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ScienceDirect
Magnetic Resonance Imaging 28 (2010) 982 – 994
MAGNETIC RESONANCE IMAGING

Adaptive smoothing of high angular resolution diffusion-weighted imaging data by generalized cross-validation improves Q-ball orientation distribution function reconstruction

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Received 22 September 2009; revised 22 December 2009; accepted 8 February 2010

Abstract

Q-ball imaging (QBI) is a high angular resolution diffusion-weighted imaging (HARDI) technique for reconstructing the orientation distribution function (ODF). Some form of smoothing or regularization is typically required in the ODF reconstruction from low signal-to-noise ratio HARDI data. The amount of smoothing or regularization is usually set a priori at the discretion of the investigator. In this article, we apply an adaptive and objective means of smoothing the raw HARDI data using the smoothing splines on the sphere method with generalized cross-validation (GCV) to estimate the diffusivity profile in each voxel. Subsequently, we reconstruct the ODF, from the smoothed data, based on the Funk-Radon transform (FRT) used in QBI. The spline method was applied to both simulated data and in vivo human brain data. Simulated data show that the smoothing splines on the sphere method with GCV smoothing reduces the mean squared error in estimates of the ODF as compared with the standard analytical QBI approach. The human data demonstrate the utility of the method for estimating smooth ODFs.

Keywords: High angular resolution diffusion-weighted imaging; Smoothing splines on the sphere; Generalized cross-validation; Q-ball imaging; Orientation distribution function

1. Introduction

Diffusion-weighted magnetic resonance imaging (MRI) has allowed unprecedented non-invasive mapping of brain microarchitecture in vivo by means of fiber tractography applications [1]. The accuracy of the tractography is dependent on the performance of fiber orientation estimates in brain white matter. Spatial resolution limitations in diffusion-weighted MRI have dictated that there will be voxels that will contain multiple fiber orientations [2–5] just as a result of partial voluming. The diffusion tensor in diffusion tensor imaging (DTI) [6] can only have a single directional maximum because of the limitations of the parametric model. High angular resolution diffusion-weighted imaging (HARDI) was proposed as a method that can reveal non-Gaussian diffusion [2–5,7] that DTI was incapable of resolving.

Earlier analysis techniques of HARDI data included using spherical harmonics to model the apparent diffusion coefficient [4,8] and using multitensor modeling [5]. Tuch [9] subsequently presented a model-independent method for reconstructing HARDI measurements. The new method was called Q-ball imaging (QBI). QBI attempts to only capture the orientational structure of the diffusion probability density function (PDF). The spherical Radon transform is applied to the diffusion-weighted signals to reconstruct the diffusion orientation distribution function (ODF). The ODF is a three-dimensional spherical function constructed to extract the dominant fiber orientations in an underlying voxel. Similar approaches used to extract the angular structure in the diffusion PDF include estimating the

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doi:10.1016/j.mri.2010.02.005

persistent angular structure (PAS) in PASMRI [10], using generalized tensor representations [11], extracting the fiber orientation distribution (FOD) in the spherical deconvolution method [12] and using the fiber orientation estimated using continuous axially symmetric tensors (FORECAST) method [13]. More recent approaches include ODF reconstruction in QBI using the spherical harmonic basis [14,15]. The primary goal of all these aforementioned methods is to extract the orientational angular structure in the diffusion function. These orientation functions portray the areas where the diffusion PDF has the most mass by forming peaks in those directions. These peaks are assumed to coincide with the underlying fiber directions [16].

With high diffusion-weightings being utilized in HARDI in order to capture complex fiber crossings, raw HARDI data have low signal-to-noise ratio (SNR) in addition to being time-intensive due to the high angular sampling. This issue of noise has been tackled previously in DTI by a number of investigators with varying approaches. These denoising methods can be categorized as either being frequency domain based or image domain based. Frequency domain based approaches mainly deal with filtering in the wavelet domain [17–19]. Of the image domain based methods included the application of partial differential equation (PDE) based anisotropic diffusion filters to the scalar-valued image [20–22], vector-based PDE anisotropic diffusion filtering applied to the eigenvector fields [23,24] and applying chains of nonlinear three-dimensional Gaussian filters [25]. In relation to HARDI data, Papadakis and Smponias [26] proposed using bi-cubic spherical splines from a piecewise spherical harmonic transform to generate a continuous smooth function from the sampled diffusion-weighted data. The choice of the degree of smoothing was ad hoc. In relation to QBI, low SNR levels of the HARDI data have prompted recent efforts in introducing different forms of regularization to improve ODF reconstruction and reliability of fiber orientation estimation in the spherical harmonic basis approaches to QBI [14,15]. None of the aforementioned methods employs objective and adaptive means of smoothing raw diffusion-weighted data.

HARDI data are samples of an originally smooth diffusion profile in each imaging voxel with an added nuisance noise term. Noise in HARDI data is of concern because it is the raw data that are used to extract the angular structure from the diffusion PDF. Methods used to construct any of the orientational structure functions will be sensitive to and directly affected by this noise. As a result, noisy diffusion data will result in noisy reconstructed ODFs. A usual practice to increase SNR in HARDI acquisitions is to average multiple acquired data sets leading to further time taxation and other biasing factors including bulk motion. A diffusivity profile that is more faithful to the true underlying smooth profile will ultimately result in more accurate ODF reconstruction. Better estimates of the diffusion ODF will be beneficial in fiber-tracking algorithms for extracting more accurate fiber orientations.

In this article, we apply an objective means of smoothing HARDI data in the three-dimensional diffusion space of each imaging voxel. We use the smoothing splines on the sphere estimator [27] to model the noisy HARDI data that naturally reside on the surface of the sphere. This estimator smoothes the measured noisy samples of the diffusion profile directly in three-dimensional diffusion space. This differs from the image domain based denoising methods used previously in denoising DTI data in that the smoothing is done in the diffusion space and not in the two-dimensional image space. The smoothing parameter is chosen objectively by generalized cross-validation (GCV) [28] that, in most situations, minimizes the mean squared error (MSE). The MSE is the sum of the square of the bias and the variance of the estimate. The smoothing splines on the sphere method has been applied recently [29] in order to smooth out spikes in the noisy MR measurements with application to the spherical deconvolution method for ODF extraction. However, the investigators did not evaluate the choice of the smoothing parameter. Kaden et al. [30] then later used smoothing spline modeling differently for fiber orientation density estimation with a non-objective means of choosing the smoothing parameter on a per voxel basis.

Objectively smoothing the diffusivity profiles is important since noise in the HARDI measurements will propagate through any reconstructed ODF obscuring the orientational structure information extracted from the diffusion PDF. In this article, we address, in particular, ODF reconstruction from noisy HARDI data by means of the Funk-Radon transform (FRT) used in the analytical QBI technique [9]. Specifically, we compare the standard QBI algorithm's performance reconstructing ODFs from noisy HARDI data with ODFs reconstructed after applying the smoothing splines on the sphere method with GCV smoothing. The comparisons are carried out for both low-density and high-density HARDI sampling schemes, at different SNR levels and for different fiber crossing angle scenarios. The two methods are also contrasted as they are applied to in vivo human brain data.

1.1. Theory

1.1.1. Q-ball imaging

QBI proposed by Tuch [7,9] reconstructs an approximate diffusion ODF. QBI reconstruction is based on applying the FRT to the sampled raw HARDI data sampled on a single sphere in diffusion reciprocal space to reconstruct this approximate ODF. Given a function defined on the sphere $f(\mathbf{r})$, where $\mathbf{r}$ is a unit vector, the FRT in the direction $\mathbf{t}$ is defined as the integration over the corresponding equator, i.e., the set of equatorial points in a plane perpendicular to $\mathbf{t}$ [9]. Formally the FRT in a direction $\mathbf{t}$ is written as

$$\mathrm{FRT}[f(\mathbf{r})](\mathbf{t}) = \int\limits_{\mathbf{r}\in\mathbf{t}^{\perp}} f(\mathbf{r})d\mathbf{r}. \tag{1}$$