How is the fractional anisotropy affected by frequency-dependent changes to the eigenvalues of the apparent diffusion tensor measured with oscillating-gradient spin-echo diffusion tensor imaging?

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Introduction: As the oscillating gradient spin-echo (OGSE) sequence has shown promise as a means to probe tissue microstructure (eg. [1,2]), it has been applied in recent work to diffusion-tensor imaging (DTI) of ex vivo monkey brain [3], ex vivo mouse brain [4], and in vivo rat brain [4,5]. In the latter study the apparent diffusion tensor (ADT) was estimated for motion-probing gradient (MPG) frequencies in the range 33.3–133.3 Hz, and regions-of-interest (ROIs) in the corpus callosum (CC), visual cortex (VC), cerebellar white matter (CBWM) and cerebellar grey matter (CBGM) were selected for detailed analysis. While there was no evidence that the orientation of the principal eigenvector varied systematically with MPG frequency, there were substantial, approximately linear changes to other aspects of the ADT. In particular, linear fits to the eigenvalues (EVs) with frequency found that the slope (α_i) was positive and significantly different from zero for all EVs of the CBWM, CBGM and VC, but only the principal EV increased strongly for the CC (Fig 1, boxes represent the standard deviation, bars are 95% confidence intervals). At the same time, linear fits to the fractional anisotropy (FA) found a substantial decrease for the CBWM, and no or only a minor dependence on frequency for the CBGM, CC and VC (Fig 2). However, although the FA is a well known function of the EVs, it is not immediately clear how the behaviour of the EVs relates to the trends in the FA. The goal of this work was to investigate how the FA is affected by changes to the EVs.

Results: Even though the FA is defined as a nonlinear function of all three EVs ($\lambda_1 \geq \lambda_2 \geq \lambda_3 \geq 0$) [7], by making the change of variables $(\mu_1, \mu_2) = (\lambda_2/\lambda_1, \lambda_3/\lambda_2)$ it can be rewritten as a function of only two independent variables

$$FA(\mu_1, \mu_2) = \sqrt{\frac{(1-\mu_1)^2 + (1-\mu_1\mu_2)^2 + {\mu_1}^2(1-\mu_2)^2}{2[1+{\mu_1}^2(1+{\mu_2}^2)]}}$$

with domain [0,1] × [0,1]. The advantage of this form is that the reduced number and finite range of the independent variables allows the changes to the FA and EVs to be simultaneously visualised on a contour plot like that shown in Fig 3. The horizontal and vertical axes correspond to μ_1 and μ_2, respectively, and the dotted contours represent lines of constant FA in steps of 0.05. Although the full domain of μ_1 and μ_2 is not shown in the figure, note that the point $\mu_1 = \mu_2 = 1$ corresponds to $FA = 0$ and from there the FA increases as either μ_1 or μ_2 decreases. Note also that the FA is always equal to 1 whenever $\mu_1 = 0$, and there are no local maxima, minima or saddle points within the domain. The positions of the closed circles correspond to the estimates of μ_1 and μ_2 at the lowest applied MPG frequency (33.3 Hz) for each of the in vivo ROIs. The solid line extending from each circle traces out the changes to the EVs and FA with increasing frequency before terminating with an arrowhead as the highest applied frequency (133.3 Hz) is reached. For the purposes of simplifying the figure, the uncertainty of the estimates has not been plotted.

Now, at any point (μ_1, μ_2) on Fig 3, $dFA/df = (\partial_{\mu_1} FA)[d\mu_1/df + \kappa\, d\mu_2/df]$, where $\kappa = \partial_{\mu_2} FA / \partial_{\mu_1} FA$ has been defined. A quick glance at the contours on the figure establishes that $\partial_{\mu_1} FA < 0$ and $\partial_{\mu_2} FA \leq 0$ throughout the domain, and therefore it is always true that $\kappa \geq 0$. Since it was found that $\lambda_i = \alpha_i f + \beta_i$ over the range of frequencies used in the experiments, it follows that

$$d\mu_j/df \cong (\alpha_{j+1}\lambda_j - \alpha_j\lambda_{j+1})/{\lambda_j}^2, \quad j = 1,2$$

is positive or negative depending on whether α_{j+1}/α_j is greater or less, respectively, than $\lambda_{j+1}/\lambda_j\,(=\mu_j)$. For example, for the CBWM ROI the 1st and 2nd EVs increase strongly with frequency at about the same rate (Fig 1), but because the value of λ_2 is substantially less than λ_1, an increase in μ_1 with f results (Fig 3).

Finally, knowing how these factors vary with frequency it can be understood from the contour plot that the FA decreases for the CBWM because both μ_1 and μ_2 increase with frequency. Similarly, the FA estimates increase for the CBGM, CC and VC because μ_1 and μ_2 both decrease with frequency, although it should be remembered that the uncertainty analysis indicates that the changes to the FA are not significant or only minor for these ROIs (Fig 2).

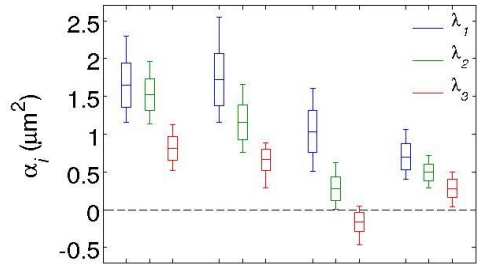

Fig 1

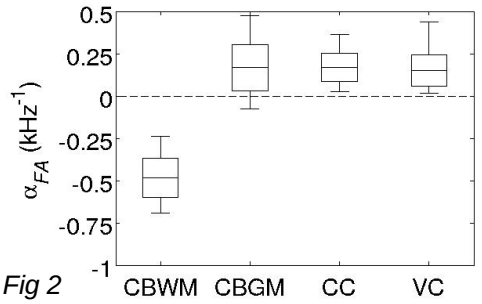

Fig 2

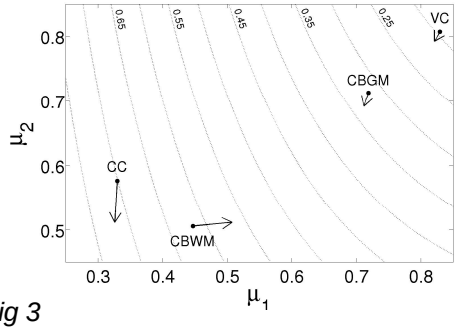

Fig 3

Conclusion: In general, the FA may either increase or decrease depending on the size of the EVs relative to each other and also on the rates of change of the EVs with frequency.

References: [1] Does *et al*, *Magn Reson Med*, 49, 206-215 (2003); [2] Colvin *et al*, *Cancer Res*, 68, 5941-7 (2008); [3] Xu *et al*, *Proc ISMRM*, 4038 (2010); [4] Aggarwal *et al*, *Magn Reson Med* 67, 98–109 (2012); [5] Kershaw et al, *Proc ISMRM*, 409 (2011); [6] Kershaw et al, *submitted to NeuroImage* (2012); [7] Basser & Pierpaoli, *J Magn Reson B*, 111, 209-219 (1996).