Robust Estimation of Kurtosis and Diffusion Tensors in Diffusional Kurtosis Imaging

A. Tabesh[1], J. H. Jensen[1], B. A. Ardekani[2], and J. A. Helpern[1,2]

[1]Radiology, New York University School of Medicine, New York, NY, United States, [2]Medical Physics, The Nathan S. Kline Institute for Psychiatric Research, Orangeburg, NY, United States

Introduction

Diffusion of water molecules in biological tissues is conventionally quantified via diffusion tensor imaging (DTI) [1]. DTI enables a Gaussian approximation to the probability distribution governing the random displacement of water molecules. In some circumstances of great interest, however, the displacement probability distribution can deviate considerably from a Gaussian form. Diffusional kurtosis imaging (DKI) allows for characterization of this deviation via inclusion of a kurtosis term in the expression for the displacement distribution [2]. The DKI model is parameterized by the diffusion and kurtosis tensors from which scalar measures such as mean diffusivity, fractional anisotropy, and axial, radial, and mean kurtoses are derived. Obtaining physically and biologically plausible estimates of these tensors in a computationally tractable framework is crucial to reliable estimation of the scalar kurtosis and diffusion metrics. In previous work concerning the estimation of generalized DTI tensors, unconstrained linear [3] and nonlinear least squares (ULLS and UNLS) [2] algorithms have been utilized. Unfortunately, in the presence of noise, unconstrained schemes do not necessarily produce plausible tensor estimates. To address this drawback, a parameterization has been proposed in a UNLS framework to guarantee a positive diffusivity function in a fourth-order tensor-only model of diffusion [4]. We present a tractable computational framework to obtain plausible estimates of kurtosis and diffusion tensors in DKI. The estimation problem is formulated as linearly constrained linear least squares (CLLS). Mean kurtosis (MK) maps for a human subject obtained using this formulation are compared to those estimated using ULLS.

Theory

For direction vector $\mathbf{g}$ and b-value b, the diffusion signal intensity $S(\mathbf{g},b)$ can be written as

$$\ln S(\mathbf{g},b) = \ln S_0 - b\sum_{i=1}^{3}\sum_{j=1}^{3} g_i g_j D_{ij} + \frac{1}{6} b^2 \bar{D}^2 \sum_{i=1}^{3}\sum_{j=1}^{3}\sum_{k=1}^{3}\sum_{l=1}^{3} g_i g_j g_k g_l W_{ijkl} \,, \tag{1}$$

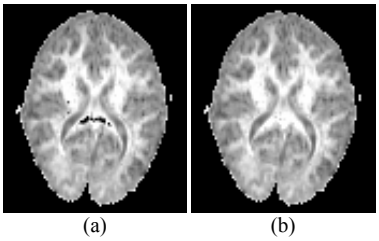
where S_0 is the signal intensity for $b = 0$, D_{ij} and W_{ijkl} are the elements of the second-order diffusion tensor $\mathbf{D}$ and fourth-order kurtosis tensor $\mathbf{W}$, respectively, and $\bar{D} = (1/3)\,\mathrm{tr}(\mathbf{D})$ is mean diffusivity, where tr(.) denotes matrix trace. Diffusivity and kurtosis along direction $\mathbf{g}$, denoted as $D(\mathbf{g})$ and $K(\mathbf{g})$, respectively, are given by

$$D(\mathbf{g}) = \sum_{i=1}^{3}\sum_{j=1}^{3} g_i g_j D_{ij} \quad \text{and} \quad K(\mathbf{g}) = \frac{\bar{D}^2}{D(\mathbf{g})^2} \sum_{i=1}^{3}\sum_{j=1}^{3}\sum_{k=1}^{3}\sum_{l=1}^{3} g_i g_j g_k g_l W_{ijkl} \,. \tag{2}$$

To ensure that the diffusivity and kurtosis parameters are physically and biologically plausible, we must have

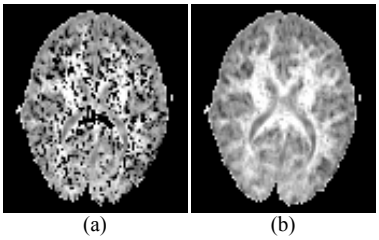
$$D(\mathbf{g}) \geq 0 \quad \text{and} \quad K_{\max}(\mathbf{g}) \geq K(\mathbf{g}) \geq K_{\min}, \quad \text{for all } \mathbf{g}\,, \tag{3}$$

where $K_{\min}$ is a constant in the [−2, 0] range, and $K_{\max}(\mathbf{g}) = C/[b_{\max} D(\mathbf{g})]$, where $3 \geq C \geq 0$. The objective in the estimation problem is to find $\mathbf{D}$ and $\mathbf{W}$ such that the mean-square error between the two sides of (1) is minimized, while the constraints in (3) are satisfied. Using the change of variable $\mathbf{V} = \bar{D}^2\mathbf{W}$ and for the typical choice of $K_{\min} = 0$, the problem of estimating $\mathbf{D}$ and $\mathbf{V}$ can be formulated as a CLLS problem. For other $K_{\min}$ values, the problem can be approximated using CLLS. The CLLS problem is a special case of convex quadratic programming which may be efficiently solved via standard methods [5].



(a) (b)

Figure 1. MK images obtained using b = 0, 1000, 2000 s/mm^2, and 30 gradient images for each b-value; (a) ULLS; and (b) CLLS.



(a) (b)

Figure 2. MK images obtained using 6 gradient directions for b = 1000 s/mm^2 and 30 gradient directions for b = 2000 s/mm^2; (a) ULLS and (b) CLLS.

Methods

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 planar imaging sequence (TR = 2300, 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 = 1000, 2000 s/mm^2). The gradient images were smoothed prior to processing using a Gaussian kernel with a full width at half maximum of 2.5 mm in the imaging plane. We used the active set method implemented in MATLAB (http://www.mathworks.com) to solve the CLLS problem. MK was also estimated using ULLS, where the constraints in (3) were relaxed. Two processing scenarios were considered: in one case MK was obtained using all the available gradient images, and in the other scenario, it was estimated using 6 of b = 1000 s/mm^2 and all of b = 2000 s/mm^2 gradient images.

Results

The total processing time for generating scalar kurtosis and diffusion maps using all gradient images was 130 and 335 seconds for ULLS and CLLS, respectively. Figures 1 and 2 show the improved quality of the MK maps obtained using the CLLS approach over those estimated via ULLS. The voxels for which the ULLS approach yielded MK estimates smaller than $K_{\min} = 0$ are marked in black. In Figure 1, such voxels are most likely to occur in high FA regions such as parts of the corpus callosum, whereas in Figure 2 they are scattered in other parts of white matter as well.

Discussion

The voxels in Figures 1 and 2 where CLLS produces improved MK estimates are those for which ULLS yields a non-positive definite (NPD) or *nearly* NPD estimate of $\mathbf{D}$. In these voxels, the smallest eigenvalue of $\mathbf{D}$, denoted as λ_3, has a small magnitude, which in turn causes the ULLS estimate of $\mathbf{D}$ to be more sensitive to noise. The constraints in (3) force a larger λ_3 yielding a more reasonable estimate of $\mathbf{D}$ and $\mathbf{W}$ in these regions. In sum, the proposed CLLS formulation offers a tractable means for parameter estimation via minimizing a convex cost function, thus avoiding local minima and achieving reasonable speed. Moreover, it achieves improved noise robustness over unconstrained schemes by ensuring that the estimated diffusivity and kurtosis remain within a physically and biologically plausible range along the imaged gradient directions. The examples using actual image data highlight the clear advantage offered by the proposed formulation over the ULLS approach. The improvement is particularly evident with fewer b = 1000 s/mm^2 acquisitions (Figure 2). Another important advantage offered by the CLLS formulation over our fast DKI estimation method [6] is that it can accept any number of b-values and different numbers of gradient directions per b-value, thus enabling further optimization of the acquisition protocol. For instance, the comparable quality of the MK maps in Figures 1(b) and 2(b) suggests that to achieve a given map quality, the CLLS formulation requires fewer gradient images at b = 1000 s/mm^2 than ULLS; in this case, offering a savings of 38% in acquisition time. Finally, it should be noted that while the improvement offered by CLLS comes at the expense of increased algorithm complexity and consequently higher run time, it is straightforward to speed up the computations via parallelization.

References: **1.** Basser PJ, et al. Biophys J 1994; 66:259. **2.** Jensen JH, et al. MRM 2005; 53:1432. **3.** Liu C, et al. MRM 2004; 51:924. **4.** Barmpoutis A, et al. NeuroImage 2009; 45:S153. **5.** Nocedal J, Wright SJ. Numerical Optimization. 2nd ed. New York: Springer; 1999. **6.** Jensen JH, et al. ISMRM 2009; 17:1403.

Acknowledgments: Supported by NIH 1R01AG027852, NIH 1R01EB007656, and Litwin Foundation for Alzheimer's Research.