Medical Image Analysis 18 (2014) 1290–1298

Contents lists available at ScienceDirect

Medical Image Analysis

journal homepage: www.elsevier.com/locate/media

Large deformation diffeomorphic registration of diffusion-weighted imaging data

Pei Zhang [a,c], Marc Niethammer [b,c], Dinggang Shen [a,c], Pew-Thian Yap [a,c,*]

[a] Department of Radiology, The University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, USA
[b] Department of Computer Science, The University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, USA
[c] Biomedical Research Imaging Center, The University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, USA

ARTICLE INFO

Article history:
Received 7 January 2014
Received in revised form 17 May 2014
Accepted 30 June 2014
Available online 21 July 2014

Keywords:
Diffeomorphism
Diffusion-weighted imaging
Image registration
Signal profile reorientation
Explicit orientation optimization

ABSTRACT

Registration plays an important role in group analysis of diffusion-weighted imaging (DWI) data. It can be used to build a reference anatomy for investigating structural variation or tracking changes in white matter. Unlike traditional scalar image registration where spatial alignment is the only focus, registration of DWI data requires both spatial alignment of structures and reorientation of local signal profiles. As such, DWI registration is much more complex and challenging than scalar image registration. Although a variety of algorithms has been proposed to tackle the problem, most of them are restricted by the zdiffusion model used for registration, making it difficult to fit to the registered data a different model. In this paper we describe a method that allows *any* diffusion model to be fitted after registration for subsequent multifaceted analysis. This is achieved by directly aligning DWI data using a large deformation diffeomorphic registration framework. Our algorithm seeks the optimal coordinate mapping by simultaneously considering structural alignment, local signal profile reorientation, and deformation regularization. Our algorithm also incorporates a multi-kernel strategy to concurrently register anatomical structures at different scales. We demonstrate the efficacy of our approach using *in vivo* data and report detailed qualitative and quantitative results in comparison with several different registration strategies.

1. Introduction

Diffusion-weighted imaging (DWI) is widely used to non-invasively study white matter microstructure and fiber tracts in the human brain. The information provided by DWI is helpful for identifying pathological damages associated with brain diseases (*e.g.*, stroke Schaefer et al., 2000, Alzheimer's disease Hanyu et al., 1998; Wee et al., 2011, 2012; Zhang et al., 2013, and schizophrenia Shi et al., 2012) and brain changes associated with normal development (Yap et al., 2011).

To quantify white matter changes, a common space is required where images of patients and healthy controls can be spatially normalized and compared. Image registration is used to build such space and to spatially normalize the images by warping them to the space.

Traditional scalar image registration techniques are not directly applicable to diffusion-weighted images. When diffusion-weighted images corresponding to different diffusion gradient directions are put together, each voxel location encodes a vector-valued signal profile that provides information on the segment of the fiber bundle that traverses the voxel. As such, registration of diffusion-weighted images requires not only the spatial alignment of anatomical structures, as in scalar image registration, but also the reorientation of signal profiles with respect to the surrounding anatomical structures, which is not considered in scalar image registration. DWI registration is thus much more complicated and challenging than scalar image registration.

A common approach to registering diffusion-weighted images is to fit some diffusion model to the images to estimate angular quantities, such as orientation distribution functions (ODFs), and then incorporate such information into a registration algorithm for structural alignment. There are a number of choices of diffusion models as well as registration algorithms, leading to a variety of DWI registration methods.

Early work uses the relatively simple diffusion tensor model (Alexander et al., 2001; Cao et al., 2006; Yeo et al., 2009,, 2010; Zhang et al., 2006). Alexander et al. (2001) introduced the preservation of principal direction (PPD) algorithm for the reorientation of diffusion tensors during image alignment. Instead of PPD, Yeo et al. (2009) used a finite strain reorientation strategy (Alexander

* Corresponding author. Address: Department of Radiology and Biomedical Research Imaging Center, The University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, USA.

E-mail address: ptyap@med.unc.edu (P.-T. Yap).

http://dx.doi.org/10.1016/j.media.2014.06.012
1361-8415/

et al., 2001) together with a diffeomorphic demons algorithm (Vercauteren et al., 2009) for registration. Zhang et al. (2006) broke down the image into uniform regions and estimated an affine transformation for each region by explicitly optimizing tensor orientation within that region. Cao et al. (2006) proposed a large deformation diffeomorphic metric mapping (LDDMM) algorithm (Beg et al., 2005) to tackle large-deformation non-linear registration of directional vector fields.

However, the diffusion tensor model can only characterize one principal fiber direction at each voxel and thus is unable to handle complex fiber configurations such as crossings. It has been found that at least one third of voxels in white matter have complex fiber configurations (Behrens et al., 2007). Obviously, failure to reorient the signal profiles in those voxels will lead to misalignments of microstructure.

To deal with crossing fibers, a number of researchers (Geng et al., 2011; Du et al., 2012; Hong et al., 2009; Raffelt et al., 2011; Yap et al., 2011; Dhollander et al., 2011; Zhang et al., 2012) attempted to use more complicated diffusion models. Geng et al. (2011) aligned ODFs represented by spherical harmonics (SHs) using an elastic registration algorithm. Du et al. (2012) integrated a similarity metric for the ODFs, which is defined in a Riemannian manifold, into a variant of LDDMM algorithm (Glaunès et al., 2008). Yap et al. (2011) extracted coarse-to-fine features from the ODFs for hierarchically refined alignment. Instead of using ODFs, Hong et al. (2009) performed registration with the help of T_2-weighted images and subsequently reoriented the fiber orientation distribution (FOD). Raffelt et al. (2011) registered DWI data by mapping the FODs through a subject-template-symmetric diffeomorphic framework.

However, the aligned data generated by the above approaches are not in the form of diffusion-weighted images. The ability to produce diffusion-weighted images as final registration outcome is important for common-space analysis using diffusion models without well-defined warping and reorientation methods.

To overcome this problem recent studies propose to register DWI data directly in the Q-space (Dhollander et al., 2011; Zhang et al., 2012). Dhollander et al. (2011) tackled the problem by virtue of an SH-based reorientation algorithm together with a diffeomorphic demons algorithm (Vercauteren et al., 2009). We (Zhang et al., 2012) achieved a similar goal by using a set of diffusion basis functions (DBFs) (Yap and Shen, 2012) and a geodesic shooting algorithm simplified proposed by Ashburner and Friston (2011). Both methods regard spatial alignment and local signal profile reorientation as two separate components, and perform optimization by alternating between (i) computing the spatial mapping without considering reorientation, and (ii) reorienting the data using the resulting mapping. Although this strategy is simple, it ignores the crucial role reorientation plays in correspondence establishment.

As shown by Yeo et al. (2009), a better but more complicated strategy is to integrate the two components into a single cost function and explicitly take into account reorientation during registration. In this paper we describe a method that is able to register DWI data in the Q-space in a single framework where image matching, data reorientation, and deformation regularization are considered simultaneously. Part of this work has been reported in our recently published conference paper (Zhang et al., 2013). Herein, we provide additional derivations, implementation details, and experimental results that are not available in the conference version. Compared with the conference paper, this paper uses a more general symmetric tensor model, instead of Watson distribution, as the DBFs (Yap and Shen, 2012). In addition, the cost function is reformulated such that the solution satisfies the Euler–Lagrange equation.

2. Outline of the approach

Our method consists of two components: (1) DWI data reorientation (Section 3) and (2) an LDDMM-based registration algorithm (Section 4). The first component achieves reorientation in the Q-space while the second one provides a registration framework where alignment and reorientation are considered simultaneously.

The first component is realized based on the work of Yap and Shen (2012), where reorientation is achieved by three steps: (i) decomposing the diffusion signal profile into a set of weighted DBFs; (ii) reorienting each DBF independently using a local transformation; (iii) recomposing the reoriented DBFs to obtain the desired profile. Compared with the SH-based reorientation scheme as used by Dhollander et al. (2011), this strategy avoids the computational complexity of SHs as well as the loss of sharp directional information when the maximum order of the SH basis functions is insufficient (see Yap and Shen (2012) for detailed discussion).

The second component involves the LDDMM algorithm (Beg et al., 2005). Based on the spatial mapping estimated by the LDDMM algorithm, a Jacobian matrix can be computed at each voxel location and used for DBF reorientation. The interaction between the two components is mathematically expressed as a single cost function (Section 4) and, during optimization, spatial alignment and local reorientation are considered simultaneously.

To simultaneously register anatomical structures at different scales we use a multi-kernel strategy (Risser et al., 2011). This is to introduce a natural multi-resolution property to our registration algorithm and to provide an intuitive way of parameter tuning based on the desired scales that should be captured by the registration. Details are given in Section 5.1.

This work has three major contributions. First, we propose a non-rigid registration algorithm for direct registration of DWI data. This allows *any* diffusion model to be fitted to the aligned data for subsequent multifaceted analysis. Second, we incorporated spatial alignment and local reorientation into a single cost function. In contrast to the works of Dhollander et al. (2011) and Hsu et al. (2012), our method does not rely on multi-shell data, which require long acquisition time. Last but not least, we derive the gradient of the cost function and describe in detail the numerical implementation.

3. Reorientation of DWI data

We now briefly review the major concepts involved in reorientation using DBFs (Yap and Shen, 2012).

3.1. Decomposition of signal profile

Let $S(\boldsymbol{q}_i)$ be the diffusion signal measured in direction $\boldsymbol{q}_i$ ($i = 1, \ldots, M$). It can be represented by a set of N DBFs:

$$S(\boldsymbol{q}_i) = w_0 f_0 + \sum_{j=1}^{N} w_j f(\boldsymbol{q}_i|\lambda_1, \lambda_2, \boldsymbol{\mu}_j),$$

where $f(\boldsymbol{q}_i|\lambda_1, \lambda_2, \boldsymbol{\mu}_j)$ is the j-th DBF, w_j is the associated weight, and f_0 is a constant component representing isotropic diffusion. Specifically, the j-th DBF is defined by

$$f(\boldsymbol{q}_i|\lambda_1, \lambda_2, \boldsymbol{\mu}_j) = \exp(-b\boldsymbol{q}_i^{\mathrm{T}}\boldsymbol{D}_j\boldsymbol{q}_i), \tag{1}$$

where b is the diffusion weighting and $\boldsymbol{D}_j = (\lambda_1 - \lambda_2)\boldsymbol{\mu}_j\boldsymbol{\mu}_j^{\mathrm{T}} + \lambda_2\boldsymbol{I}$ is a symmetric diffusion tensor. λ_1 and λ_2 control the shape of the tensor, $\{\boldsymbol{\mu}_j\}$ is a pre-defined set of tensor principal directions and $\boldsymbol{I}$ is an identity matrix representing an isotropic tensor. We generated $\{\boldsymbol{\mu}_j\}$ via spherical tessellation by subdividing the faces of an icosahedron.

If $\lambda_1 \gg \lambda_2, \boldsymbol{D}_j$ can be approximated by $\lambda_1\boldsymbol{\mu}_j\boldsymbol{\mu}_j^{\mathrm{T}}$. Then, we have