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A fast schema for parameter estimation in diffusion kurtosis imaging

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A B S T R A C T

Diffusion kurtosis imaging (DKI) is a new model in magnetic resonance imaging (MRI) characterizing restricted diffusion of water molecules in living tissues. We propose a method for fast estimation of the DKI parameters. These parameters – apparent diffusion coefficient (ADC) and apparent kurtosis coefficient (AKC) – are evaluated using an alternative iteration schema (AIS). This schema first roughly estimates a pair of ADC and AKC values from a subset of the DKI data acquired at 3 *b*-values. It then iteratively and alternately updates the ADC and AKC until they are converged. This approach employs the technique of linear least square fitting to minimize estimation error in each iteration. In addition to the common physical and biological constrains that set the upper and lower boundaries of the ADC and AKC values, we use a smoothing procedure to ensure that estimation is robust. Quantitative comparisons between our AIS methods and the conventional methods of unconstrained nonlinear least square (UNLS) using both synthetic and real data showed that our unconstrained AIS method can significantly accelerate the estimation procedure without compromising its accuracy, with the computational time for a DKI dataset successfully reduced to only 1 or 2 min. Moreover, the incorporation of the smoothing procedure using one of our AIS methods can significantly enhance the contrast of AKC maps and greatly improve the visibility of details in fine structures.

1. Introduction

Diffusion tensor imaging (DTI) is a non-invasive technique for characterizing the motion of water molecules in living tissues [1]. It assumes that the random displacement of water molecules approximately follows a Gaussian distribution. Although DTI has been successfully applied in many neuroimaging studies, the assumption of a Gaussian distribution of motion is not strictly accurate because of the effects of tissue microstructure on the diffusion of water. New methods have been proposed to account for the non-Gaussian components of this diffusion, such as the Multi-Exponential model [2,3] or the q-space imaging technique. The Multi-Exponential model assumes that a single voxel may consist of multiple compartments, and diffusion in each compartment satisfies Gaussian model. The consolidated diffusions in all these compartments thus results in non-Gaussian phenomenon. In contrast, the q-space imaging technique makes no assumptions about the number of tissue compartments, but instead directly evaluates the displacement probability distribution function of water molecules [4,5].

Jensen and his colleagues recently proposed a new and efficient model, called diffusion kurtosis imaging (DKI) [6], for studying the non-Gaussian characteristics of water diffusion in tissue structures [7]. This model makes no assumption about the number of tissue compartments, and requires less scanning time (approximately 10 min) than does the q-space imaging. It introduced a kurtosis

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term into the expression of displacement distribution to evaluate the deviation from a Gaussian model. This kurtosis coefficient was then incorporated into a tensor model [8–10]. However, the kurtosis value could be over-estimated significantly in certain cases, and investigators have developed a method that uses a framework for estimation of constrained maximum likelihood (CML) with a Rician-noise model to prevent this from happening [11]. Anyway, compared to conventional DTI indices, the kurtosis value provides additional information of microstructure complexity in both white and gray matter, and is more sensitive to the presence of tissue heterogeneity [12–14]. Due to these advantages of the kurtosis term, DKI has been successfully applied to human studies on aging [15], attention deficit hyperactivity disorder [16], cerebral glioma [17], epilepsy [18], head and neck cancer [19], and animal models [20].

The DKI model uses conventional diffusion weighted imaging (DWI) data, but it requires data acquired with no less than 3 different b-values. The key parameters of the DKI model, including the apparent diffusion coefficient (ADC) and the apparent kurtosis coefficient (AKC), can be estimated using an unconstrained nonlinear least squares (UNLS) method [6]. This method performs robustly but usually requires at least 10 min to complete processing one single DKI dataset typically containing 30 slices acquired using 6 b-values along 30 gradient directions, which is excessively time consuming for clinical applications in practice. To shorten the processing time, Jensen et al. suggested directly solving the nonlinear function using 3 b-value data [21], which would allow a dataset to be evaluated in real time. Unfortunately, this method works only for cases of 3 b-values, and is therefore not a general solution. Recently, a new method, namely constrained linear least squares (CLLS), was proposed, achieving a fast speed of computation and comparatively better accuracy [22]. The CLLS method re-parameterizes the nonlinear function of DKI, and transforms it into a 2-variable linear problem. However, this approach needs to acquire data along more than 15 diffusion gradient directions to estimate ADC and AKC tensors, which therefore requires lengthy acquisition time.

We propose a method for rapid estimation of DKI parameters that uses an alternative iteration schema (AIS). It calculates ADC and AKC alternatively using a simple calculation formula and thus significantly reduces the calculation complexity. In addition, it adopts an iteration framework, which can easily incorporate extra constraints and smoothing procedures to improve the accuracy and robustness of the estimation. More specifically, the AIS method estimates ADC and AKC for each gradient direction independently, with each individual direction using data acquired at multiple b-values. In this algorithm, we first estimate initial values of the ADC and AKC using data acquired at baseline and two non-zero b-values from a DKI dataset. Second, we use an iterative framework to calculate these two parameters alternately until the results converge. Furthermore, we incorporate constraints and a smoothing procedure in each iteration to ensure the accuracy and robustness of the estimation (see Section 2). Thus, we have evaluated three versions of the AIS method: the original or unconstrained AIS (UAIS, Section 2.2), the constrained AIS (CAIS, Section 2.3), and the smoothed and constrained AIS (SCAIS, Section 2.4). In the evaluations, we used both synthetic and real data, against a number of other methods popularly in use. In a recent study on epilepsy [18], we successfully applied the proposed method to DKI data and achieved satisfactory results.

2. Method

In this section, we first briefly introduce the conventional UNLS method, discussing its high computational complexity due to the nonlinearity of DKI. Then we present an assumption on the nonlinear function that leads to an alternative iteration schema to simplify the calculation, thereby yielding the UAIS method. In addition, constraints and an additional smoothing procedure are subsequently incorporated into the iteration framework to improve the estimation accuracy and precision, resulting in the CAIS and SCAIS methods. Finally, an overview will be given to elaborate the algorithmic details of the AIS methods.

2.1. The UNLS method

The DKI model containing the ADC and AKC terms is a nonlinear function:

$$S(b) = S(0)\exp\left(-bD + \frac{1}{6}\cdot b^2D^2K + O(b^3)\right) \tag{1}$$

in which D and K denote ADC and AKC, respectively, and b denotes the b-value. $S(b)$ and $S(0)$ are the signal intensity of DWI data and the baseline measurement without applying any diffusion gradient, respectively.

Conventional UNLS methods optimize ADC and AKC value simultaneously using nonlinear curve fitting [6]. The fitting procedure aims to minimize the Euclidean Norm of difference between $S(b_n)/S(0)$ and $\exp(-b_n + 1/6\cdot b_n^2D^2K)$, as shown below:

$$\min_{D,K}\sum_{n=1}^{N}\left(\frac{S(b_n)}{S(0)} - \exp\left(-b_nD + \frac{1}{6}\cdot b_n^2D^2K\right)\right)^2 \tag{2}$$

where N denotes the total number of b-values involved in nonlinear fitting, and n is the current index of b-value. In Eq. (2), the 2nd order term of b-value accounts for the main difference between the DKI and DTI models.

The Levenburg–Marquadt algorithm is commonly used to solve the minimization problem of the nonlinear cost function [23], namely Eq. (2). However, the calculation of this method needs iterations and requires a matrix inversion and partial derivatives in each iteration. In addition, the parameters are normally estimated in a voxel-wise fashion. The computational burden is therefore very heavy for a DKI dataset because of the involvement of a large number of voxels.

In fact, logarithm can be applied to Eq. (1) for computational efficiency, thus the minimization turns to be log-nonlinear least squares fitting as follows:

$$\min_{D,K}\sum_{n=1}^{N}w_n\left(\ln\left(\frac{S(b_n)}{S(0)}\right) + b_nD - \frac{1}{6}\cdot b_n^2D^2K\right)^2 \tag{3}$$

where w_n is a weight for DWI measurement of the nth b-value, and should be set as $w_n = S(b_n)^2$ [24].

2.2. The UAIS method

Considering that avoiding nonlinear fitting may significantly shorten computation time, we introduce as follows an iterative schema, i.e., the UAIS method, to update ADC and AKC alternatively and progressively. The nonlinear fitting thus degenerates into a process of linear fitting.

2.2.1. The iteration framework

Supposing that we want to calculate an updated ADC value from Eq. (3), while a current estimation of the ADC and AKC values have already been obtained from a previous step, thus the following equation should be satisfied:

$$\frac{\partial}{\partial D_{i+1}}\left(\sum_{n=1}^{N}w_n\left(\ln\left(\frac{S(b_n)}{S(0)}\right) + b_nD_{i+1} - \frac{1}{6}\cdot b_n^2D_{i+1}^2K_i\right)^2\right) = 0 \tag{4}$$