USING THE CHARMED MODEL TO ELUCIDATE THE UNDERPINNINGS OF CONTRAST IN DIFFUSIONAL KURTOSIS IMAGING

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Introduction

Conventional DTI measures [1] are affected by a lack of specificity that complicates the interpretation of the results, because very different configurations of axon density, size and myelination may generate the same measured DTI parameters. Moreover, in white matter (WM) diffusion-induced MRI signal loss deviates from mono-exponential decay, particularly at high diffusion weightings or b-values. To address these issues, both model-based and model-free approaches have been proposed. Diffusional kurtosis imaging (DKI) [2] is a model-free technique that estimates the kurtosis from the expansion of the logarithm of the MRI signal intensity in powers of b, without *a priori* hypotheses on the biophysics. CHARMED model [3] expresses the signal as a superimposition of a hindered Gaussian extra-axonal compartment and one or more restricted intra-axonal compartments and is thus tailored for WM. The aim of this work was to investigate the relationship between DKI and CHARMED metrics in WM, to understand whether (and where) the information contained in the kurtosis orthogonal to the main fibre direction (K_{ORTHO}) overlaps with the information extracted by CHARMED.

Subjects and Methods

The theoretical kurtosis *K* was numerically calculated for the propagator in the CHARMED model, which in turn is based on Neuman's model of restricted diffusion within impermeable cylinders [4]. *K* was calculated in the directional orthogonal to the fibre and investigated as a function of the CHARMED parameters (restricted volume fraction *RF* and axonal diffusivity *D)*. The correlation between these measures was then investigated *in vivo* in 5 healthy young subjects that underwent a combined CHARMED/DKI protocol at 3T[5], according to the following parameters: TE/TR=114/17000ms, 130 unique gradient directions, maximum b-value=7500s/mm^2. A cardiac-gated DTI protocol was also used (TE=93ms, 45 directions, maximum b-value=1200s/mm^2) to derive maps of the intra-voxel directional coherence (IVDC) [6], a measure of the local fibre dispersion. Inter-subject alignment and statistical analysis were performed combining the TBSS approach [7] with an automatic region-of-interest (ROI) selection using WM labelling in standard space. Non-parametric Spearman correlation and multiple linear regression coefficients were calculated in Matlab.

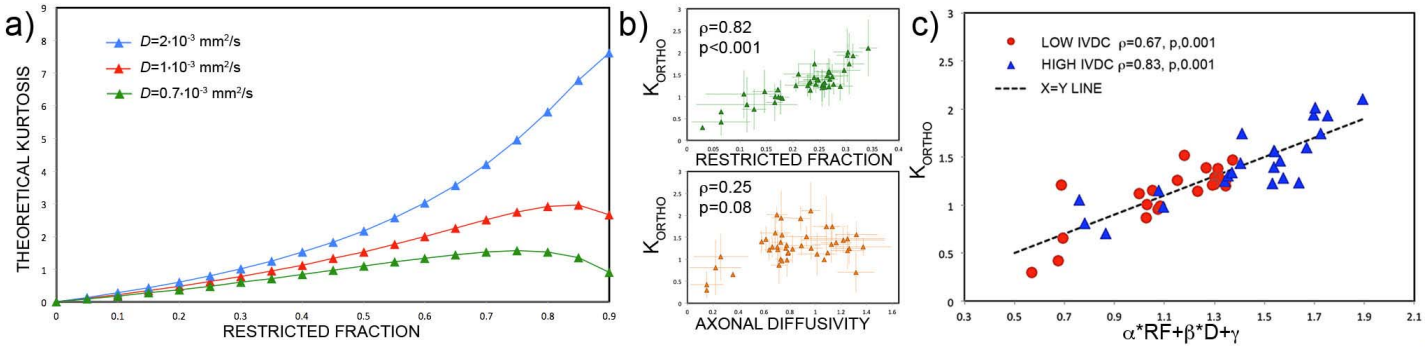

Figure 1: a) Kurtosis theoretical value *K* as a function of *RF* and for three different values of the axonal diffusivity. b) Scatter plot of the mean values of K_{ORTHO} vs *RF* (upper plot) and K_{ORTHO} vs *D* (lower plot) and associated standard deviations across all the subjects. c) Multilinear regression of K_{ORTHO} with respect to the model $\alpha RF+\beta D+\gamma$, shown separately for the two groups, according to low (red circles) or high (blue triangles) IVDC. The continuous line represents the x = y line.

Results

For a fixed diffusion time, the value of *K* from the theory has a monotonically increasing trend for both increasing *RF* values and increasing *D* (Fig1a). A significant positive correlation ($p<0.001$) was found *in vivo* between the kurtosis orthogonal to the main fibre direction (K_{ortho}) and *RF* (Fig1b). The positive correlation found between K_{ORTHO} and *D* is not statistically significant at a 0.05 level. A multivariate linear regression showed that K_{ORTHO} values are better explained by a mixed contribution of both RF and D ($p<0.001$), according to the model $K_{ORTHO}=\alpha RF+\beta D+\gamma$ (whit $\alpha=4.65/\beta=0.12/\gamma=0.22$). In Fig.1c, the data are divided into two equally sized groups, corresponding to low and high values of IVDC. The correlation coefficient calculated separately for the two groups shows that in ROIs characterized by high inter-voxel directional coherence among fibres, the correlation between K_{ORTHO} and the regression model $=\alpha RF+\beta D+\gamma$ is stronger ($\rho=0.83$) as compared to the correlation calculated in ROIs of lower inter-voxel directional coherence ($\rho=0.67$).

Discussion and Conclusion

We report for the first time the dependency of the kurtosis on the CHARMED parameters *RF* and *D* by calculating *K* directly from the propagator used in the CHARMED model and verifying the correlation between K_{ORTHO} and the CHARMED parameters *in vivo*. By calculating the kurtosis associated to the CHARMED model, it is possible to interpret the results of a model-free approach in terms of the underlying biophysics. When the correlation between the kurtosis and the CHARMED model parameter is calculated separately for high and low values of IVDC, a stronger correlation is found in ROI characterised by higher IVDC. This suggests that DKI and CHARMED overlap where the hypothesis of a simple cylindrical geometry holds, showing instead a different information content in areas of non negligible fibre dispersion.

References

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