Experimentally and Computationally Fast Method for Estimation of the Mean Kurtosis

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Introduction: Diffusion kurtosis imaging (DKI) is a popular extension of diffusion tensor imaging (DTI) accounting for nongaussian aspects of diffusion in biological tissue[1]. Recently, several studies have indicated enhanced sensitivity of mean kurtosis (MK) to tissue pathology, including stroke[2-4]. However, the relatively lengthy acquisition time and postprocessing required to estimate kurtosis metrics remains a barrier for further investigations, and hence current research efforts are directed at speeding up DKI [5]. Here we propose a very fast acquisition and postprocessing scheme for estimation of a new mean kurtosis, which is demonstrated on a large diffusion MR data set from fixed rat brain and a large data set from in-vivo human brain to be very similar to MK. We then introduce and evaluate a fast experimental protocol for estimation of this new mean kurtosis. This protocol requires only 13 diffusion weighted images, which can be acquired in less than one minute, followed by a postprocessing time of seconds. Thus, our new measure is shown to be a clinically feasible alternative to MK, even in an acute setting.

Theory: The mean kurtosis is tedious to estimate because it is the orientational average of the apparent kurtosis $K(\hat{n})$ in the direction $\hat{n}$, which is multiplied by the apparent diffusivity $D(\hat{n})$ in the cumulant expansion of the signal

$$\log S(b,\hat{n}) = -bD(\hat{n}) + \frac{b^2}{6} D(\hat{n})^2 K(\hat{n}) + O(b^4) = -bD(\hat{n}) + \frac{b^2}{6}\bar{D}^2 W(\hat{n}) + O(b^4) \tag{1}$$

Therefore, it is necessary to decouple $D(\hat{n})$ and $K(\hat{n})$ before averaging over directions. Here, $W(\hat{n})$ is related to the kurtosis tensor[1] W_{ijkl} as $W(\hat{n}) = \sum_{ijkl} W_{ijkl} n_i n_j n_k n_l$. To circumvent this difficulty, we propose instead to consider, $\bar{W}$ the orientationally averaged value of $W(\hat{n})$

$$\bar{W} = \frac{1}{4\pi}\int_{S_2} d\hat{n} W(\hat{n}) = \frac{1}{4\pi}\sum_{ijkl} W_{ijkl}\int_{S_2} d\hat{n} n_i n_j n_k n_l = \frac{1}{5}(W_{xxxx} + W_{yyyy} + W_{zzzz} + 2W_{xxyy} + 2W_{xxzz} + 2W_{yyzz}) = \frac{1}{5}\mathrm{Tr(W)} \tag{2}$$

Because of Eq. (1), linear combinations of $W(\hat{n})$ along different directions as in Eq. (2) can be *directly estimated by combining log of signals with diffusion gradients along corresponding directions*. For example, we find that with 9 directions

$$\frac{1}{15}\left(\sum_{i=1}^{3}\log S(b,\hat{n}^{(i)}) + 2\sum_{i=1}^{3}\log S(b,\hat{n}^{(i+)}) + 2\sum_{i=1}^{3}\log S(b,\hat{n}^{(i-)})\right) = -b\bar{D} + 1/6\, b^2\bar{D}^2\bar{W} \tag{3}$$

where $\hat{n}^{(i)}$, $\hat{n}^{(i+)}$ and $\hat{n}^{(i-)}$ (i=1,2,3), are defined as $\hat{n}^{(1)} = (1,0,0)^{\mathrm{T}}$, $\hat{n}^{(1+)} = (0,1,1)^{\mathrm{T}}$, $\hat{n}^{(1-)} = (0,1,-1)^{\mathrm{T}}$, and similarly for i= 2 and 3; i.e., superscript i in $\hat{n}^{(i+)}$ and $\hat{n}^{(i-)}$ labels the position of the '0'. Finally, in order to extract $\bar{W}$, we need to obtain an estimate of D. We do so by acquiring an additional 3 images along $\hat{n}^{(i)}$ at a lower b-value, and using the procedure in [5] to estimate the apparent diffusivity along these 3 directions, followed by averaging to obtain $\bar{D}$. We will refer to this protocol as the 1-3-9 protocol, and the associated estimate of $\bar{W}$ as $\bar{W}_{139}$.

Methods: Fixed rat brain was imaged[6] at 16.4T (Bruker Biospin) using a standard spin echo diffusion weighted sequence. Nine b=0 images were acquired and 144 diffusion weighting directions were chosen to constitute a 144 point spherical 16-design[7] and distributed equally on 16 shells from b=1...15 ms/μm^2. The remaining diffusion and imaging parameters were: TR=3 s, TE=14.7 ms, data matrix 128×128, field of view 12.8 mm×12.8 mm, slice thickness 0.5 mm, and Δ/δ=8/2 ms. Imaging in a human volunteer was performed on a Siemens Trio using a 32 channel head coil. For comparison to the $\bar{W}$, we obtained two 160 image data sets for estimation of the full kurtosis tensor and MK in a traditional way. These data sets were recorded using the optimized DKI protocol from[8] with 10 b=0 images and 30 encoding directions on 5 shells at 500, 1000, 1500, 2000, and 2500 s/mm^2. The fast 1-3-9 protocol was based on the same sequence but used instead one b=0 image, 3 low b-value measurements at b = 1000 s/mm2, and 9 directions at b=2500 s/mm^2. In both data set types, we obtained full brain coverage at 3 mm isotropic resolution. Acquisition time for the fast protocol was 55 secs, followed by smoothing (linear interpolation) and a 2 sec (Matlab® on standard PC) postprocessing procedure as described above. This is to be compared to 11.5 min acquisition time for the 160 image data set, with an associated postprocessing time of about 4 hours in our implementation.

Results: To compare the similarity of information in MK and $\bar{W}$, Fig. 1 shows maps of both metrics as computed explicitly from the full kurtosis tensor determined from a fit of the rat data to Eq. (1). The contrast is highly comparable but the arrow indicates a region where the two maps differ appreciably. A scatter plot of the two maps against each other has a linear correlation of 0.88, and in fact, more than 90% of the MK values are within 10% of the $\bar{W}$ value in the same pixel. The similarity between MK and $\bar{W}$ is also seen in the human data: Fig. 2 shows MK and $\bar{W}$ estimated from a fit to a 160 image DKI data set. Again the contrast is comparable, and a scatter plot of the human data in Fig. 2 revealed a linear correlation of 0.99 with 96% of the MK values within 10% of corresponding $\bar{W}$ value. Having thus established the similarity of MK and $\bar{W}$ we now turn to comparing $\bar{W}$ as obtained from a 160 image data set to $\bar{W}$ as obtained using the fast 1-3-9 protocol, $\bar{W}_{139}$. Figure 3 shows maps of $\bar{W}$ and $\bar{W}_{139}$ and it is seen that the contrast is still comparable. The contrast in $\bar{W}_{139}$ from the fast protocol is clearly of a similar nature to that from the full data set, however, differences are visible. Most notably, $\bar{W}_{139}$ values from the fast protocol seem to underestimate the extent of regions with higher values of $\bar{W}$. Comparing the $\bar{W}$ maps obtained from two 160 image data sets to eight $\bar{W}_{139}$ maps obtained from 8 acquisitions of the 1-3-9 data sets, we find an average linear correlation of 0.97, and an average of 87% of the $\bar{W}$ values from the full data sets were estimated with a 10% accuracy by $\bar{W}_{139}$. Lastly, we consider in Fig. 4 the robustness of the fast protocol, by comparing the percentage difference between 2 repetitions (A) to a similar measure for mean kurtosis (B) using the full data set for the latter. Most of the voxels change less than 10%, and the robustness of $\bar{W}_{139}$ is seen to be comparable to MK, despite being based on a much smaller data set. Figure 4C examines the coefficient of variation over the 8 repetitions of the 139 protocol, showing that it is less than 10% over most parts of the brain.

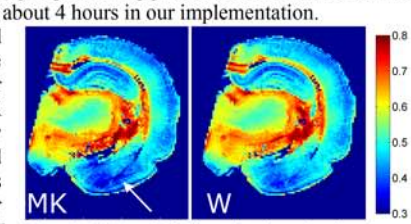

Fig. 1: MK and $\bar{W}$ in a fixed rat brain.

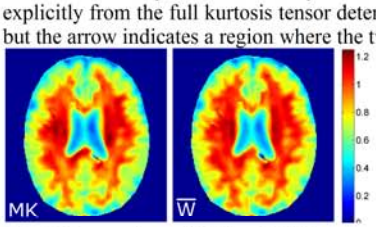

Fig.2: Comparison of MK and $\bar{W}$ in normal human brain.

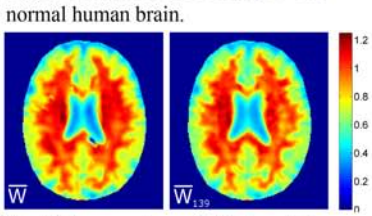

Fig. 3: Comparison of $\bar{W}$ from full kurtosis tensor and W139 obtained using the fast protocol.

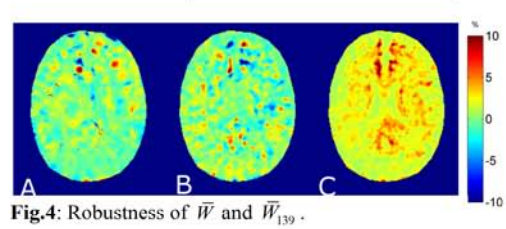

Fig.4: Robustness of $\bar{W}$ and $\bar{W}_{139}$.

Conclusions: We have suggested a new kurtosis metric $\bar{W}$, which can be defined as the isotropic part of the kurtosis tensor. We showed experimentally that $\bar{W}$ maps had very similar contrast to the conventional mean kurtosis, MK. Therefore, we expect $\bar{W}$ to share many of the same characteristics as MK, in particular it gives reason to believe that $\bar{W}$ could be a valuable marker of tissue pathology. In contrast to MK, however, $\bar{W}$ is extremely fast to measure, and the scheme proposed here would enable $\bar{W}$ to be estimated in practically any clinical setting with negligible acquisition time overhead and a post-processing time of a few seconds. We believe our method will facilitate a more rapid exploration of the potential applications of DKI.

References: 1. Jensen, J.H., et al., Magn. Reson. Med., (2005). **53**;2. Hui, E.S., et al., Stroke, (2012);3. Jensen, J.H., et al., NMR Biomed, (2011). **24**;4. Latt, J., et al. in *Proc. Int. Soc. Magn. Reson. Med.* 2009;5. Jensen, J.H., et al. in *Proc. Int. Soc. Magn. Reson. Med.* 2009. Honolulu, Hawaii.; 6. Jespersen, S.N., et al., Neuroimage, (2010). **49**;7. Hardin, R.H. and N.J.A. Sloane, Discrete & Computational Geometry, (1996). **15**;8. Poot, D.H., et al., IEEE Trans Med Imaging, (2010). **29**;