The Mean Kurtosis evaluation measurements show a considerable disparity from the analytically evaluated ones for a clinically used range of b-values

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Target Audience: Researchers and clinicians interested in applications and interpretations of Diffusion Kurtosis imaging.

Purpose: Diffusion Kurtosis Imaging is an extension of DTI based on the fourth order cumulant expansion of MR signal [1] and aims to approximate the Diffusion Weighted Signal in a more precise manner by accounting for the leading non-Gaussian diffusion effects. Recently, multiple studies reported a significant sensitivity of this imaging modality for tissue pathologies, and its potential usefulness for neurites structural modeling [2-5]. In DKI imaging studies, a wide range of different gradient strengths (b-values) is used, which is known to affect the estimated diffusivity and kurtosis parameters [6]. Hence there is a need to assess the validity of the DKI expression and the accuracy of the estimated parameters as a function of b-value. The purpose of this work was to examine the error in a mean kurtosis parameter with respect to the ground truth, using a biophysical model with parameters determined from real data.

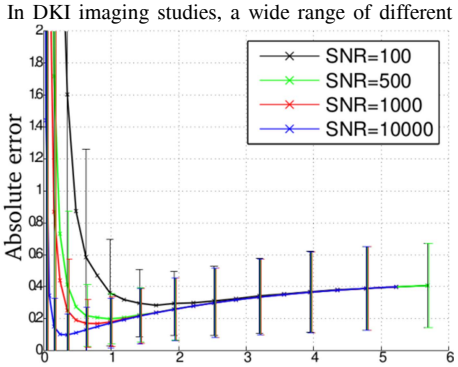

Figure 1: Error between the analytically evaluated mean kurtosis tensor and the one evaluated from the results of the fit as a function of a maximum b-value

Theory: The kurtosis expression originates from a Taylor expansion in b of the logarithm of the diffusion signal around $b = 0$ [7]. Thus, while strictly speaking it is only valid at $b = 0$, we are interested in finding the maximum b-value that produces maximal acceptable error. Practically, maximum b-values have been limited to the range of $b \leq \frac{3}{DK}$ or $b \leq 6\ \mathrm{ms/\mu m^2}$, for a fixed brain tissue, guaranteeing a monotonically decreasing diffusion signal [8]. Also, according to [8], the estimates of $b \leq 2-3\ \mathrm{ms/\mu m^2}$ provide maximum b-values for a reliable assessment of diffusivity and kurtosis based on the assumptions of a bi-exponential model. Yet, there are rising concerns about the validity of a bi-exponential diffusion model for evaluation of neural tissue parameters [9]

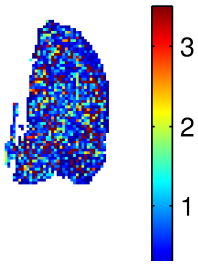

Figure 2: Highest b_{max} value that allows 10% error for an ideal SNR = 10000

In this study the full neurite model [10] was used to provide ground truth diffusion parameters as well as a simulated diffusion signal. This model was previously shown to be highly correlated with histology and to approximate the diffusion signal reliably close to the one from the biological sample. Diffusion data from a rat brain (see methods) was fit to the neurite model using nonlinear least squares, and from the obtained model parameters, the mean tensor kurtosis [11] was computed analytically.

This provided maps of ground truth W (W_{th}). The fitted model parameters were subsequently used a second time to generate synthetic signals at 14 directions and 12 b values from b=0…b_{max}, noise corresponding to a variable SNR levels was added to the signal. The noisy synthetic signals were then nonlinearly fit to the DKI model, emulating an experimentally determined W, (W_{exp}) from which mean kurtosis tensor may be calculated using $\bar{W} = \frac{1}{5}(W_{xxxx} + W_{yyyy} + W_{zzzz} + 2W_{xxyy} + 2W_{xxzz} + 2W_{yyzz}) = \frac{1}{5}\mathrm{Tr(W)}$. These values were then compared to W_{th} as a function of b_{max}, and results reported in terms of the absolute error between $\bar{W}_{\mathrm{exp}}$ and $\bar{W}_{\mathrm{th}}$.

The mean of the kurtosis tensor $\bar{W}$ as described in [11] was proved to be a parameter finely correlated with mean kurtosis, while an analytical expression of it using the parameters of the neurite model [10] could be found, thus the error in evaluation of this parameter using full kurtosis model fit is explored.

Methods: Diffusion weighted MRI data were acquired in a fixed 6-weeks old adult wistar rat brain. The signal initially acquired in 14 spherical directions in 12 b-values of $0-8\ \mathrm{ms/\mu m^2}$. Imaging was performed on a Bruker Biospec 9.4T equipped with a 15 mm quadrature coil. Imaging parameters were: TE = 26 ms, TR = 6500 ms, delta/Delta = 5/15 ms, resolution 250 µm isotropic. For analysis one coronal image plane containing both gray and white matter was used. The data was consequently fit with the neurite model [10] using non-linear least squares algorithm. This fit was then used to generate ground truth signals for different identically sized sets of gradients (b-values), with an altering b_{max}, while the random noise of different intensity was introduced. Subsequently the generated signals were fit with a 22-independent parameters full kurtosis model using non-linear least squares in Matlab. The mean of the kurtosis tensor $\bar{W}$ as described in [11] was proved to be a parameter finely correlated with mean kurtosis. An analytical expression of $\bar{W}$ based on the parameters of the neurite model [10] could be found by Taylor expansion of the model. The absolute error in evaluation of this parameter using full kurtosis model fit is explored.

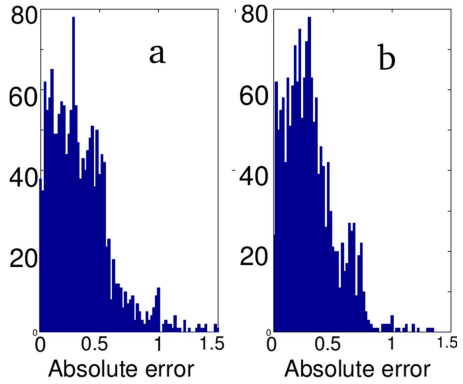

Figure 3: Histogram of the absolute error for b_{max}= 1 (a) and b_{max}=2.5(b) ms/µm² and a realistic SNR=100

Results: In Fig. 1 the absolute error of $\bar{W}$ evaluation is shown for a number SNR values as a function of maximum b-value. It can be seen that while the minimum error is achieved for $b_{\mathrm{max}} \approx 0.4\ \mathrm{ms/\mu m^2}$ even for a moderate values of $b_{\mathrm{max}} = 1\ \mathrm{ms/\mu m^2}$ about 20% error in kurtosis evaluation is reached. In Fig 2 the map of maximum b-value that allows 10% in evaluation of $\bar{W}$ is shown. The critical values found here do not correlate with a convergence radius of the isotropic variant of neurite model found by numerically evaluating the function singularities in the complex plane (as proposed in [7]). In Fig 3 histograms of an absolute error for b_{max} being equal to the commonly used b-values are given, and a wide distribution of absolute error for these b-values could be observed.

Discussion and Conclusion: The present work examined the degree of deviation of the 'true' mean kurtosis values from the experimentally evaluated ones. We made three important observations: 1) the most accurate determination of the mean kurtosis requires surprisingly small b values (b=0.4 $\mathrm{ms/\mu m^2}$), 2) the error for infinite SNR was at least 20% in average per slice 3) for realistic SNRs, the highest accuracy was obtained already at b=1.5 while the error was larger than 30%. At the typically used b-values, mean kurtosis was surprisingly inaccurate with absolute errors averaging 30-40%. Our results suggest caution when relating kurtosis parameters to tissue structure, and when using them in efforts to build reliable neural tissue models. These results do not subtract from the value of the kurtosis model in providing sensitive biomarkers.

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References: [1]Jensen, JH,et al Magn. Reson. Med., (2005). 53;[2] Hui, ES, et al., Stroke, (2012);[3] Latt, J, et al. in Proc. Int. Soc. Magn. Reson. Med. 2009;[4] Cheung MM, et al Neuroimage, (2009);[5]Novikov DS, et al, NMR in Biomed (2010); [6] Veraart K, et al Magn. Reson. Med., (2011); [7] Kiselev VG, in Diffusion MRI:Theory, Methods and Applications, pp152-168 (2011); [8] Jensen, JH, et al, NMR in Biomed. (2010); [9] Kiselev, VG, MRM (2007);[10] Jespersen, SN, et al, Neuromage, (2007); [11] Hansen, B, et al, Magn. Reson. Med., (2013)