Characterization of neural tissues in humans using diffusion kurtosis imaging

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Introduction: Diffusion kurtosis imaging (DKI) was recently proposed to probe non-Gaussian diffusion property [1-7]. A recent study by Hui et al. demonstrated that various kurtosis estimates can reveal information different from diffusivity estimates by diffusion tensor imaging (DTI) [4]. Additionally, the mean kurtosis (MK) was found to be equally applicable to both grey and white matter (GM/WM) in human brains as it does not require the microstructure of the tissue to be spatially oriented while conventional DTI measures are limited to WM [3]. However, it has never been reported whether directional kurtosis estimates in addition to MK improve tissue characterization in various human brain tissues. We aimed to characterize human neural tissues using kurtosis estimates and to compare them with conventional diffusivity estimates.

Methods: Nine healthy volunteers (5 male, 4 females; mean age = 24 ± standard deviation (SD) = 2) were studied after signed, informed consent. All studies were approved by the local institutional review board. All scans were performed on a Philips 3T MRI Achieva scanner (Philips Healthcare, Best, The Netherlands) with a body coil excitation and an 8-channel SENSE head coil for reception. Four averaged minimally weighted (b₀) and 2 averaged 32 gradient directions with two b values (1000 and 2000 s/mm²) were acquired using single-shot EPI sequence. The imaging parameters were: TR/TE = 2000/69 ms, nominal resolution = 2.55x2.55x3 mm³, reconstruction resolution = 2x2x3 mm³, 44 axial slices with no interslice gap to cover the whole brain, SENSE factor = 2, 3/4 partial Fourier encoding, total scan time = 19 min. 39 s. For anatomical reference, a three-dimensional T1-weighted image were also acquired using 3D-MPRAGE sequence with the following parameters: TR/TE = 7.0/3.2ms, TI = 800 ms, nominal/reconstruction resolution = 1x1x1 mm³, 167 slices, scan duration 10 min. 41 s. Data were processed using a custom-written program in MATLAB (Mathworks, Natick, MA, USA). The diffusion-weighted images were first co-registered to b0 followed by spatial Gaussian smoothing with full-width-half-maximum of 2.5 mm using Automated image registration (AIR5) [8]. Most of DTI- and DKI-derived indices were estimated as described in Jensen et al. [7] while MK was computed in a conventional way [3-6]. Eight regions-of-interest (ROIs) (5 GM areas including caudate head (ch), putamen (put), globus pallidus (gp), thalamus (th) and cortical GM (cGM); 3 WM areas including internal capsule (ic), corpus callosum (cc) and frontal WM (fWM)) were manually drawn using ImageJ (National Institutes of Health, Bethesda, MD, USA) and then transferred to all DTI-and DKI-derived maps for quantification. Spearman-rho analysis was performed to test the correlation between DTI- and DKI- indices using SPSS (Chicago, IL, USA).

Results: Fig.1 illustrates representive DTI- and DKI-derived maps from one subject. Although the maps for FA, MD, λ_{\parallel} and λ_{\perp} are qualitatively similar to those typically obtained with DTI, a recent study by Veraart et al. [9] showed that diffusivity measures by DKI provide more accurate estimation compared with conventional DTI. The maps for MK, K_{\parallel} and K_{\perp} provide additional information that quantifies diffusional non-Gaussianity. The calibration bars for the diffusivities are in units of µm²/ms, while those for the FA and kurtosis are dimensionless. Fig. 2 shows the scatter plots between DTI- and DKI-indices measured for various neural tissues from all subjects. Between MD and MK, no significant correlation was observed, however a negative correlation existed if only GM tissues were considered (r = -0.452, p = 0.002). A strong negative correlation was found between λ_{\perp} and K_{\perp} while a moderate correlation existed between λ_{\parallel} and K_{\parallel} . Our results agree well with a study demonstrated in rodent brains [4].

Conclusion: In present study, kurtosis estimates were computed for various WM and GM tissues and compared to the diffusion tensor estimates, for the first time in human brains. By measuring directional diffusivity and kurtosis, DKI offers a more comprehensive and sensitive detection of subtle changes in tissue microstructure. Such imaging advance can provide better MR diffusion characterization of neural tissues, both WM and GM while conventional DTI is limited to WM. DKI in

Fig. 1. DTI- and DKI-derived maps. WM GM 1.4 1.2 ♦ ic O ch put 1.2 ▲ fWM △ gp Oth <u>=</u> 0.8 - cGM = -0.289p < 0.010.4 0.6 0.8 1.8 2.2 0.9 1.2 0.6 1.4 0.3 0.6 1.2

 $\lambda_{\parallel} (\mu m^2/ms)$

combination with DTI may provide further information in normal, developmental and pathological states in human brains.

Fig. 2. Spearman-rho correlations between various DKI and DTI estimates measured for WM and GM tissues from all subjects.

 $\lambda_{\perp} (\mu m^2/ms)$

References: [1] Jensen JH et al., Magn Reson Med, 2005. [2] Lu H et al., NMR Biomed, 2006. [3] Falangola MF et al., J Magn Reson Imaging, 2008. [4] Hui ES et al., NeuroImage, 2008. [5] Cheung MM et al., Neuroimage, 2009. [6] Wu EX et al., NMR Biomed, 2010. [7] Jensen JH et al., NMR Biomed, 2010. [8] Woods RP et al., J Comput Assist Tomogr, 1998. [9] Veraart et al., Magn Reson Med, 2010.

 $MD (\mu m^2/ms)$