An improved method for diffusional kurtosis estimation

B. A. Ardekani[1,2], A. Tabesh[1,3], J. H. Jensen[3], J. A. Helpern[1,3], A. Bachman[1], and H. Kushner[4]
[1]Center for Advanced Brain Imaging, The Nathan S. Kline Institute for Psychiatric Research, Orangeburg, NY, United States, [2]Department of Psychiatry, New York University School of Medicine, New York, New York, United States, [3]Department of Radiology, New York University School of Medicine, New York, NY, United States, [4]Statistical Sciences and Research Division, The Nathan S. Kline Institute for Psychiatric Research, Orangeburg, NY, United States

Introduction

Recently, diffusion-weighted imaging techniques have been developed that make the measurement of new diffusion metrics feasible in clinical settings. In particular, we have generalized DTI in order to determine diffusional kurtosis (DK), a quantitative measure of the non-Gaussianity of the diffusion process [1-3]. The DK is of interest, for example, as an indicator of the diffusional heterogeneity generated by diffusion barriers, such as cell membranes and organelles. This paper presents an improved method for estimating the DK from a diffusional kurtosis imaging (DKI) dataset. In particular, we present a simpler algorithm, than what has been previously described [4], for imposing positive-definiteness on the fourth order tensor in our signal attenuation model. Experimentally, we show this to be an important condition for obtaining high quality parametric maps. In addition, we propose to use Mardia's multivariate coefficient of kurtosis [5] as a measure of overall diffusional non-Gaussianity, as an alternative to the mean univariate kurtosis measure that is currently used in DKI literature [3]. Mardia's kurtosis is both more straightforward to compute and more widely accepted in the statistical literature as an extension of the concept of kurtosis to multivariate distributions.

Theory

We employ the standard DKI model for the diffusion-weighted signal [2, 3]:

$$S(\boldsymbol{q}) = S_0 \exp\left(-b \sum_{i,j=1}^{3} D_{ij} g_i g_j + b^2 \sum_{i,j,k,l=1}^{3} K_{ijkl} g_i g_j g_k g_l\right). \quad \text{(Eq. 1)}$$

Here **D** and **K** are totally symmetric second and fourth order tensors with 6 and 15 unknown parameters, respectively. For a second order DTI model, Koay et al. [6] showed how positive-definiteness of **D** may be enforced using the Cholesky decomposition for use in non-linear least squares estimation. For a fourth order DTI model [7], Barmpoutis et al. [4] developed a method to enforce positive-definiteness by representing the fourth order tensor as ternary quartics and applying the Hilbert's theorem on ternary quartics along with the Iwasawa parameterization. In this paper, we first note that a fourth order three-dimensional totally symmetric Cartesian tensor such as **K** may be written in terms of a second order six-dimensional symmetric tensor with only 15 unique elements. This observation enables us to use the Cholesky parameterization to impose positivity not only on **D**, but also on **K**, circumventing the need for using a different and more complicated method for imposing positive-definiteness on **K**.

As a measure of non-Gaussianity, we propose to use Mardia's kurtosis. Let $\boldsymbol{x} = [x_1 \quad x_2 \quad x_3]^T$ be a random vector representing the displacement of a water molecule over a diffusion time Δ. For DKI, Mardia's kurtosis in 3D may be written as: $\mathrm{E}(\boldsymbol{x}^T \boldsymbol{\Sigma}^{-1} \boldsymbol{x})^2 - 15$, where $\boldsymbol{\Sigma} = \mathrm{E}(\boldsymbol{x}\boldsymbol{x}^T)$ represents the covariance matrix of $\boldsymbol{x}$. Here 15 is subtracted to make the kurtosis for the 3D Gaussian distribution equal to 0. In addition to being the most widely accepted multivariate generalization of kurtosis, an advantage of using Mardia's kurtosis is that it may be explicitly written in terms of the second and fourth order moments of $\boldsymbol{x}$ without the need for integration, as is required for mean (i.e., directionally averaged) univariate DK. If we consider our attenuation model (Eq. 1) to approximate the Fourier transform (characteristic function in statistical parlance) of the probability density function of the displacement, we can show that the moments may be written in terms of **D** and **K** as follows:

$$\mathrm{E}(x_i x_j) = 2D_{ij} \qquad \mathrm{E}(x_i x_j x_k x_l) = 4D_{il}D_{jk} + 4D_{jl}D_{ik} + 4D_{kl}D_{ij} + 24K_{ijkl}. \quad \text{(Eq. 2)}$$

Therefore, Mardia's kurtosis may be written explicitly in terms of the elements of **D** and **K**. It can be shown that positive-definiteness of **K** implies that the univariate excess kurtosis in any given direction is positive. This is consistent with the compartmental tissue model which predicts positive excess kurtosis in any given direction.

Experiments and Results

A DKI scan was performed on a healthy volunteer using a 3 T Siemens Trio system with an 8-channel head coil. Diffusion-weighted images were acquired along 30 gradient directions with a twice-refocused spin-echo echo-planar imaging sequence (TR = 2300 ms, TE = 109 ms, matrix = 128 × 128, FOV = 256 × 256 mm², 15 slices, slice thickness = 2 mm, gap = 2 mm, NEX = 6 for b = 0, NEX = 2 for b = 500, 1000, 1500, 2000, 2500 s/mm²). The 22 parameters in (Eq. 1) (i.e., **D**, **K**, and S_0) were estimated for each voxel, initially using an unconstrained weighted linearized least squares (WLS) method. If the initial estimate of **D** or **K** were nonpositive-definite, then the constrained weighted non-linear least squares (CWLS) approach outlined above was used to enforce positivity. Of the 58408 voxels in the brain that were processed, in the initial WLS, only 104 voxels (0.2%) violated the positivity condition for **D**, while 6998 voxels (12%) violated the condition for **K**. Therefore, the tensor were re-estimated in these voxels using CWLS. Figure 1 shows Mardia's kurtosis maps obtained without (a) and with (b) imposing positivity. In 322 voxels (dark voxels in (a) inside the brain), Mardia's kurtosis was estimated to be negative using the unconstrained method. There were no negative kurtosis estimates by the CWLS method. Panel (c) shows the conventional mean univariate kurtosis map.

Discussion

Imposing the positivity constraint on the fourth order tensor is crucial for obtaining high quality parametric maps in DKI. In the data presented, 12% of the voxels had nonpositive-definite **K**, which implies that for some direction(s), the excess kurtosis would be negative. This is inconsistent with the compartmental tissue model of diffusion which predicts a positive kurtosis [2]. Many of these voxels are located in high anisotropy regions (e.g., splenium of the corpus callosum). This problem is alleviated by using the CWLS method. Mardia's kurtosis map (b) is similar to the mean univariate kurtosis map (c) but easier to compute. It also appears to have a slightly better gray-to-white matter contrast as well as contrast within white matter regions.

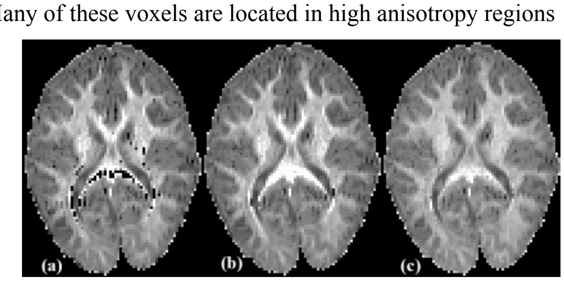

Figure 1: Estimated Mardia's kurtosis image obtained using unconstrained (a) and constrained (b) methods. (c) Mean univariate kurtosis using constrained estimation.

References

[1] Jensen JH & Helpern JA. Proc Intl Soc Mag Reson Med. 2003;11:2154.
[2] Jensen JH, et al. MRM 2005; 53:1432-1440.
[3] Lu H, et al. NMR Biomed 2006; 19:236-247.
[4] Barmpoutis A, et al. Neuroimage 2009; 45:S153-S162.
[5] Mardia KV. Biometrika 1970; 57: 519-530.
[6] Koay CG, et al. MRM (2006); 55:930-936.
[7] Özarslan E, et al. MRM (2003); 50:955-965.