Evaluation of DTI Property Maps as Basis of DTI Atlas Building

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ABSTRACT

Compared to region of interest based DTI analysis, voxel-based analysis gives higher degree of localization and avoids the procedure of manual delineation with the resulting intra and inter-rater variability. One of the major challenges in voxel-wise DTI analysis is to get high quality voxel-level correspondence. For that purpose, current DTI analysis tools are building on nonlinear registration algorithms that deform individual datasets into a template image that is either precomputed or computed as part of the analysis. A variety of matching criteria and deformation schemes have been proposed, but often comparative evaluation is missing. In our opinion, the use of consistent and unbiased measures to evaluate current DTI procedures is of great importance and our work presents two possible measures. Specifically, we propose the evaluation criteria generalization and specificity, originally introduced by the shape modeling community, to evaluate and compare different DTI nonlinear warping results. These measures are of indirect nature and have a population wise view. Both measures incorporate information of the variability of the registration results in the template space via a voxel-wise PCA model. Thus far, we have used these measures to evaluate our own DTI analysis procedure employing fluid-based registration on scalar DTI maps. Generalization and specificity from tensor images in the template space were computed for 8 scalar property maps. We found that for our procedure an intensity-normalized FA feature outperformed the other scalar measurements. Also, using the tensor images rather than the FA maps as a comparison frame seemed to produce more robust results.

Keywords: Diffusion Tensor Imaging, Nonlinear Registration, Principal Component Analysis, Model Specificity, Model Generalization, Voxel-wise Analysis

1. INTRODUCTION

Diffusion tensor imaging (DTI) is a relative new but rapidly developing MRI imaging modality. With DTI, the pathways of the major fiber tracks in brain white matter can be visualized and the integrity of the brain white matter can be studied for the first time in vivo (Basser et al., 1994).

Atlas based group analysis of DTI has been increasingly used to investigate normal white matter development, degradation and pathological changes by comparing white matter properties between different groups. To build an DTI atlas, all the individual DTI volumes need to be brought to a common space, which can either a pre-computed, usually a standard anatomy atlas space, such as the MNI and the Talairach atlas (Chau and McIntosh, 2005), or computed as part

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of the analysis procedure, which is usually a space with averaged shape and properties, such as a data set specific unbiased atlas (Joshi et al., 2004; Lorenzen et al., 2005). To achieve high quality voxel-wise level correspondence across all the subjects under investigation, nonlinear registration algorithms are used to deform the individual datasets into the template space. Unlike scalar image registration, after spatial transformation of the voxel coordinates, the tensor field needs to be re-sampled and reoriented. The tensor interpolation should be done in a Riemannian manifolds to preserve the symmetric, positive and definite properties. To simply the computation, log-Euclidian metric (Arsigny et al., 2006) was introduced in tensor calculations. Reorientation ensures the principle directions of the tensors preserve accordance with the underlying anatomical structures after spatial transformations(Alexander et al., 2001).

In atlas space, region of interest (ROI) based analysis, voxel-wise analysis (Liu et al., 2009) and fiber tract oriented analysis (Goodlett et al., 2009) can be conducted to draw clinically meaningful conclusions. Compared to region of interest (ROI) based analysis, voxel-based analysis gives better localization and avoids manual ROI delineation with its inherent problems of intra and inter-rater variability and ROI definition bias. One of the major and fundamental challenges in voxel-wise DTI analysis is to get high quality voxel correspondence across all the subjects (Liu et al., 2009). For this purpose, a variety of matching criteria and deformation schemes have been proposed, but thorough comparative evaluation is still missing. In our opinion, the use of consistent and unbiased measures to evaluate current DTI procedures is of great importance. We present two such possible measures in this paper.

In this work, we propose the use of the evaluation criteria generalization and specificity, which are originally introduced by the shape modeling community (Styner et al., 2003), to evaluate and compare the voxel-wise correspondence of different DTI nonlinear warping results. As is the case with any correspondence evaluation metric, they bias the analysis to their specific viewpoint on what constitutes correct correspondence. These measures are of indirect nature and have a population wise view. Both measures incorporate information of the variability of the nonlinear registration results in the template space via a voxel-wise principal component analysis (PCA) model.

Basically, generalization captures the ability to describe instances outside of a given training set, while specificity gives the ability to represent only valid instances of the object class.

2. METHODS

2.1 Modified PCA model computation

PCA involves a mathematical procedure that transforms a number of possibly correlated variables into a smaller number of uncorrelated variables called principal components. The first principal component accounts for as much of the variability in the data as possible, and each succeeding component accounts for as much of the remaining variability as possible.

In shape modeling, PCA is employed to capture the mean and variability of a group of objects, commonly referred to as training objects, each represented by a scalar vector of same dimensionality. The procedure is in essence a decomposition of an existing feature space (the object vectors) into its mean and principal directions of variance computed from the covariance matrix. The principal directions are determined by computing and sorting the eigen values and eigenvectors of the covariance matrix. The principal directions span a shape space with the mean vector at its origin.

Objects in this space are described as a linear combination of the eigenvectors on the mean vector. For common scalar images, such as a DTI fractional anisotropic (FA) image, the vector representation is simply a direct linearization of the image traversing the image in a single TV-scan procedure. For tensor images, we propose to use a method adapted to the nonlinear tensor space also called principal geodesic analysis (PGA) introduced by (Fletcher et al., 2004; Fletcher et al., 2009).

The PCA/PGA space employed here is different from standard PCA procedure in that the average object/image, and thus the center of the PCA/PGA space, is not computed from the object data directly, but rather is given by the DTI analysis procedure itself. Most current procedures are based on mapping the individual data into a template image that is either pre-computed or computed as part of the analysis procedure. We are choosing that template as the center of the PCA/PGA space.

2.2 Model generalization

The model generalization metric quantifies the ability of a PCA space to represent the unseen instances of the same object class. Because the PCA model is calculated from a limited training set of the object class and learned the characteristics of the object class, generalization property is important for the model not to be over constrained to the training set. If a PCA space is over-fitted to the small training object set, it will lost the ability to generalize to new examples to the training set.

To measure the generalization ability of a model, a leave-one-out procedure is conducted. First, the PCA space is calculated using all but one member of the training set. Then the model is fitted to the excluded example to measure how it captures the characteristics of the example. The accuracy to which the PCA space can describe the new example is measured by the model generalization. Model generalization ability is then defined as the approximation error averaged over the complete set of trials. It is measured as a function of the number of principal directions employed in the reconstruction procedure.

Specifically for the DTI atlas setting, lower generalization errors would indicate a registration method's ability to identify voxel correspondences with similar local properties across all DTI brain scans from the same subject population (pathology, age etc). Thus, a new unseen image of the same subject population is likely to be registered equally well as the training data. This property is very important for DTI atlas building, where the appropriateness of the computed atlas for unseen data is of high relevance. The lower the generalization errors in the atlas coordinate space, the better the subjects are aligned.

2.3 Model specificity

Using a model computed from a training set should only generate similar instances of the object class to those in the training set. This is called model specificity. This property of a PCA model is commonly assessed by randomly sampling a population of instances from the PCA space and comparing them to the training set. The quantitative measure of model specificity as a function of the number of principal directions is defined as the average distance of these randomly generated objects to their nearest member in the training set.

In the DTI registration and atlas settings, lower specificity errors indicate that the registration was able to cluster the training data datasets well across the whole subject population. Low values of specificity are important in DTI simulation studies, as well as when DTI atlases are used to detect subjects from another population, such as the detection of pathology via a DTI atlas from healthy subjects.

2.4 Error metric

For the distance between two DTI scalar images, it is computed in our experiments using the mean squared intensity difference. The mean Log-Euclidean tensor distance is used for distance between DTI volumes.

2.5 Our DTI registration setup

With voxel-based analysis methods of DTI datasets, high fidelity registration accuracy is crucial in presence of large deformations due to inter-subject differences as well as the susceptibility artifact induced image distortions present in DTI. In our study we employed a high-dimensional, unbiased atlas computing method, which uses a fluid based nonlinear registration algorithm (Goodlett et al., 2006). The atlas building procedure is initialized by affine registration and followed by fluid-based nonlinear registration of a DTI derived feature image, which is sensitive to the geometry of brain structures, especially white matter. With the deformation field data, we warped each of the tensor images into the unbiased space to get the average DTI atlas via principal axis realignment and strain preservation. We studied the following selected set of scalar maps from DTI study with our nonlinear registration setup:

1) Average baseline (b = 0) image

2) Fractional Anisotropy (FA) image

3) Curvature FA image computed with the method used in(Goodlett et al., 2006)

4) Mean Diffusivity (MD) image,

5) Curvature MD image, calculated in the same way as curvature FA

6) Combination of Curvature FA and Curvature MD

7) Isotropically-weighted diffusion imaging (IDWI)

8) Intensity-histogram normalized FA image

3. RESULTS

We created an unbiased atlas with 15 subjects, and then evaluated the warping quality of the 15 subjects in atlas space with model generalization and model specificity described above. For all DTI derived features maps, we examined the performance of our unbiased atlas computation via generalization and specificity errors of the FA images mapped in the atlas/template space. As mentioned before the origin of the PCA space is defined by that atlas space. Figure 1 and figure 2 show the model generalization and specificity respectively. In the 2 figures, both the least model generalization and specificity errors came from the atlas building result using FA images as registration feature maps. This implies that among all the 8 scalar maps we tested, using FA images outperformed the other scalar measurements and their combinations, giving the most matching quality in atlas space. The second best result came from the intensity normalized FA images (denoted as nFA in Figure 1 and Figure 2). IDWI gave the worst result, mainly because the rather smoothed appearance of IDWI maps lacked of contrast to drive the matching procedure. Curvature FA feature maps gave the result worse than FA and intensity normalized FA, but better than other scalar maps listed in section 2.5.

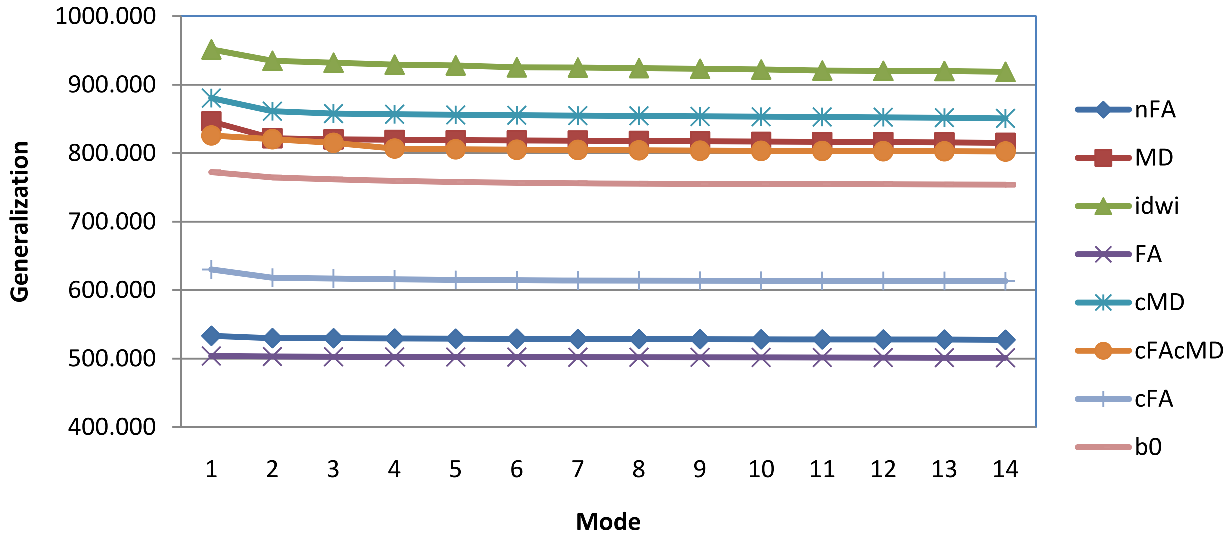

Figure 1 Generalization plotting of nonlinearly warped FA images of 15 subjects in DTI atlas space

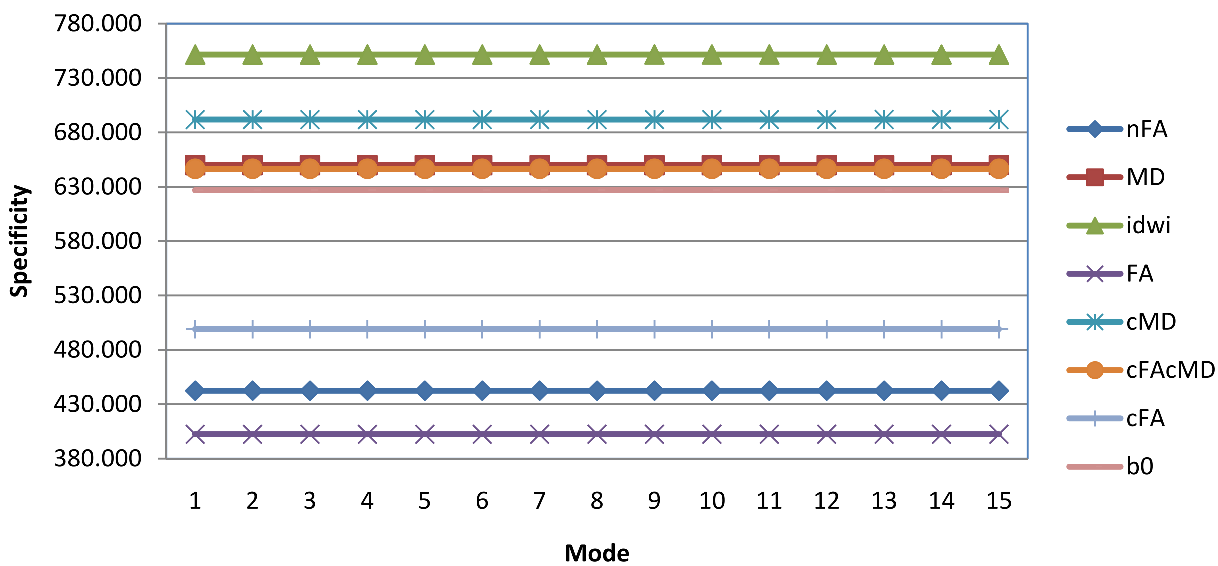

Figure 2. Specificity plotting of nonlinearly warped FA images of 15 subjects in DTI atlas space

While doing actual analysis, it is always desirable to avoid directly using FA maps as registration feature maps in order not to produce any bias in group-wise FA comparison. Thus, we recommend using intensity normalized FA maps in nonlinear DTI registration to drive the deformation field computation procedure.

In our study, we also found that using the tensor images rather than the FA maps as a comparison frame seemed to produce more robust results. In our future studies, we will compare our atlas building procedure against other ones using both FA images and tensor images in atlas space.

4. CONCLUSION

Atlas based group analysis is of great importance in DTI studies, especially for voxel-wise group comparisons. The atlas itself gives limited information about how well the individual are aligned in the atlas space. To measure the correspondence of the subjects mapped in atlas space, we proposed a modified PCA model in which the model generalization and specificity are used as correspondence measures in atlas space. From our study, among the scalar feature images derived from a DTI study used to drive a fluid based nonlinear DTI registration and unbiased atlas building, FA gives the best individual correspondence in atlas space. Intensity normalized FA gives the second best result. To avoid any bias possibly introduced during FA based registration, the intensity normalized FA image is the best choice in a fluid based nonlinear registration based DTI registration setup. In our future studies, we will investigate other DTI atlas building schemes using this comparison framework.

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