ADC-Weighted Joint Registration-Estimation for Cardiac Diffusion Magnetic Resonance Imaging

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Abstract

The purpose of this work is to develop a method for the groupwise registration of diffusion weighted datasets of the heart which automatically provide smooth Apparent Diffusion Coefficient (ADC) estimations, by making use of a novel multimodal scheme. To this end, we have introduced a joint methodology that simultaneously performs both the alignment of the images and the ADC estimation. In order to promote diffeomorphic transformations and to avoid undesirable noise amplification, we have included appropriate smoothness constraints for both problems under the same formulation. The implemented multimodal registration metric incorporates the ADC estimation residuals, which are inversely weighted with the b-*values to balance the influence of the signal level for each diffusion weighted image. Results show that the joint formulation provides more robust and precise ADC estimations and a significant improvement in the overlap of the contour of manual delineations along the different* b-*values. The proposed algorithm is able to effectively deal with the presence of both physiological motion and inherent contrast variability for the different* b-*value images, increasing accuracy and robustness of the estimation of diffusion parameters for cardiac imaging.*

1 Introduction

Diffusion weighted imaging (DWI) is an imaging technique sensitive to water molecule displacement allowing to measure micro-structure density and membrane tortuosity within the tissue. DWI is increasingly employed in clinical practice as it is a relatively quick non-contrast technique that provides quantitative markers, such as the well-known apparent diffusion coefficient (ADC), showing usefulness in early diagnosis of cardiovascular accidents due to its ability to detect early signs of ischemia [1]. ADC has been shown to be a positive indicator of tumor response [2] due to its ability to measure displacement of water molecules, giving evidence about cellular organization and permeability in the tissue [3].

Nonetheless, in most cases, a previous registration step is performed in order to obtain proper ADC estimations, since images are acquired in different apneas. However, this is not an easy task since a signal intensity dropout is observed when increasing the intensity of the diffusion gradient (hereinafter referred to as *b*-value), leading to images with very different signal to noise ratios (SNR). This phenomenon, associated to the very nature of the DWI acquisition process, is illustrated in Fig. 1.

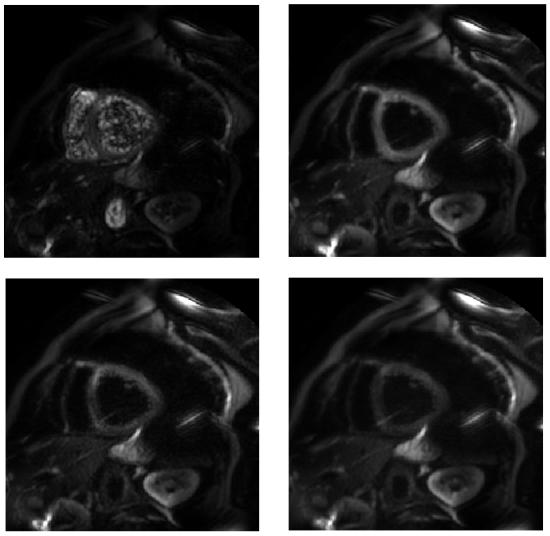

Figure 1. *Axial slices of DWI acquisition in a healthy patient for* b-*values of 0, 50, 150 and 300* s/mm^2 *(from upper left to bottom right).*

Physiological motion is the most dominant confounding factor, specially in cardiac imaging. Breath-hold acquisitions are a popular way of avoiding motion artifacts. However, when different images are acquired at different breath-holds and, later, used for ADC estimation, considerable artifacts can arise [4] that stem from the fact that two inspiration levels are never identical. Therefore, the aforementioned registration step is mandatory in order to relate anatomical relevant information from multiparametric acquisitions.

Image registration, to put it short, is concerned with the search of an optimal transformation for the alignment of at least two images. It has many applications in imaging, such as fusion of image information [5], material point tracking [6] or atlas construction [7]. As for the groupwise registration problem, it may be posed as finding a spatial transformation so that every point in each image is matched to a point in a reference image that is built out of the whole image set to be registered.

The cost function (metric) associated to the registration problem is usually designed to measure the image similarity/dissimilarity within the dataset. Examples of common voxel-based metrics are cross correlation [8], mutual information [9] or sum of squared differences, which have proven useful for different image alignment problems.

Different methodologies for multiparametric registration towards robust ADC estimation have been designed for distortion correction [10] and motion compensation [11], but from a pairwise standpoint. Groupwise approaches have also been addressed in [12]. However, none of them consider explicitly the diffusion process. For these reasons, we hypothesize that a registration metric that takes into account the parameters to be estimated, as proposed in [13, 14], will help diminish the impact of motion artifacts as well as robustify the subsequent ADC estimation.

Therefore, we propose a joint formulation that solves simultaneously the estimation and the registration problems. We aim at finding the optimal transformation over the cardiac DWI dataset which leads to optimal ADC estimates. We have incorporated within the registration metric some weighting parameters that balance the influence of the different images on the registration process according to the DW signal content.

2 Materials and Methods

2.1 Materials

For the validation of the proposed approach, a synthetic experiment has been carried out using a simulation environment based on the 4D digital extended cardio-torso (XCAT) phantom [15]. The phantom consists of a whole body model that contains high level detailed anatomical labels, which feed a high resolution image synthesis procedure. The 4D XCAT phantom incorporates state of the art respiratory and cardiac mechanics, which provide sufficient flexibility to simulate cardio-torso motion from user-defined parameters. Therefore, the phantom provides us not only with the images themselves, but also with a ground-truth displacement field. Diffusion processes are simulated as the molecular displacement, often referred to as Brownian motion. For restricted diffusion, the resulting motion can be modeled as a random walk process [16], where motion presents a non-Gaussian distribution with lower apparent diffusion. Common approaches assume a monoexponential decay in the DW signal [17].

Additionally, we have performed MRI acquisitions over a healthy volunteer. An axial SENSitivity Encoding (SENSE) DWI sequence has been acquired on a Philips Achieva 3T scanner on free breathing conditions. Cardiac gating has also been activated during the acquisition. The following subset of b-values (N_b=4) has been acquired: $b \in \{0, 50, 150, 300\} s/mm^2$. Acquisition and resolution details for these experiments are shown in Table 1.

Parameters	XCAT	DW-MRI
Δ_p	1	1.1719
Δ_l	1	8
N_p	192	256
N_s	70	11
T_R	8000	1052.6
T_E	93	51.74
N_g	1	3

Table 1. *Details on the image sequences used in the paper. Δ_p : Spatial Resolution (mm). Δ_l : Slice Thickness (mm). N_p: Number of pixels along each direction. N_s: Number of slices. T_R : Repetition Time (ms). T_E: Echo Time (ms). N_s: Number of diffusion gradients.*

2.2 Methods

The proposed method has been applied to the groupwise registration of two-dimensional cardiac DWI acquisitions and, specifically, for robust ADC estimation. Bearing in mind this application, local transformation τ has been represented as a combination of B-spline FFDs [18].

Therefore, we intend to find optimal alignment of DWI dataset $\mathbf{S}$ by solving the following joint registration-estimation problem:

$$[\widehat{\text{ADC}}, \widehat{\tau}] = \underset{\text{ADC},\tau}{\operatorname{argmin}} \int_{\chi} H(\mathbf{S}, \text{ADC}, \tau)) + \beta ||\text{ADC}||_{TV} + \lambda Reg(\tau) d\mathbf{x}, \quad (1)$$

where $Reg(\tau(\mathbf{x}))$ is a penalty term which favors the transformation τ to be invertible [19] and $||\text{ADC}(\mathbf{x})||_{TV}$ represents the spatial total variation regularization term as defined in [20]. The total variation term has been introduced so that it contributes to noise removal in the final estimated ADC map dealing with the inhomogeneities derived from the inherent low SNR of each b-value image [21]. The influence of these two regularization terms is balanced by trade-off parameters λ and β, respectively, which have been set empirically.

As for the metric H, our proposal aims at directly minimizing the residuals in the ADC estimation, so it is defined as:

$$H(\mathbf{S}, \text{ADC}, \tau) = \sum_{j=1}^{N_b} W_j^i (S_j(\tau(\mathbf{x})) - \widehat{S_j}(\text{ADC}^i(\mathbf{x})))^2, \quad (2)$$

where S_j represents the acquired image and $\widehat{S_j} = S_0 \exp(-b_j \text{ADC}^i)$ for the current (i-th iteration) ADC estimate. S_0 is the image with no diffusion gradient applied.

The proposed metric extends the one presented in [13] by adding proper weighting parameters related to the underlying noise distribution of the magnitude images as a trade-off between the different b-values. Those weights, initially unitary, are redefined along iterations with the predicted DW signals (see [22]) as follows:

$$W_j^i = \exp(-2 b_j \mu(\widehat{\text{ADC}^i}), \quad (3)$$

where $\mu(ADC)$ represents the median of the current ADC distribution in the myocardium.

We will solve Eq. (1) by sequentially solving the estimation and registration problems separately, via *ceteris-*

paribus analysis. Hence, we iteratively alternate between estimating model parameters and the optimal transformation until convergence is reached both in transformation τ and metric H. First, the diffusion parameters are estimated by means of the NESTA algorithm [20] as described:

$$\widehat{\text{ADC}} = \underset{\text{ADC}}{\text{argmin}} \int_{\chi} [H(\mathbf{S}, \text{ADC}, \tau) + \beta ||\text{ADC}(\mathbf{x})||_{TV}] \, d\mathbf{x}. \tag{4}$$

As stated before, the measured images are not spatially aligned and therefore the ADC map cannot be directly computed. Therefore, we have introduced a groupwise registration framework using the registration metric defined in Eq. (2). To constraint the transformation τ to be locally invertible, we have resorted to a simple quadratic regularization scheme described in [19]. A gradient-descent optimization scheme has been employed [23] to solve the registration problem posed in Eq. (5) as:

$$\widehat{\tau} = \underset{\tau}{\text{argmin}} \int_{\chi} H(\mathbf{S}, \text{ADC}, \tau) + \frac{\lambda}{2} \sum_{l=1}^{L} \sum_{j=1}^{N_b} \sum_{m,n} [\\ (\tau^l_{m+1,n,j} - \tau^l_{m,n,j})^2 + (\tau^l_{m,n+1,j} - \tau^l_{m,n,j})^2] d\mathbf{x}, \tag{5}$$

where $\tau^l_{m,n,j}$ represents each of the (displacements) components of the transformation ($L = 2$ for the 2D case).

3 Results

In this section, we test robustness and accuracy of our joint formulation in comparison with other methodologies in the literature. Demons [24] pairwise registration algorithm has been implemented using a mutual information based metric. As for groupwise approaches, apart from our Joint scheme, we have tried Entropy of the Distribution of Intensities [25], Normalized Cross-Correlation [8] and Sum of Squared Differences metrics.

With the data provided by the XCAT phantom and for each method mentioned above we have measured the overlap degree —using the Dice coefficient [26]— between the myocardial contours for each *b*-value and cardiac phase with those at the diastolic instant of the S_0 image.

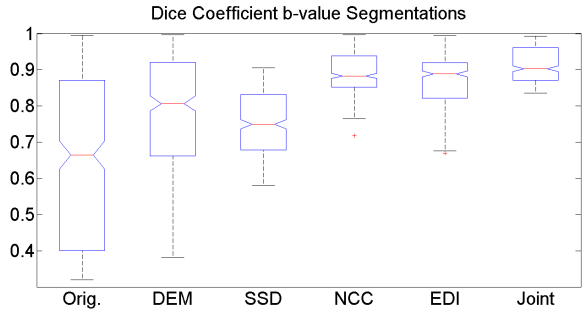

Figure 2. *Boxplot diagrams of Dice Coefficient distributions between segmentations in different* b*-values.*

In Figure 2 we show the boxplot diagrams of the Dice coefficient obtained from the aforementioned registration methods and our joint formulation proposal. The joint formulation shows a considerable improvement in terms of overlapping compared with the other two methods. Mann-Whitney U-tests have been performed on the Dice coefficient distributions, finding significant improvement when introducing any registration step when compared to the non-registered sequence ($p < 10^{-6}$) for all methodologies. The joint formulation presents also significant improvement both over the pairwise (DEM) and monomodal (SSD) approaches ($p < 10^{-6}$ for both). These results conclusively support the hypothesis that the joint formulation is a better option than sole groupwise multimodal registration schemes ($p < 10^{-3}$ for both EDI and NCC metrics).

In addition, for the real data we have tested the performance of the aforementioned procedures for the estimation of diffusion parameters. In this experiment, we have measured the mean, variance and coefficient of variation ($CV = std/mean$) of ADC estimates obtained inside the myocardium for each method (see Table 2).

$Method$	$Mean(mm^2/s)$	$Variance$	$CV\%$
$Orig.$	$1.4863 \cdot 10^{-3}$	$2.5517 \cdot 10^{-7}$	33.99
DEM	$1.4264 \cdot 10^{-3}$	$2.7957 \cdot 10^{-7}$	37.06
SSD	$1.2088 \cdot 10^{-3}$	$4.2366 \cdot 10^{-7}$	53.84
NCC	$1.5348 \cdot 10^{-3}$	$2.5435 \cdot 10^{-7}$	32.86
EDI	$1.5490 \cdot 10^{-3}$	$2.5530 \cdot 10^{-7}$	32.62
$Joint$	$1.7091 \cdot 10^{-3}$	$1.7380 \cdot 10^{-7}$	24.39

Table 2. *Mean, variance and CV of ADC estimates over the myocardium of a healthy patient.*

As indicated in the table, the CV of the estimated ADC parameters obtained with the joint formulation is significantly lower compared to other methodologies, specially to the monomodal approach. Besides, robustness of ADC estimates was increased and bias in estimation seems greatly diminished, leading to more accurate measures.

Finally, visual inspection of a registered DWI sequence reveals that our approach is able to preserve structure while reducing artifact impact, as it can be seen in Fig. 3. Therefore, boundaries will be more clearly identified (as well as tissue heterogeneity or anatomical structure), leading to reconstructed ADC maps with higher quality.

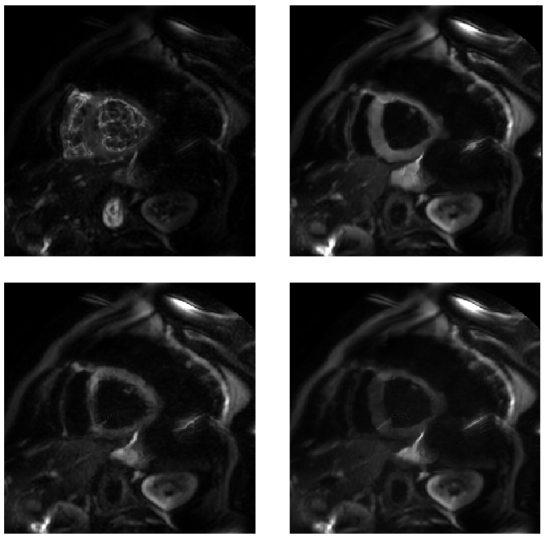

Figure 3. *Axial slices of registered DWI sequence for* b*-values of 0, 50, 150 and 300* s/mm^2 *(from upper left to bottom right).*

4 Conclusions and Future Work

We have presented an image processing methodology for the simultaneous ADC estimation and non-rigid registration of cardiac DWI with a novel multimodal metric that weights each *b*-value by the residuals derived from the estimation. This methodology, under the groupwise paradigm, has proven to be reliable for missalignment correction and robust in the estimation of diffusion parameters, being able to provide high-quality denoised ADC maps of the heart.

Results have shown that a joint formulation approach is effective in correcting the characteristic boundary smearing of cardiac DW datasets, increasing SNR on the images while preserving myocardial anatomical structure.

5 Acknowledgments

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