A more accurate and b-value independent estimation of diffusion parameters using Diffusion Kurtosis Imaging

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Introduction/Purpose: In diffusion tensor imaging (DTI), one assumes that diffusion of water molecules through brain structures occurs in a free and unrestricted environment. The chance of those molecules diffusing from one location to another in a given time period is described by a Gaussian probability distribution of which the standard deviation is proportional to the diffusion coefficient [1]. However, due to the complex cellular microstructures (cell membranes, organelles, extra - and intracellular water compartments) in biological tissue, the diffusion will appear non-Gaussian. This implies that the signal attenuation of the diffusion weighted signal with respect to the b-value can no longer accurately be approximated by the monoexponential function assumed by DTI. Because of this, the estimation of the diffusion coefficient and the associated diffusion parameters such as the fractional anisotropy (FA), mean diffusivity (MD) and radial diffusivity (RD) depends on the *b*-value of the acquisition [2]. In order to quantify the apparent non-Gaussian behavior of the diffusion, Jensen et al. recently developed Diffusion Kurtosis Imaging (DKI) [3]. They proposed to extend the DTI model by adding the second order term of the Taylor series. The DKI model not only enables a more accurate fit of the diffusion weighted signal attenuation. It is also possible to associate the additional coefficient with the apparent kurtosis, a dimensionless measure which quantifies the degree of non-Gaussianity. In this study, it will be demonstrated that DKI allows a more accurate estimation of the diffusion parameters compared to conventional DTI, which is, in addition, characterized by a reduced *b*-value dependency.

Methods: For one adult Sprague-Dawley rat, a set of diffusion weighted images (DWIs) was acquired at the Bio Imaging Lab (University of Antwerp) on a 9.4T Bruker Biospec scanner (Ettlingen, Germany) using a spin echo EPI sequence with an encoding scheme of 30 DW-gradient directions using TR/TE=6500/24ms, δ=5ms/Δ=12ms, acquisition matrix = 96 x 64 with resolution = 0.3 x0.3mm^2 and 35 slices with slice thickness = 0.6mm**.** Eight *b*-values (0, 400, 800, 1200, 1600, 2000, 2400 and 2800 s/mm^2) were used along each direction. In addition, the sequence was repeated 4 times resulting in a set of 868 DWIs.
The diffusion parameters were calculated by means of the eigenvalues of the DTs which were estimated using (I) the DTI model, including all DWIs corresponding to 2 *b*-values, 0 and 400,800,1200,1600,2000,2400 or 2800 respectively, over all repetitions. Next, (II) the DKI model was used to estimate the DTs using all images corresponding to 3 *b*-values, 0 and several 2-combinations out of the non-zero *b*-values with the condition that at least one *b*-value exceeds 1500s/mm^2. Hereby, only the first 2 repetitions are considered in order to preserve the number of DWIs over the entire experiment (n=120). Histograms of all diffusion parameters were calculated over the entire brain, including cerebral spinal fluid, grey and white matter.

Results: The results concerning MD are visualized in figure 1. (A) Using DTI, a *b*-value dependency is noticeable. The MD histogram translates to lower values by increasing the *b*-value. Even for commonly used b-values (800 and 1200 s/mm^2), one can observe a clear shift with respect to the parameter map calculated using DKI, including all 868 DWIs, which is in this study considered as the *ground truth*. Further, the ground truth tensors were estimated with a Maximum Likelihood, including noise term, approach. (B) Although small differences in variance between the histograms remain, all peaks are located at the same MD value, which implies a more accurate estimation of MD using DKI. (C) In addition, it is demonstrated that including a third *b*-value reduces the influence of the selected *b*-values. However, the calculated MD values are significantly less compared to the *ground truth.* Similar results were obtained for all diffusion parameters. However, the b-value dependency and the shift to lower values when using DTI compared to DKI were less pronounced for FA. Further, the effect was noticeable in all brain structures.

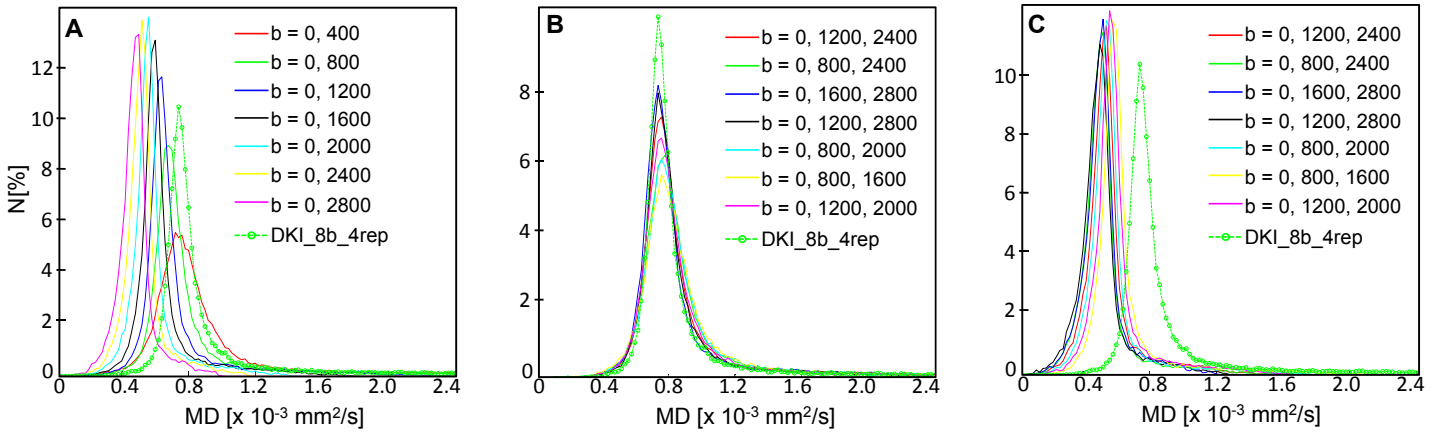

Figure 1 Normalized MD histograms using (A) DTI with a single non-zero *b*-value, (B) DKI involving 2 non-zero *b*-values, with at least one larger than 1500 s/mm^2, (C) DTI using 2 non-zero *b*-values.

Conclusion: DKI appears to be a useful model to quantify the diffusion parameters, such as FA, MD and RD, more accurately compared to conventional DTI. All parameters, with exception of FA, appear to be significantly increased when using DKI. A small FA decrease in white matter structures is noticed because of a larger increase of radial diffusivity with respect to axial diffusivity. That finding is in agreement with the more hindered diffusion in the direction perpendicular to the fiber orientation. In addition, one can clearly notice a reduced *b*-value dependency of the parameters using DKI. The variability in the histograms' width in (B) is explained by the fact that the precision of the parameters' estimation is decreased due to the increased model's complexity and depends on the acquisition scheme. This effect could be minimized by acquiring images using an optimized gradient set [4]. By including a third *b*-value in the DTI model, one can already reduce the *b*-value dependency, but, unfortunately, the parameter estimations are biased.

Acknowledgment: This work is supported by the Institute for the Promotion of Innovation through Science and Technology in Flanders (IWT-Vlaanderen).

References: [1] LeBihan et al. (2001) JMRI 4(6):534-546 [2] Hui et al. (2009) NeuroImage, in press. [3] Jensen JH et.al. (2005) MRM 53(6):1432-1440, [4] Poot et al. ISMRM, p. 1394, Honolulu, USA, 2009