# A GENERAL FRAMEWORK FOR DIFFUSION TENSOR WARPING

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#### ABSTRACT

The need for warping diffusion tensor after applying a geometric transformation to an image of this modality has been previously reported. However, a careful justification of this requirement has not been provided. In this paper, on the basis of the image acquisition procedure, the effects of geometric transformations in both diffusion weighted images and in the diffusion tensors computed from them are analyzed. This provides the grounds for the description of how the tensors should be warped if the image is transformed, and it supplies a general framework in which the warping strategies previously proposed in the literature can be viewed as approaches to such theoretical warping.

## 1. INTRODUCTION

Diffusion tensor imaging (DTI) is an image modality that measures the water diffusion in tissues [2]. In brain, it allows to visualize the fiber structures since diffusion is constrained by the myelin coat of the axons. Note that it is a macroscopic imaging technique, meanwhile fibers are formed by neuron axons, that have microscopic diameters. For this reason, instead of the microscopic fiber structure, the macroscopic tracts in which fibers are bundled are visualized.

The processing techniques that deal with this modality must take into account its special features, since the diffusion tensor (DT) at each voxel is related to the underlying structure. Thus, if a geometric transformation is applied to the image, the DT should be also transformed to remain consistent with the structures. This is essential for registration of these images, and therefore some strategies have been developed to warp the tensors consistently with the transformation [1, 7]. They argue that only rotations should be applied to tensors because they define microscopical tissue properties that cannot change, an argument whose accuracy will be discussed in further sections. Moreover, both the requirement for warping and the simplification to rotations have not been rigorously justified. Thus, in this paper we provide the rationale behind the requirement for tensor warping. On this basis, it will be possible to define an approach to the tensor warping directly related to the actual effect of image transformation, as well as, to analyze the validity of previously proposed methods inside this framework.

This paper is structured as follows: in Section 2 a description of the problem can be found. Then, in Section 3 the methods proposed in the literature are described. The need for tensor warping and its description are exposed in Section 4, and the experiments with real data are described in Section 5. Finally, some conclusions are drawn in Section 6.

#### 2. PROBLEM ASSESSMENT

Let *I* be an image defined in a compact support  $\Omega$  and let be *T* a transformation that maps the  $\Omega$  into a deformed domain  $\Omega'$ . That is, for a given point  $\vec{x} \in \Omega$ , we obtain a point  $\vec{x'} \in \Omega'$ ,  $\vec{x'} = T(\vec{x})$ . Thus, the local deformation in a point  $\vec{x}$  is assessed as the gradient of the transformation at the given point, that is the Jacobian matrix  $\mathbf{J}(\vec{x}) = \frac{\partial T(\vec{x})}{\partial \vec{x}}$ . In a scalar image, a transformed image *I'* is built by mapping the intensity values at  $\vec{x} \in \Omega$  to the new positions in the  $\Omega'$  domain. However, in the case of tensor data, the value at the location  $\vec{x}$  is a tensor  $\mathbf{D}_{\mathbf{x}}$ . If this value is directly mapped to the transformed domain, the tensor  $\mathbf{D}_{\mathbf{x}'}$  could not preserve the coherence with underlying structures in the transformed image. For this reason, it is necessary to warp the original tensor  $\mathbf{D}_{\mathbf{x}}$ , in order to obtain the appropriate transformed tensor  $\mathbf{D}'_{\mathbf{x}'}$ .

The requirement for tensor warping can be viewed in the synthetic example in Fig. 1, where tensors are represented by ellipses, whose axes length and directions are given respectively by the tensor eigenvalues and eigenvectors. Since diffusion is constrained by the axons myelin coat, the areas where diffusion has a predominant direction can be identified as fibers oriented in such direction. Thus, a synthetic fiber can be distinguished in Fig. 1.(a). This image is rotated, and the tensors are translated to the new locations, so the image in Fig. 1.(b) is obtained, where the main diffusion direction does not coincide with the new fiber orientation. Therefore, the same rotation should be applied to tensors in order to be aligned with the fiber direction, as shown in Fig. 1.(c).

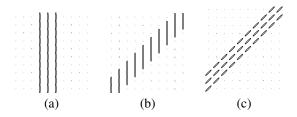


Figure 1: Synthetic example that shows the need for warping tensors after the image transformation: (a) Synthetic image with a vertical fiber; (b) rotation of (a) without tensor warping; (c) rotation of (a) with tensor warping.

Although in this example the warping that must be applied to tensors seems to be obvious, if more complex transformations are applied to the image the assessment of such

The authors acknowledge the Comisión Interministerial de Ciencia yTecnología for research Grant TEC2007-67073. First author is funded by the Junta de Castilla y León and the European Social Fund (ESF).

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(a) (b)	

Figure 2: Effect of the direct application of the local deformation matrix: (a) Original isotropic tissue; (b) Warped DT.

warping is not straightforward. The strategies that have been proposed to tackle this problem are detailed in next section.

## 3. BACKGROUND

In general, the methods that compute the warping are based on the local deformation at every voxel, that is given by the Jacobian matrix,  $\mathbf{J}(\vec{x})$ , of the transformation at the voxel (the transformation is assumed to be differentiable). Thus, the first and most simple approach to the warping that should be applied to the tensor  $\mathbf{D}_{\mathbf{x}}$  is the one mentioned in [5], that computes the warped tensor  $\mathbf{D}'_{\mathbf{x}'}$  at the location  $\vec{x'} = T(\vec{x})$  as:

$$\mathbf{D}_{\mathbf{x}'}' = \mathbf{J}^T(\vec{x})\mathbf{D}_{\mathbf{x}}\mathbf{J}(\vec{x}) \tag{1}$$

According to [5], it is not clear that diffusion tensors deform following this model. The problem is that the shape of the ellipsoids that represent the tensor is not preserved. It is argued that the tensor shape should be preserved, specially in areas of high anisotropy where the fiber tracts are, that is, the deformation should only affect to the directional properties of the diffusion, but not to its size or shape. For this reason, it is proposed to rescale the tensor  $\mathbf{D}'_{\mathbf{x}'}$  obtained by Eq. (1) to preserve the ellipsoid volume. Another proposal is to normalize the higher eigenvalue, to be the same that in  $D_x$ . This method is analyzed by the example in Fig. 2 where it is shown that it can lead to some situations that does not correspond to the physical interpretation of the data. Fig. 2.(a). represents a tissue area where diffusion is isotropic. Since the diffusion is isotropic and equal in every point of the tissue, the diffusion in the area enclosed by each voxel will be equal in every direction. That is, the measured tensor should be isotropic independently of the measurement frame. Therefore, for any transformation applied to the domain, DT should preserve its shape. If the local deformation is applied to the tensors to warp them<sup>1</sup>, we obtain anisotropic tensors as the shown in Fig. 2.(b), what is not coherent with the underlying tissue, where diffusion is isotropic. Even though the tensor was rescaled to preserve the volume or the higher eigenvalue of the original data, the warped tensors would be anisotropic. Therefore, the direct application of the local deformation tensor provides a warped DT that is not realistic. Actually, the authors in [5] state that more research is required to clarify how the tensor should be transformed.

Other research line is based on the assumption that only rotations should be applied to the tensors, and the rotation component of  $\mathbf{J}(\vec{x})$  is searched. Once the rotation matrix **R** is obtained, the warped tensor is computed as:

$$\mathbf{D}_{\mathbf{x}'}' = \mathbf{R}^T \mathbf{D}_{\mathbf{x}} \mathbf{R} \tag{2}$$

Two methods are proposed in [1] in order to find the rotation matrix: Finite strain (FS), and preservation of principal direction (PPD). The former is based on the polar decomposition theorem, that states that for any non-singular square matrix there are unique symmetric positive definite matrices  $\mathbf{P}$  and  $\mathbf{Q}$  and a unique orthonormal matrix  $\mathbf{R}$  that satisfy that:

$$\mathbf{J} = \mathbf{R}\mathbf{P} = \mathbf{Q}\mathbf{R}.\tag{3}$$

Thus, the FS computes the rigid rotation component  $\mathbf{R}$  of the transformation as follows:

$$\mathbf{R} = \mathbf{J}(\mathbf{J}^T \mathbf{J})^{-\frac{1}{2}} \tag{4}$$

In [4], a different but equivalent way to compute the rotation matrix is provided. It is based on the singular value decomposition (SVD) of  $\mathbf{J} = \mathbf{U}\Sigma\mathbf{V}^T$ . Both matrices  $\mathbf{U}$  and  $\mathbf{V}$  are orthonormal and  $\Sigma$  is a diagonal matrix whose elements are the scale factor in each direction. Thus, the scaling is ignored, and the rotation matrix is computed as  $\mathbf{R} = \mathbf{U}\mathbf{V}^T$ . The equivalence between these two rotation matrices is easy to prove if  $\mathbf{J}$  is replaced by its SVD decomposition in Eq. (4).

FS ignores the deformation component, also related to rotational effects that depends on the original data orientation. This effect is addressed by PPD [1] as follows: First, a rotation matrix  $\mathbf{R}_1$  is obtained as the one that maps the first eigenvector,  $\vec{e_1}$ , into the unitary vector in the direction given by  $\mathbf{J}\vec{e_1}$ . Then, a matrix  $\mathbf{R}_2$  is obtained as the one that maps the second eigenvector,  $\vec{e_2}$ , into the unitary vector in the direction of the projection of the vector given by  $\mathbf{J}\vec{e_2}$  in the plane perpendicular to  $\mathbf{J}\vec{e_1}$ . Finally, the matrix that should be applied to the tensor is computed according to  $\mathbf{R} = \mathbf{R}_2\mathbf{R}_1$ .

Both methods in [1] consider that only rotations can be applied to tensors. This simplification is justified saying that size and shape of the DTs reflects microstructural properties of the tissue, that cannot be changed. However, this statement is not completely true. It is true that the microstructural properties of the tissue must not change. However, the DT is a macrostructural measure of the properties of this tissue. Each voxel could contain various tissue kinds that contribute to the global diffusion measure. Since the underlying region comprised by the voxel can change due to the transformation, the diffusion tensor at the voxel can change both in shape and size. This can be better understood by the example in Fig. 3.

The four images in Fig. 3 simulate acquisitions of the same region with different voxel size. Two tissues can be distinguished: the background, where diffusion is small and isotropic; and the fibers, where the diffusion is higher in the major eigenvector direction, so the ellipses approach lines in this direction. In Fig. 3.(a), five fibers can be clearly identified, whereas in Fig. 3.(d), only two of these fibers (the two broadest fibers) are so clearly distinguished. Since the voxel size is higher, each DT represents the diffusion in a wider area, that includes both background points and fiber. The contribution of the anisotropic diffusion to the measure is decreasing as the voxel area comprises more isotropic tissue. For this reason the fibers are *dispelled* into the isotropic tissue as the voxel size is getting larger. In conclusion, since the DT is a macroscopic measure of the microscopic tissue properties, DT size or shape changes may occur due to the acquisition procedures. The DT that is measured is not a microscopic tissue property, and for this reason, the two previous methods are based on a questionable assumption. In this

<sup>&</sup>lt;sup>1</sup>For this example, a random local deformation matrix has been generated:  $\mathbf{J} = \begin{pmatrix} 0.9 & 0.1 \\ 0.2 & 0.8 \end{pmatrix}$ 

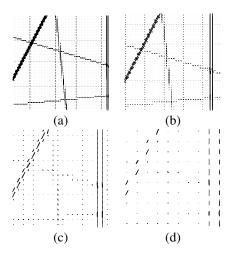


Figure 3: Acquisition of the same tissue area with different voxel size: (a)  $0.01 \text{ } mm^2$ ; (b)  $0.09 \text{ } mm^2$ ; (c)  $0.225 \text{ } mm^2$ ; (d)  $0.36 \text{ } mm^2$ 

paper these methods are analyzed and grounded on physical principles to validate its performance.

Other more complex approach is proposed in [7]: major eigenvector is viewed as a random sample of the true fiber direction and the rotation matrix is computed by Procrustean estimation. Again, the method is also grounded on the same assumption about the preservation of size and shape.

## 4. DIFFUSION TENSOR WARPING

In this section, the basis of DTI acquisition and tensor computation are described to understand how the DT at each voxel is related to the underlying structures. Taken this issue in mind, we can assess how the tensors should be warped.

## 4.1 DTI Acquisition and Computation

DTIs are computed from a set of diffusion weighted magnetic resonance images (DWIs), that are acquired by means of a gradient pulse in a given direction  $\vec{g}$ , and measure the diffusion in such direction. A conventional MRI without diffusion weighting, the baseline image, is also required to compute the tensor. Each of the DWIs are related to the baseline by means of the Stejskal-Tanner equation [6]:

$$S_i = S_0 e^{-b\vec{g}_i^T \mathbf{D}\vec{g}_i}, \ i = 1, ..., N$$
 (5)

where  $S_i$  stands for the DWI acquired by means of the pulse gradient in the direction given by the unitary vector  $\vec{g}_i$ ,  $S_0$ represents the baseline image, and *b* is a parameter related to the sequence applied to measure the diffusion. Since **D** is described by a symmetric  $3 \times 3$  matrix, six matrix components must be computed, so at least six different DWI are required.

The intensity value of  $S_i$  is related to the quantity of diffusion in the direction given by  $\vec{g_i}$ . This vector is defined by its coordinates with respect to a reference framework. If this framework changes, due, for instance, to a geometric transformation, the vector should be expressed with respect to the new framework. Next, we show how the gradient directions should be changed to correctly estimate the tensors from the transformed DWIs. For the sake of simplicity, we firstly analyze the case of a rigid rotation, and then the effect of higher degree of freedom transformations.

### 4.2 Rotation

Let suppose that the coordinate system in which the images (both DWIs,  $S_i$ , and baselines) are defined is changed by a rotation matrix **R**. The tensor should be therefore estimated from the set of rotated images. To correctly estimate the tensor components, the gradients in Eq. (5) must be expressed in the same reference framework than the diffusion images.

The value of intensity at the voxels of the transformed images,  $S_{R_i}$  is related with the diffusion in the direction given by the gradients in the new reference frame, that are computed as  $\vec{h_i} = \mathbf{R}\vec{g_i}$ . Thus, it is possible to find the relationship between the tensors  $\mathbf{D_x}$  computed from the original dataset, and  $\mathbf{D'_{x'}}$  computed in the rotated domain. Let us consider a voxel  $\vec{x}$ , whose original intensity values are  $S_i(\vec{x}), i = 0, ..., N$ , where N is the number of acquired diffusion images. After rotation, these values will be located at a position  $\vec{x'} = \mathbf{R}\vec{x}$ , that is,  $S_{R_i}(\vec{x'}) = S_i(\vec{x})$ . To compute the DT at  $\vec{x'}$ , we evaluate Eq. (5) in  $\vec{x'}$  and substitute the original gradient by  $\vec{h_i}$ :

$$S_{R_i}(\vec{x}') = S_{R_0}(\vec{x}')e^{-b\vec{h_i}'\,\mathbf{D}'_{\mathbf{x}'}\vec{h_i}}$$
(6)

$$S_{R_i}(\vec{x'}) = S_{R_0}(\vec{x'})e^{-b\vec{g}_i^T R^T \mathbf{D'}_{\mathbf{x'}}R\vec{g}_i}$$
(7)

On the other hand, the tensor computed in the original domain at  $\vec{x}$  is obtained by evaluating Eq. (5) at this point:

$$S_i(\vec{x}) = S_0(\vec{x})e^{-b\vec{g}_i^T \mathbf{D}_{\mathbf{x}}\vec{g}_i}$$
(8)

Since  $S_{R_i}(\vec{x'}) = S_i(\vec{x})$ , the right terms in both previous equations can be equated. Simplifying the common terms in the resulting equation, and taking logarithms, the relation between the DT at the position  $\vec{x}$  in the original image, and the warped tensor at the transformed location  $\vec{x'}$  is obtained:

$$\mathbf{R}^T \mathbf{D}'_{\mathbf{x}'} \mathbf{R} = \mathbf{D}_{\mathbf{x}} \tag{9}$$

$$\mathbf{D}_{\mathbf{x}'}' = \mathbf{R} \mathbf{D}_{\mathbf{x}} \mathbf{R}^T \tag{10}$$

Therefore, after applying a rotation to the image, the same rotation should be applied to the tensors, in order to preserve the information provided by the images. This agrees with the intuitive approach previously mentioned.

#### 4.3 Elastic Transformations

If a more complex transformation has been applied to the image, the change in the gradient direction will be different at each voxel, depending on the local deformation  $\mathbf{J}(\vec{x})$ . If this matrix is applied to the unitary gradient vector  $\vec{g}_i$ , we will obtain a vector  $\vec{h}_i = \mathbf{J}\vec{g}_i$ . Let note that, if  $\mathbf{J}$  is not an orthonormal matrix,  $\vec{h}_i$  is not unitary. For this reason, normalization is required in order to obtain the unitary vector in the transformed gradient direction, that would be given by:

$$\vec{h}_i(x) = \frac{\mathbf{J}(x)\vec{g}_i}{||\mathbf{J}(x)\vec{g}_i||}, i = 1, ..., N,$$
(11)

where N is the number of gradients. Note that, due to the shear effect that may appear in the deformation, the orientation of  $\vec{h}_i$  depends on the original direction  $\vec{g}_i$ . For this reason, it is not possible to obtain a unique rotation matrix for

every gradient, but a different rotation is applied to each of them. According to the polar decomposition theorem, every non-singular matrix can be decomposed into a rigid rotation  $\mathbf{R}$  and a strain component  $\mathbf{U}$ . The reorientation effect of the pure rotation matrix is independent of the original vector direction, but the rotational effect of the strain component depends on the original gradient direction. Therefore, to obtain an expression similar to Eq. (9) the strain component should be ignored so only the rigid rotation component would be applied. This will lead directly to the definition of the FS previously described. That is, the FS method simplifies the real warping by discarding the deformation component.

Eq. (11) shows that the non rigid transformation causes a warping of the tensor that is more complex than rotation. Therefore, the assumption that only allows tensor rotations is a simplification of the real case, and the proposed algorithms for tensor reorientation do not represent the real tensor warping, since they do not allow changes of shape or size. Thus, to correctly warp the tensors, the DWI should be warped and then the tensor should be recomputed with the reoriented gradient directions. We denote such method as gradient warping (GW). However, this procedure may be costly, and some problems may appear if transformation with a high deformation component is applied to the gradients. To estimate the tensor, it is advisable that gradient directions were equally distributed in the space. However, since a different rotation is applied to every gradient, the resulting gradients may be separated by a small angle, what may lead to problems in tensor estimation, such as negative tensor eigenvalues, what is not realistic. As show in Section 5, this problem may be negligible in real registration problems, since transformations are smooth enough. Nevertheless this problem involves that a general method cannot be described without taking into account the conditions required to correctly estimate the tensor. Moreover, this method may be computationally costly and for this reason, it can be simplified to perform in registration algorithms. Next we show that such simplifications will lead to the known reorientation strategies.

### 4.4 DT Warping Simplifications

In previous subsection, it was deduced that a closed expression for tensor warping can be obtained from the Stejskal-Tanner equation to describe the effect on tensors of image rigid rotation. However, this expression cannot be obtained if other kind of transformations are applied, unless their deformation component is ignored, which lead to the definition of the FS strategy, as shown in Subsection 4.3.

This can also be analyzed as a Procrustean problem. To preserve the norm of the transformed vectors, the matrix that multiply them must be orthonormal. The search for the orthonormal matrix that better approach a given matrix  $\mathbf{J}$  is a Procrustean problem, whose solution is given by  $\mathbf{R} = \mathbf{U}\mathbf{V}^T$ , where U and V are the matrices obtained by SVD of  $\mathbf{J}$ , what coincides with the computation of the rotation matrix described in [4], that is itself equivalent to the FS approach.

Therefore, FS is a simplification that ignores the rotational effect due to the strain component of the transformation. The PPD strategy [1] was proposed to consider the reorientation due to this component, that depends on the original orientation of the data. Again, it is a simplification of the real warping, since it only allows tensor rotations. It approximates better the shear effect, but it still ignores the possible

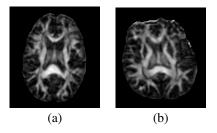


Figure 4: (a) Target image and (b) Source image between which registration is performed.

changes in shape and size that can appear. The simplifications that lead to this method are detailed just below.

As aforementioned, a problem appears if high shears are applied to DTs, because it may lead to undesired situations where gradients are not separated enough to obtain realistic DT. To avoid it, the angle among gradients should be preserved, which means that the same rotation should be applied to every gradient. Note that it is a simplification to avoid problems in DT estimation. Since shear involves a rotation that depends on the original direction, if only a rotation is chosen, it should rotate correctly unless the most meaningful diffusion direction. In the domain of DWIs, the most important direction is the one in which  $S_i$  is minimum and the diffusion is maximum. However, more information may be obtained from DT because it integrates the information of the DWIs and describes diffusion in every direction. Thus, diffusion is maximum along the direction given by the main eigenvector,  $\vec{e_1}$  and therefore, shear should be applied to this direction. To include the shear in other directions, another rotation matrix could be computed, as long as it did not affect the already rotated main eigenvector,  $\vec{e_1}'$  and reorient the second eigenvector  $\vec{e_2}$  in the direction that better approaches the direction  $\vec{e_2}'$  resulting of the application of J. Such direction is given by the projection of the  $\vec{e_2}'$  on the plane orthogonal to  $\vec{e_1}'$ . If this were applied over the gradients, it could be applied only to orthogonal directions, since in other case it would not be possible to find a rotation matrix that does not change the rotated gradient corresponding to the minimum  $S_i$  preserving the angle between gradients. For this reason, it is simpler to compute the rotation over the DT instead of the gradients, what lead to the definition of the PPD algorithm.

#### 5. EXPERIMENTS

As shown in previous sections, the FS and PPD strategies for tensor reorientation are simplifications of the warping that should be applied to the tensors. Now, the effect of such simplifications in the performance of registration is analyzed, as well as, the feasibility of the use of GW in a real case.

To avoid assumptions about tensor warping model, synthetic data have not been considered, since the transformation of the tensors should be described according to a theoretical model, what could bias the conclusions. Therefore, real data acquired by a GE 1.5T scanner, with 15 diffusing directions and b = 1000 have been used in the experiments. Volumes where the brain orientation is noticeably different, as shown in Fig. 4 have been chosen to better analyze the effect of warping after registration.

Registration is carried out by a block matching algo-

rithm based on the correlation coefficient between fractional anisotropy (FA), that is a measure of the diffusion anisotropy computed from the DT eigenvalues. The displacement field is interpolated by B-Splines, so the Jacobian can be analitically computed. Hence, the same transformation is considered by each of the warping methods, so the differences between the registered images are only due to such algorithms.

Note that registration usually aim to obtain a smooth transformation in order to preserve the image topology. Thus, it is usual to include smoothing filters in the algorithms to improve the registration results. Since the reorientation depends on the Jacobian of such transformation, that is smaller as the transformation is getting smoother, the effect of warping with respect to certain smoothing parameter is analyzed. For instance, let suppose that the final transformation is smoothed by a Gaussian filter described by its variance  $\sigma$ . The angle between the major eigenvectors of the tensors in the target images and the registered images with different  $\sigma$  values is computed. Such angles are averaged in regions where the linear coefficient<sup>2</sup> is higher than 0.4, that is, molecules diffuses mostly along the direction described by the major eigenvector. The threshold is chosen to consider the areas where fiber tracts are, where the diffusion direction is more significant. In Table 1 is shown the improvement in the angle matching achieved by using warping strategies. This improvement is measured as the difference (in radians) between the average angle computed for the registration without tensor warping and the average angle computed for each of the three warping strategies.

σ	1	5	10
FS	0.0106	0.0082	0.0062
PPD	0.0020	0.0019	0.0013
GW	0.0106	0.0084	0.0093

Table 1: Improvement in the average angle between target and registered major eigenvectors due to warping methods.

Thus, improvement in the angle between eigenvectors is less noticeable as transformation is smoother (higher  $\sigma$ ). However, realistic transformations usually are required to be smooth, and in such cases the improvement obtained by warping tensors is less significant. In any case, the difference between reorientation strategies is small, what is hard to perceive visually and has little effects in applications such as fiber tracking, that are based on the major eigenvector to track the fiber trajectory. This small difference was also pointed in the experiments with real data compiled in [3].

On the other hand, the applicability of the GW has been analyzed. As shown in Table 1 the results achieved with this method are better than with FS or PPD, although the difference is very small. Regarding the problem related to the loss of uniformity in the distribution of the gradient direction, the performed experiments have shown that tensors with negative eigenvalues only appear in a negligible percentage of voxels, namely from 0.002% to 0.004% of the voxels, as  $\sigma$  value decreases. Thus, GW can be applied in real cases where transformations are smooth enough. Nevertheless, the improvement in the alignment is so small that FS or PPD simplifications can be used instead, without a very significant loss of performance.

## 6. CONCLUSIONS

The need of warping tensors has been reported since registration was applied to DTI. However, a rigorous analysis of such requirement has not been made, and the strategies have been grounded in an uncertain argument that said that tensor represents microstructural properties of the tissue. In this paper we have shown that this assessment is not true, and we have deduced how tensors should be warped from the basis of the Stejskal-Tanner equation that relates the diffusion tensor with the acquisition parameters. However, it is shown that such theoretical warping could not be used in general, because the warped DWIs and gradients could not correspond to real physical situations. Empirically, we have shown that this problem is negligible if the transformation is smooth enough and results are similar to the results obtained by means of FS or PPD, that are simplifications of the GW.

Warping methods have been compared for a real case of DTI registration, and it has been shown that results achieved with these methods are similar because of two reasons: first, the real data are usually acquired with little orientation differences, and second, the registration usually searches for smooth transformations, so the local deformation at every voxel is small and the resulting warping is also small. In some cases, it could be suitable to estimate a global rigid rotation to align the data and use the local deformation to refine the results. These results encourage us to a thorough analysis of tensor warping for different real cases to conclude how the local deformation refinement improves the result of the matching.

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<sup>&</sup>lt;sup>2</sup>Linear coefficient is defined as  $\frac{\lambda_1 - \lambda_2}{\lambda_1}$ , where  $\lambda_i$  are the ordered tensor eigenvalues, and measures the linearity of the diffusion.