A fast and robust method for simultaneous estimation of mean diffusivity and mean tensor kurtosis

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Target audience: Researchers with an interest in diffusion kurtosis imaging, diffusion-MR method development, and the clinical application of kurtosis imaging.

Purpose: 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, relatively lengthy acquisition time and postprocessing required to estimate kurtosis metrics hamper further investigations. Recently a fast acquisition and postprocessing scheme for estimation of mean tensor kurtosis was proposed and demonstrated on large diffusion MR data sets from fixed rat brain and in-vivo human brain[5]. This protocol requires only 13 diffusion weighted images (scan time less than one minute), followed by postprocessing of few seconds in duration. Here we consider a refinement with increased accuracy in the estimate of mean tensor kurtosis with minimal additional scan time and no added computational time.

Theory: The method in ref. 5 aims to estimate the orientational average $\overline{W}$ of the kurtosis $W(\hat{n}) = \sum_{ijkl} W_{ijkl} n_i n_j n_k n_l$ observed along a direction $\hat{n}$: $\overline{W} = 1/(4\pi)\int d\hat{n}\, W(\hat{n}) = \mathrm{Tr(W)}/5$. Here W_{ijkl} is the kurtosis tensor[1] appearing in the cumulant expansion of the diffusion signal S (here normalized to b=0):

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

where $D(\hat{n})$ is the diffusivity. Because of Eq. (1), linear combinations of $W(\hat{n})$ along different directions as in the trace operation can be *directly estimated by combining log of signals with diffusion gradients along corresponding directions*. In ref. 5 a set of nine directions were proposed fulfilling

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

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'. In order to extract $\overline{W}$ using Eq. 2, an estimate of $\overline{D}$ is required. This was previously[5] done by acquiring an additional 3 images along $\hat{n}^{(i)}$ (x,y,z) at a b-value assumed low enough to neglect nongaussian diffusion, and estimating the mean apparent diffusivity from these 3 directions. This allows $\overline{W}$ to be estimated from one b0 image (for normalization), three images at b_1 (eg. ≈ 1000 s/mm²) and nine images at b_2 (eg. ≈ 2500 s/mm²). As in ref. 5, we refer to this protocol as the 1-3-9 protocol, and the associated estimate of $\overline{W}$ as $\overline{W}_{139}$. However, it has been shown that estimates of $\overline{D}$ are improved by including the kurtosis term even at relatively low b-values[6]. Therefore, we consider an extension of the above strategy where signals from the nine directions listed above are acquired at two b-values, b_1 and b_2. Thereby, we can form eq. 2 at two different b-values producing a system of two equations with two unknowns ($\overline{D}$, $\overline{W}$). Solving these, we obtain for $\overline{W}$ and $\overline{D}$:

$$\overline{W} = 6b_1b_2\left(A_1b_2 - A_2b_1\right)\left(b_1 - b_2\right)\Big/\left(A_1b_2^2 - A_2b_1^2\right)^2 \quad \text{(3a)} \quad \text{and} \quad \overline{D} = \left(b_1^2A_2 - b_2^2A_1\right)\Big/\left(b_1b_2^2 - b_1^2b_2\right) \quad \text{(3b)}$$

where A_1 and A_2 denote the left hand side of eq. (2) for the first b-value (b_1) and second b-value (b_2) respectively. We refer to this protocol as the 1-9-9 protocol, and the associated estimate of $\overline{W}$ as $\overline{W}_{199}$. An additional advantage of the new approach is the direct formula for $\overline{W}$ (eq. (3a)), which allows e.g. its accuracy and precision to be explicitly computed as a function of diffusion weighting (b_1, b_2). Here we demonstrate this by analyzing the precision of the $\overline{W}$ estimate in the human cortex for various choices of b_1 and b_2 assuming the diffusion signal to be Rician with SNR as in the experiments.

Methods: To evaluate the efficiency of the 1-9-9 scheme, we acquired ten data sets in a normal volunteer in one session. The data consisted of: a) two large data sets of 160 diffusion weighted images each (*T* protocol in[8]) and b) eight data sets using the 1-9-9 scheme. Each of the two large data sets (a) provided the full kurtosis tensor through a fit to eq. (1). Two ground truth maps of $\overline{W}$ were then produced from the trace of the full kurtosis tensor. From each of the 1-9-9 data sets both $\overline{W}_{139}$ and $\overline{W}_{199}$ were obtained.

Results: As expected[5], $\overline{W}_{139}$ provides a good estimate of the true $\overline{W}$ (fig. 1). We therefore focus on assessing the improvement in $\overline{W}$ estimate obtained with the 1-9-9 scheme over the 1-3-9 scheme. On inspection, maps of $\overline{W}_{139}$ and $\overline{W}_{199}$ are both quite similar to maps of $\overline{W}$ (fig. 1). A closer scrutiny reveals slight improvements in agreement between $\overline{W}_{199}$ and $\overline{W}$ over $\overline{W}_{139}$, e.g. as marked in fig. 1 with a black ellipse in the $\overline{W}_{199}$ map. Generally, improved agreement is seen in areas of high $\overline{W}$ which have extents found[5] to be underestimated in $\overline{W}_{139}$ maps compared to the true $\overline{W}$. For a more quantitative depiction of the difference, we show in fig. 2 areas where the relative accuracy difference between the two protocols was in the ±1% range as gray (neutral), agreement improved by more than 1% as white and agreement worsened by more than 1% as black. Neutral voxels are most numerous, but voxels with improved agreement outnumber the pixels where agreement went down. In fig. 3, we illustrate how the sum (over a large cortical ROI) of squared relative errors of $\overline{W}$ depends on b_1 and b_2. This map shows that slightly increased accuracy may be achievable using different values of b_1 and b_2.

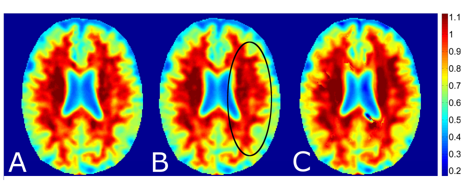

Fig. 1: A) $\overline{W}_{139}$; B) $\overline{W}_{199}$; C) 'True' $\overline{W}$.

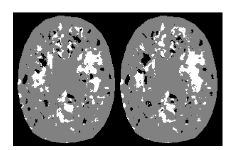

Fig. 2: White areas had improved $\overline{W}$ estimate over eight trials of $\overline{W}_{199}$ vs. eight trials of $\overline{W}_{139}$. Black areas had average reduction in accuracy. Gray pixels were neutral. Comparison vs. two maps of $\overline{W}$ shown.

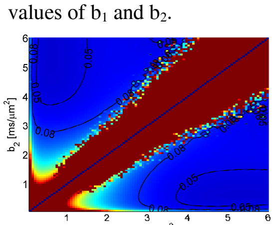

Fig. 3: map of sum of errors in $\overline{W}$ estimate in the 1-9-9 scheme as function of b-values. Clearly, b_1 and b_2 should not be too close (red areas).

Discussion and conclusion: The 1-9-9 scheme has six additional measurements compared to the 1-3-9 scheme. This adds only a small amount of scan time, so even with the 1-9-9 scheme whole brain estimation of $\overline{W}$ is possible in ~2 min including postprocessing. The 1-9-9 strategy can naturally be extended to include more b-values (1-9-9-9...) allowing parameters to be calculated from an over-determined data set. This might increase parameter estimate accuracy in situations where the cost of longer scan time is acceptable. A possible further refinement to these strategies is inclusion of the inverted directions at each b-value to compensate for the effects of eddy currents. With almost 50% more data than 1-3-9, the 1-9-9 scheme gave a surprisingly small increase in accuracy. This is encouraging for clinical use of the faster 1-3-9 scheme which has been shown[5] to provide an accurate estimate of $\overline{W}$. A clear advantage of the 1-9-9 scheme is that it allows explicit numerical optimization of the b-values used. Future study will show if the predicted improvement is experimentally discernible and whether optimized b-values from the 1-9-9 scheme can fruitfully be transferred to the faster 1-3-9 protocol.

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. Hansen et al. MRM 69(6) 2013; 6. Veraart et al. MRM 65, 2011; 8. Poot, D.H., et al., IEEE Trans Med Imaging, (2010). 29.