.

Reference: [1]. Jensen JH, et al., Magn Reson Med.53:1432-40, 2005. [2]. Zhuo J, et al., NeuroImage. 59(1):467-77, 2012. [3]. Jensen JH, Helpern JA. NMR Biomed. 23(7):698-710. 2010. [4] Tabesh A, et al., Magn Reson Med. 65(3):823-36. 2011.