Comparison of Cardiac Motion Across Subjects Using Non-rigid Registration

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Abstract. We present a novel technique that enables a direct quantitative comparison of cardiac motion derived from 4D MR image sequences to be made either within or across patients. This is achieved by registering the images that describe the anatomy of both subjects and then using the computed transformation to map the motion fields of each subject into the same coordinate system. The motion fields are calculated by registering each of the frames in a sequence of tagged short-axis MRI images to the end-diastolic frame using a non-rigid registration technique based on multi-level free-form deformations. The end-diastolic untagged short-axis images acquired shortly after the tagged images were obtained are registered using non-rigid registration to determine an inter-subject mapping, which is used to transform the motion fields of one of the subjects into the coordinate system of the other, which is thus our reference coordinate system. The results show the transformed myocardial motion fields of a series of volunteers, and clearly demonstrate the potential of the proposed technique.

1 Introduction

Despite the advent of increasingly sophisticated cardiac imaging and surgery techniques, cardiovascular disease remains the leading cause of death in the western world [1]. It most frequently appears as coronary heart disease, in which an atherosclerosis of the coronary arteries reduces the oxygen supply to the muscles of the heart, causing them to become ischemic. This leads to a loss of function of the heart and a reduced contractility. Tagged MRI imaging [2,3] provides a means to investigate the deformations that the heart undergoes through the cardiac cycle, and is thus a potential tool for coronary heart disease diagnosis. It relies on the perturbation of magnetisation in the myocardium in a specified spatial pattern at end-diastole. These appear as dark stripes or grids when imaged immediately after the application of the tag pattern, and, since the myocardial tissue retains this perturbation, the dark stripes or grids deform with the heart as it contracts, allowing local deformation parameters to be estimated.

Many of the techniques for the analysis of tagged MR images are based on deformable models [4,5,6,7,8,9] or optical flow [10,11]. More recently, Chandrashekar et al. [12] described a fully automated method for tracking the cardiac motion in a sequence of tagged MRI images using non-rigid registration. In this algorithm, a sequence of free-form deformations is used to represent myocardial motion and the motion field is extracted by maximising the mutual information between images in the cine sequence.

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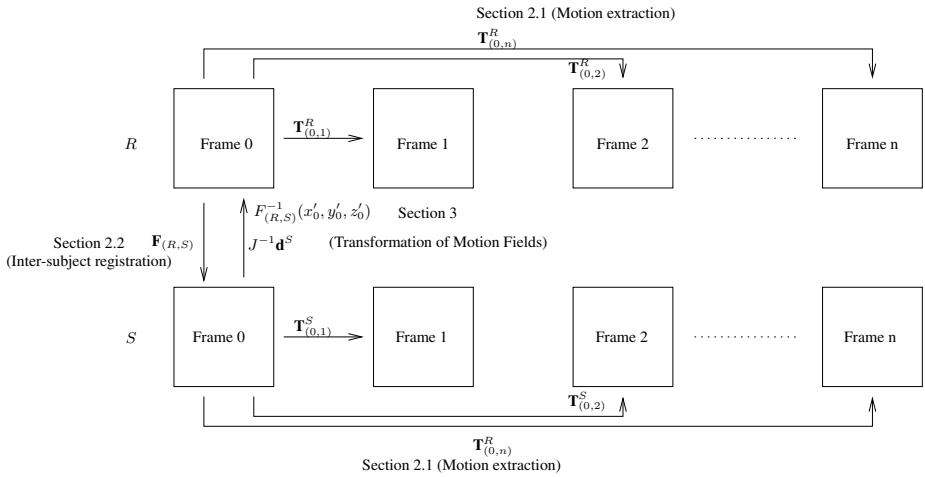


Fig. 1. Overview of proposed technique for mapping cardiac motion between subjects

The result of this algorithm is a set of motion fields for each time frame relative to an end-diastolic reference image. It would be extremely useful if we could compare the motion fields of two different image sequences obtained using this technique. There are two principal reasons for this: Firstly it would enable us to compare the motion fields of a single subject obtained at different times. This would, for example, facilitate an assessment of the cardiac function of a subject before and after undergoing pharmacological or surgical interventions. Secondly, it would enable a comparison to be made of the cardiac function of two different subjects. Unfortunately, we cannot make our comparison of the two sets of motion fields as they stand, because they are defined with respect to the coordinate systems of the end-diastolic images used to calculate them, which in general will be different.

In this paper we present a novel technique to map the myocardial motion fields that describe the cardiac motion of a subject S into the coordinate system of a reference subject R to facilitate comparisons between the cardiac function of each of the subjects. The original (unmapped) myocardial motion fields are calculated using both short-axis and long-axis tagged MRI sequences as described by [12], while the corresponding untagged MRI sequences are used to determine the mapping of anatomical information between subjects. This inter-subject transformation facilitates the final mapping of myocardial motion fields into the reference coordinate system. An overview of the various operations required by our method along with the section in which their calculation is described, is given in Figure 1.

In the next section we explain the non-rigid registration algorithm we used to determine the original myocardial motion fields and calculate the inter-subject mapping. We go on to describe in detail each of the stages of our technique, before showing results with four subjects in section 4.

2 Non-rigid Registration

Image registration entails the determination of a transformation that maps points within one image to their corresponding points in another image. For our purposes we will

require the mappings between corresponding points at different time frames of a sequence of MR images taken of a single subject, as well as the mappings between corresponding points of two MR images of different subjects. We model the transformations using the non-rigid registration technique of Rueckert et al. [13]. This algorithm expresses the required transformation as the sum of a global and local component:

$$\mathbf{T}(x, y, z) = \mathbf{T}_{global}(x, y, z) + \mathbf{T}_{local}(x, y, z)$$

$\mathbf{T}_{global}$ is modelled by an affine transformation that incorporates scaling, shearing, rotation and translation. $\mathbf{T}_{local}$, the local deformations, are modelled using a free-form deformation (FFD) model based on B-splines that manipulates an underlying mesh of control points ϕ, thus changing the shape of the object. The resulting deformation can be expressed as the 3D tensor product of the standard 1D cubic B splines

$$\mathbf{T}_{local}(x, y, z) = \sum_{l=0}^{3} \sum_{m=0}^{3} \sum_{n=0}^{3} B_l(u) B_m(v) B_n(w) \phi_{i+1,j+m,k+n}$$

where B_l denotes the l-th B-spline basis function. In our algorithm the optimal transformation **T** is found by maximising a voxel-based similarity measure, normalised mutual information [14], which measures the degree of alignment between images. The normalised mutual information of two images A and B is defined as

$$I(A, B) = \frac{H(A) + H(B)}{H(A, B)}$$

where $H(A)$,$H(B)$ are the marginal entropies of images A and B, and $H(A, B)$ denotes the joint entropy of the combined images A, B. We are using normalised mutual information as a similarity measure because it only measures the statistical dependencies between the intensity distributions in both images and therefore can be used in tagged MR images where the image intensities can change as a result of tag fading.

2.1 Motion Modelling from Tagged MR Using Non-rigid Registration

The first step in our process requires the calculation of the myocardial motion fields for the subject S that we will later map into the coordinate system of R, the reference subject. To facilitate this we must first choose an image in our tagged image sequence S_i, $i = 0, ..., n$, to be our temporal reference point, i.e. the one in whose coordinate system all calculated motion fields of S will be expressed and will be relative to. We choose the end-diastolic image S_0 to be this reference because cardiac motion is minimal at this time, and we denote its coordinate system as the triple (x', y', z'). Similarly, we define the end-diastolic image of subject R, R_0, to be the analogous reference point for this subject, denoting its coordinate system as (x, y, z). This makes (x, y, z) the coordinate system to which we ultimately would like to map the myocardial motion fields of S.

To calculate the myocardial motion fields we are using an extension of the free-form deformation (FFD) model described in the previous section. In this extension a number of single-level FFDs are combined in a multi-level FFD framework [15]. This approach has been previously applied successfully for myocardial motion tracking in tagged MR images [12]. The estimation of the motion field proceeds in a sequence of registration

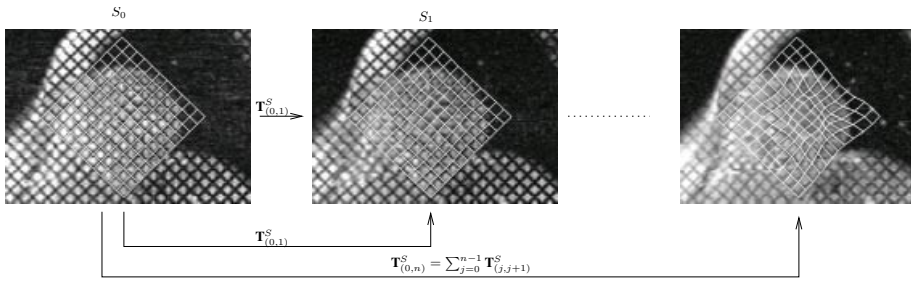


Fig. 2. Extraction of cardiac motion parameters for Subject S: A virtual tag grid which has been aligned with the tag pattern at time $t = 0$ is overlaid on different time frames of the tagged MR sequence to illustrate the tag tracking with non-rigid registration. As time progresses the virtual tag grid is deformed by the MFFD and follows the underlying tag pattern in the images. An animated colour version of this figure can be found at
`http://www.doc.ic.ac.uk/~dr/projects/animations/MICCAI02`.

steps as shown in Figure 1: After registering the image S_1 to S_0 we obtain a multi-level FFD (MFFD) consisting of a single FFD representing the motion of the myocardium at time $t = 1$. To register volume S_2 to S_0 a second level is added to the sequence of FFDs and then optimised to yield the transformation at time $t = 2$. This process continues until all the volumes in the sequence are registered, allowing us to relate any point in the myocardium at time $t = 0$ to its corresponding point throughout the sequence. The transformation between the end-diastolic time frame S_0 and the image S_i at time frame $t = i$ is then given by:

$$\mathbf{T}^S_{(0,i)}(x', y', z') = \sum_{j=0}^{i-1} \mathbf{T}^S_{(j,j+1)}(x', y', z')$$

Figure 2 shows the short axis tagged images of a subject taken at different time frames overlayed with a virtual grid which has been aligned with the tag pattern of the end-diastolic frame. As time progresses, the virtual tag grid is deformed by the calculated MFFD and is seen to follow the underlying tag pattern in the images. This demonstrates the success of the tracking algorithm used.

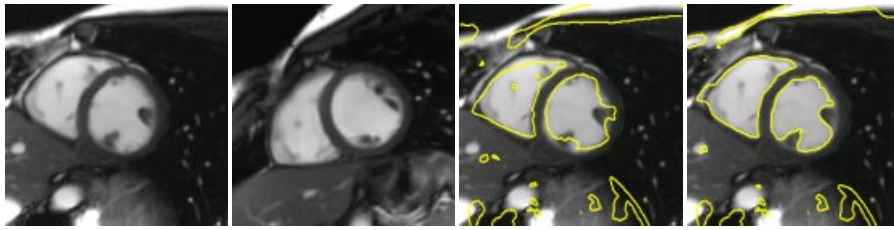
The actual myocardial motion fields $\mathbf{D}^S_{(0,i)}(x', y', z')$ that we require are given by

$$\mathbf{D}^S_{(0,i)}(x', y', z') = \mathbf{T}^S_{(0,i)}(x', y', z') - (x', y', z')$$

Using the same approach we can calculate the myocardial motion fields $\mathbf{D}^R_{(0,i)}(x, y, z)$ for subject R.

2.2 Non-rigid Registration of Untagged MR between Subjects

We now need to calculate a mapping between the end-diastolic MR images of subject and reference, S_0 and R_0, so that we can map the myocardial motion fields $\mathbf{D}^S_{(0,i)}$ into the coordinate system of R , (x, y, z). Since the untagged images are obtained shortly after the tagged images, the end-diastolic untagged frames of each subject are already aligned with the end-diastolic tagged frames of each subject that were used to define the



(a) (b) (c) (d)

Fig. 3. This figure illustrates the short axis views of a reference end-diastolic image (a), a subject end-diastolic image (b), the subject image after global registration (c), and non-rigid registration (d)

co-ordinate systems of R and S. This means that we can use the end-diastolic untagged images of each subject to calculate the inter-subject co-ordinate system mapping. The transformation between subjects R and S is determined using the non-rigid registration algorithm described in the introduction of section 2, giving a mapping $\mathbf{F}_{(R,S)}$ between coordinate systems (x, y, z) and (x', y', z'):

$$\mathbf{F}_{(R,S)} : (x, y, z) \longmapsto (x'(x, y, z), y'(x, y, z), z'(x, y, z))$$

In this case there will be a non-zero global component as we are registering between subjects. Note that here the registration algorithm is being used to calculate a transformation of co-ordinates of the reference anatomy that aligns it with the subject anatomy, in contrast to its use in section 2.1 where it was used to calculate the motion of the heart in a fixed co-ordinate system.

Figure 3 shows the short-axis end-diastolic image of a reference subject (a), and of a second subject (b). In Figure 3(c) we see the overlayed anatomy contours of the second subject on the reference subject anatomy if we register the images using only the affine global component, while figure 3(d) shows the contours if we include the local deformations in the registration. It is clear that the anatomies are much better aligned when we include local deformations in our registration.

3 Transformation of Myocardial Motion Fields

We are now in a position to transform the motion fields $\mathbf{D}^S_{(0,i)}(x', y', z')\ i = 1, ...n$ into the coordinate system of R, (x, y, z). If the motion vector at a point P with positional coordinate (x'_0, y'_0, z'_0) in the coordinate system of S is equal to $\mathbf{d}^S$, this transforms to the vector $\tilde{\mathbf{d}}^S$ at the location (x_0, y_0, z_0) in the coordinate system of R, where

$$(x_0, y_0, z_0) = \mathbf{F}^{-1}_{(R,S)}(x'_0, y'_0, z'_0) \quad \text{and} \quad \tilde{\mathbf{d}}^S = J^{-1}\mathbf{d}^S$$

Here, J is the Jacobian matrix of the transformation $\mathbf{F}_{(R,S)}$ evaluated at P:

$$J = \left[\begin{array}{ccc} \frac{\partial x'(x,y,z)}{\partial x} & \frac{\partial x'(x,y,z)}{\partial y} & \frac{\partial x'(x,y,z)}{\partial z} \\ \frac{\partial y'(x,y,z)}{\partial x} & \frac{\partial y'(x,y,z)}{\partial y} & \frac{\partial y'(x,y,z)}{\partial z} \\ \frac{\partial z'(x,y,z)}{\partial x} & \frac{\partial z'(x,y,z)}{\partial y} & \frac{\partial z'(x,y,z)}{\partial z} \end{array}\right]\Bigg|_{(x,y,z)=(x_0,y_0,z_0)}$$

which can be determined analytically. Transforming the vectors of each of the $\mathbf{D}^S_{(0,i)}$ (x', y', z') in the above manner yields the transformed myocardial motion fields for S, $\tilde{\mathbf{D}}^S_{(0,i)}(x, y, z)$

4 Results and Discussion

We applied and evaluated our technique on sets of untagged and tagged short-axis images of four healthy volunteers. The untagged and tagged MR images have been acquired shortly after each other to minimise any motion between the image acquisitions. All images were acquired using a Siemens Sonata 1.5T scanner. For the tagged sequences, a cine breath-hold sequence with a SPAMM tag pattern was used to acquire ten short-axis slices covering the entire LV. For the untagged images a cine breath-hold TrueFisp sequence was used to acquire ten slices in the same anatomical planes as the tagged imaging planes. In both cases the images have a resolution of 256 x 256 pixels with a field of view ranging between 300 and 350mm depending on the subject and a slice thickness of 10mm. In both cases imaging was done at the end of expiration and all images have been visually assessed for motion between the acquisitions.

Firstly, the myocardial motion fields of each subject relative to the end-diastolic frame in their respective sequence, were calculated using the tagged image sequences. Our previous experiments [12] have shown that the non-rigid registration algorithm is able to track the myocardial motion with an RMS of less than 0.5mm in simulated data and with an RMS error between 1 and 2mm on tagged MR images. One of the four subjects was designated a reference subject, and the untagged end-diastolic images of the other were registered to this one. The calculated transformations were then used to map the myocardial motion fields of each of these three subjects into the co-ordinate system of the reference subject.

In figure 4 we show the transformed myocardial motion fields describing cardiac motion between end-diastole and end-systole for each of the four subjects. We chose to show the motion fields at end-systole because this is when the deformation of the heart is greatest. The field in the top left of the figure shows the myocardial motion field of the reference subject, while the other fields show the transformed myocardial motion fields of the three other subjects when mapped into the correct anatomical location of the reference. Vector magnitude is indicated by the length of the arrows. For clarity, we show only the motion fields for the middle short-axis slice and have projected the motion fields onto this plane, even though we had also obtained long-axis tagged and untagged images. It is clear that the transformed motion fields of the three subjects bear a high degree of similarity to that of the reference, and the mapping allows us to make comparisons of the cardiac motion of each subject.

5 Conclusions and Future Work

In this paper we have developed a non-rigid registration based technique to compare cardiac motion patterns derived from tagged MR images within patients and across patients. The comparison of cardiac motion patterns within subjects has a number of potential applications, including the comparison in changes of the cardiac function over time in patients as a result of pharmacological or surgical interventions. In these patients the effect of pharmacological or surgical interventions could be assessed by comparing

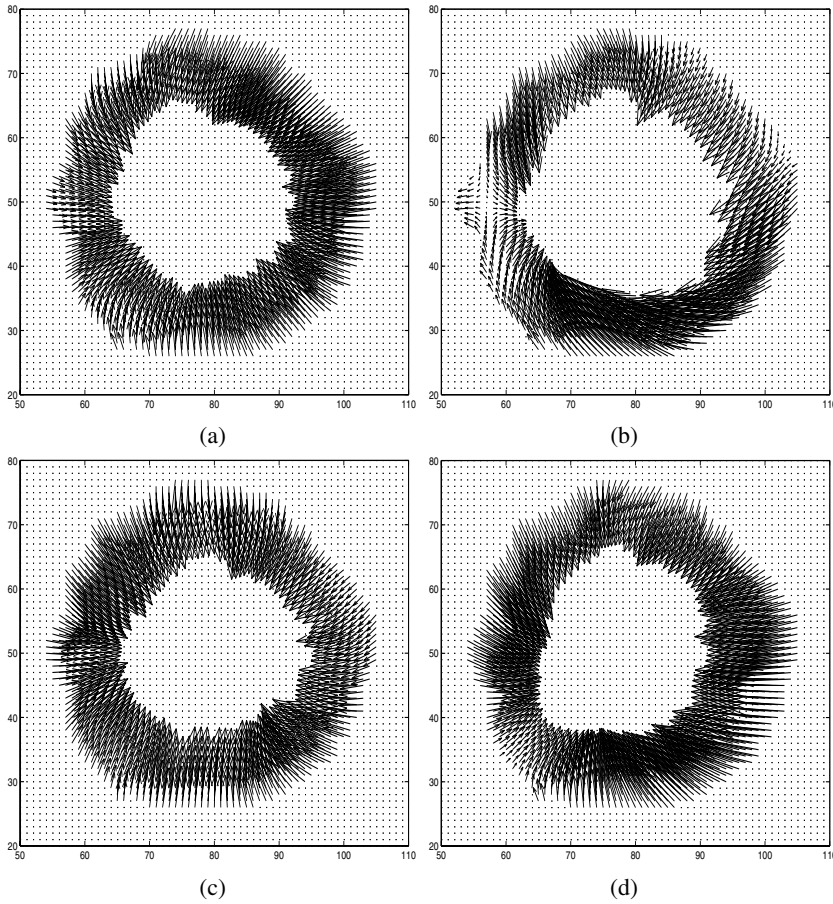


Fig. 4. The myocardial motion field of a chosen reference subject between end-diastole and end-systole is shown in (a). Images (b)-(d) shows the transformed myocardial motion fields of 3 other subjects placed at the correct anatomical location of the reference subject. Colour versions of these fields can be found at
`http://www.doc.ic.ac.uk/~dr/projects/animations/MICCAI02`.

images acquired before and after the intervention. By mapping images acquired after intervention into the same spatial frame of reference as images acquired before the intervention, one can study in detail the effect of the intervention on the cardiovascular physiology. It is likely that the same methodology will be applicable to other clinical scenarios in which changes in cardiovascular morphology and function over time need to be assessed. In particular, it may be possible to assess cardiac and vascular remodelling as a result of ischemia, infarction and other pathologies.

Future work will focus primarily on the temporal normalisation of image sequences. Even if the temporal resolution of the acquired cine MR images remains constant the variability of the heart beat rate within a single subject (i.e. in rest and stress) and across subjects will necessitate a temporal normalisation of the acquired images. In addition,

future work will focus on the construction of a subject-independent reference space in which to perform comparisons on cardiac anatomy and function. Ideally, such a reference space should not be based on a single individual subject, but rather correspond to the space which minimises any patient-specific spatial and temporal variability of anatomical and functional landmarks as a result of differences in position, orientation, size and heart rate during the image acquisition.

References

1. American Heart Association. Heart and stroke statistical update. http://www.americanheart.org/, 2002.
2. E. A. Zerhouni, D. M. Parish, W. J. Rogers, A. Yang, and E. P. Shapiro. Human heart: Tagging with MR imaging – a method for noninvasive assessment of myocardial motion. *Radiology*, 169(1):59–63, 1988.
3. L. Axel and L. Dougherty. MR imaging of motion with spatial modulation of magnetization. *Radiology*, 171(3):841–845, 1989.
4. A. A. Amini, Y. Chen, R. W. Curwen, V. Mani, and J. Sun. Coupled B-snake grids and constrained thin-plate splines for analysis of 2D tissue deformations from tagged MRI. *IEEE Transactions on Medical Imaging*, 17(3):344–356, June 1998.
5. A. A. Amini, Y. Chen, M. Elayyadi, and P. Radeva. Tag surface reconstruction and tracking of myocardial beads from SPAMM-MRI with parametric B-spline surfaces. *IEEE Transactions on Medical Imaging*, 20(2):94–103, February 2001.
6. Alistair A. Young, Dara L. Kraitchman, Lawerence Dougherty, and Leon Axel. Tracking and finite element analysis of stripe deformation in magnetic resonance tagging. *IEEE Transactions on Medical Imaging*, 14(3):413–421, September 1995.
7. J. Park, D. Metaxas, and L. Axel. Analysis of left ventricular wall motion based on volumetric deformable models and MRI-SPAMM. *Medical Image Analysis*, 1(1):53–71, 1996.
8. S. Kumar and D. Goldgof. Automatic tracking of SPAMM grid and the estimation of deformation parameters from cardiac MR images. *IEEE Transactions on Medical Imaging*, 13(1):122–132, March 1994.
9. J. Huang, D. Abendschein, V. G. Dávila-Román, and A. A. Amini. Spatio-temporal tracking of myocardial deformations with a 4-D B-spline model from tagged MRI. *IEEE Transactions on Medical Imaging*, 18(10):957–972, October 1999.
10. J. L. Prince and E. R. McVeigh. Motion estimation from tagged MR images. *IEEE Transactions on Medical Imaging*, 11(2):238–249, June 1992.
11. L. Dougherty, J. C. Asmuth, A. S. Blom, L. Axel, and R. Kumar. Validation of an optical flow method for tag displacement estimation. *IEEE Transactions on Medical Imaging*, 18(4):359–363, April 1999.
12. R. Chandrashekara, R. H. Mohiaddin, and D. Rueckert. Analysis of myocardial motion in tagged MR images using non-rigid image registration. In *Proc. SPIE Medical Imaging 2002: Image Processing*, San Diego, CA, February 2002. In press.
13. D. Rueckert, L. I. Sonoda, C. Hayes, D. L. G. Hill, M. O. Leach, and D. J. Hawkes. Non-rigid registration using free-form deformations: Application to breast MR images. *IEEE Transactions on Medical Imaging*, 18(8):712–721, August 1999.
14. C. Studholme, D. L. G. Hill, and D. J. Hawkes. An overlap invariant entropy measure of 3D medical image alignment. *Pattern Recognition*, 32(1):71–86, 1998.
15. J. A. Schnabel, D. Rueckert, M. Quist, J. M. Blackall, A. D. Castellano Smith, T. Hartkens, G. P. Penney, W. A. Hall, H. Liu, C. L. Truwit, F. A. Gerritsen, D. L. G. Hill, and D. J. Hawkes. A generic framework for non-rigid registration based on non-uniform multi-level free-form deformations. In *Fourth Int. Conf. on Medical Image Computing and Computer-Assisted Intervention (MICCAI '01)*, pages 573–581, Utrecht, NL, October 2001.