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Cardiac Motion Analysis in Ischemic and Non-Ischemic Cardiomyopathy Using Parallel Transport

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Abstract

In this study, we used the multi-detector computed tomographic (MDCT) images of heart left ventricles at end-diastole and end-systole to perform quantitative analysis and comparison of heart motion in patients with anterior wall myocardial infarction and ischemic cardiomyopathy (ICM) versus those with global non-ischemic cardiomyopathy (NICM). MDCT ventricular images of 25 subjects (13 with ICM) with ejection fraction (EF) < 35% were analyzed. We used parallel transport in diffeomorphism under the large deformation diffeomorphic metric mapping framework to translate within subject motion related deformation in a global template coordinate system. We then performed a hypothesis testing on the ventricular motion variation in the global template coordinate. Statistical analysis indicates that there are meaningful ventricular motion differences between ICM and NICM groups. Additionally, subjects with ICM demonstrated less wall thickening at ES in the anterior wall where the pathology is located.

Index Terms

parallel transport; cardiac motion analysis; cardiomyopathy

1. Introduction

Despite recent advances in medical and surgical therapies, heart failure remains a leading cause of cardiovascular morbidity and mortality [1]. Heart failure patients with prior myocardial infarction (MI) due to coronary artery disease (CAD) are considered to have ischemic cardiomyopathy (ICM). The remaining heart failure patients are classified as nonischemic (NICM) which is a heterogeneous group. Death of myocardial cells from ischemia, toxic or infectious agents, or pressure or volume overload leads to scar formation, alteration in ventricular geometry, and electric and anatomic remodeling. Because ventricular function is influenced by this remodeling, metrics related to motion may be particularly sensitive to disturbances in myocardial organization that occur during disease progress and may have great value in risk prediction and treatment evaluation. Identifying the etiology of heart failure is clinically relevant since it determines the prognosis and course of treatment.

Assessing regional differences in left ventricular motion requires examining within-subject time-dependent deformation of left ventricle (LV) across population. To perform hypothesis testing related to time-dependant within-subject deformation, it is essential to define a common coordinate system across subjects. Previously, it has been suggested to map individual anatomy to a single common atlas (template) using warping techniques [2]. However, this approach does not distant between inter and cross subject shape variation along different cardiac time

phases. Simply matching every image to a single template may conceal within-subject variation when between-subject variation is large. To overcome this difficulty, we have used a novel method, parallel transport in diffeomorphism [3], to translate within-subject motion related deformation at one cardiac cycle to a global template eliminating across-subject deformation.

In this work, we will apply methods of computational anatomy (CA) and parallel transport in the framework of diffeomorphism to perform quantitative analysis of left ventricular motion at two time points, end-diastole (ED) and end-systole (ES), using imaging data collected from two patient populations diagnosed with ischemic or nonischemic cardiomyopathy all of whom have received implantable cardioverter-defibrillator (ICD) placement. The goal is to define anatomical motion differences that are reliable markers for discriminating between these two populations.

2. Methods

2.1. Subjects

All human studies were approved by The Johns Hopkins Institutional Review Board for human investigation, and all subjects gave written informed consent following explanation of the study and protocol. All patients were enrolled in a single-center prospective study of clinically-indicated ICD placement for the primary prevention of sudden cardiac death. All patients had left ventricular ejection fraction (LVEF) $\leq 35\%$ as measured by echocardiography or radionuclide studies, and all patients had undergone coronary angiography. Patients with significant coronary artery stenosis and a history of MI or revascularization were classified as having ICM. Patients were classified as NICM if they had no history of myocardial infarction (MI) or revascularization, and no evidence of coronary artery stenoses $> 50\%$ of 2 or more epicardial vessels or left main or proximal left anterior descending (LAD) coronary artery stenosis $> 50\%$. Patients underwent cardiac magnetic resonance imaging and multi-detector CT.

Twenty five patients (ICM ten men and three women; NICM eight men and four women) were selected such that the average LVEF was matched between the two groups. Mean age was 55.9 ± 10.9 (SD) years and 51.7 ± 13.2 years ($p = 0.39$) for ICM and NICM subjects, respectively. LVEFs by MRI were $29.1 \pm 6.5\%$ and $22.6 \pm 9.9\%$ ($p = 0.07$) for the ICM and NICM groups, respectively. The MI location in the ICM group varied from anterior to anterior apical and anterior/septal. Each subject was studied either in a 32 ($n = 8$) or 64-detector ($n = 17$) multi detector computed tomography (MDCT) scanner (Aquilion 32(64), Toshiba Medical Systems Corporation, Otawara, Japan). Plane resolution varied from $0.36 \text{ mm} \times 0.36 \text{ mm}$ to $0.45 \times 0.45 \text{ mm}$, thickness = 0.5 mm . Axial images were reconstructed using a multi-segment reconstruction algorithm at 10 time points (the centre of the reconstruction window between 0% and 90% of the cardiac cycle, at 10% intervals).

2.2. Pre-processing

Axial images were interpolated to an isotropic voxel size of 1 mm^3 , and then cropped to isolate the LV. A box oriented in the long axis direction of each LV was then positioned manually and images were re-sampled in accordance with the planes parallel to this axis. Images were then segmented manually by outlining epicardial and endocardial surfaces (papillary muscles and trabeculations were excluded). ES and ED cardiac phases were determined by visual examination of heart images using short axis views at the mid-ventricular level.

2.3. Template construction and parallel transport

We have employed the large deformation diffeomorphic metric mappings (LDDMM) algorithm [4] along with the theory of geodesic shooting to create global ED average LV

template using the heart images from all 25 subjects. The first step in this iterative process is to estimate an optimal diffeomorphic transformation, using the LDDMM algorithm, which maps a provisional template to the individual target images in a cohort population. This step provides optimal initial velocity vector fields that will be used in the second step to compute average initial velocity vectors. The final step is to propagate these averaged initial velocity vectors along the direction of minimal energy path (geodesic). The final result is an evolved template that is in closer proximity to the true average shape. These steps are iterated until the magnitude of the averaged initial velocity becomes small enough.

Fig. 1 summarizes the process of parallel transport. Once the global ED template is created, we first select a subject related template (I_0^n for $n = 1, \dots, 25$) in the time sequence (ED in this study) and perform a cross-subject alignment of this subject-related ED template to a common template ($I_{globalTemp}$, global ED). To improve cross-subject alignment, our LDDMM based image matching is preceded by an affine registration of subject related template (ED) to the global template. The same affine transformation is then applied to the corresponding subject related ES image. At the end of this first step, we generate a sequence of scalar fields,

$\zeta_0^1, \dots, \zeta_0^{25}$, such that $\mu_0^n = \zeta_0^n N_0^n$, N_0^n being the oriented unit normal to the level sets of I_0^n , is the initial momentum of geodesic between I_0^n and $I_{globalTemp}$ [5]. The momentum signature (μ_0^n) is a vector that can be used to uniquely determine the evolution from the group template to the global template. Subsequent to this cross-subject alignment, we estimate deformations that mapped affine-transformed subject-related ES image (I_1^n) to its corresponding affine-transformed ED template (I_0^n). This provides new scalar fields, $z_0^1, \dots, z_0^{25}$, such that $m_0^n = z_0^n N_0^n$ is the initial momentum of the geodesic between I_0^n and I_1^n . The final step is to parallel translate momentum m_0^n from I_0^n to $I_{globalTemp}$, in order to perform between-subject comparisons. This requires, for each n , to follow this procedure: Let J_t^n be the image at time t for the geodesic between I_0^n and $I_{globalTemp}$, ζ_t^n the momentum at time t and $v_t = K(\zeta_t^n \nabla J_t^n)$. Let also $\xi_t = -\langle \nabla J_t^n, v_t \rangle$. Here t represents steps in geodesic evolution equation that is different from time points in cardiac phase. K is a smoothing kernel: $K = L^{-1}$ where $L = (\Delta^2 + \alpha Identity)^3$. The parallel translation of z_0^n along J_t^n is given by:

$$\begin{aligned} (\nabla J_t^n)^T K(\partial_t z_t^n \nabla J_t^n) &= \frac{1}{2} (\nabla \eta_t^n v_t - \nabla \xi_t^n w_t + \\ & (\nabla J_t^n)^T K(\zeta_t^n \nabla \eta_t - z_t^n \xi_t) - \\ & (\nabla J_t^n)^T K(\nabla \cdot (z_t^n v_t + \zeta_t^n w_t) \nabla J_t^n)) \\ \eta_t &= -(\nabla J_t^n K(z_t^n \nabla J_t^n)) \\ w_t &= K(z_t^n \nabla J_t^n) \end{aligned}$$

2.4. Statistical analysis

To make statistical inference about ICM and NICM groups with regards to ED to ES motion-related deformation, we designed a nonparametric randomized test based on rank-sums. (i) We first computed the matrix containing the dot products of parallel transported initial momenta among all subjects, normalized by the product of the norms of the momenta. The coefficients of this matrix therefore provide the angle cosines between two initial momenta. (ii) For each subject, we generated an ordered list of angle cosines between this subject and all other subjects in both ICM and NICM groups, and summed the obtained ranks of subjects belonging to the same group. This provides a number per subject that should be large if two groups are distinct (high cosines for subjects in the same group). (iii) Finally, we summed over all these numbers to obtain a single statistics. To obtain the p value, a permutation test with 10,000 permutations was used.

2.5. Visualization

To visualize the group effect on ED to ES ventricular motion, we first normalized the parallel transported momenta and then computed the average momenta that corresponded to the ventricular motion in ICM and NICM groups separately. This results in two averaged momenta that are aligned with the global ED template. From these two averaged momenta, we can compute two deformations by solving EPDiff equations [3]. Applying these deformations to the global ED template creates two shapes that illustrate average deformation from ED to ES for ICM and NICM groups.

3. Results

Fig. 2 illustrates one example using parallel transport to represent within-subject ventricular motion deformation from ED to ES in the global ED template coordinate. Top row represents a sample long axis 2D view of left ventricle in ED (right) and ES (left) respectively. Bottom left panel represents the corresponding 2D plane of left ventricle for the ED global template (right). Bottom left depicts the left ventricular image of this subject at ES represented in the global template coordinate. Careful examination of this figure indicates that the technique of parallel transport can capture the ED to ES ventricular deformation as it is evident from the pattern of wall thickening and chamber size.

The non parametric statistical analysis of angle cosines among the initial momenta suggests that there are statistically significant ventricular motion differences between ICM and NICM groups ($p \approx 0.03$). To illustrate average ventricular motion variation between ICM and NICM groups, we used the evolution equations to deform the global ED template and create average parallel translated ES images for ICM and NICM groups respectively (Fig. 3). Visual assessment of group average ES shapes indicates that the anterior wall thickening that normally occurs in ventricular contraction is less noticeable in ICM group (light color arrow in Fig. 3). The similar reduced thickening is identifiable at inferior-apical wall in the ICM group (dark light arrow in Fig. 3). In contrast to ICM group, NICM group on average demonstrates greater wall thickening in both anterior and inferior walls at apical and mid-wall regions.

4. Discussion

In this work, we introduced application of parallel transport in diffeomorphism on analyzing motion variation of *in-vivo* heart images in patients with LV dysfunction. The results indicate that this method can identify and quantify motion variation in remodeled myopathic heart and that can potentially be used to discriminate between patients with ischemic cardiomyopathy and those with global non-ischemic cardiomyopathy. Additionally, we observed regional difference in wall thickening between ICM and NICM groups. Ischemic patients on average demonstrate less wall thickening in the anterior wall which is consistent with the anterior location of infarction. This suggests that our approach has high sensitivity to locate the pathology.

Time series analysis, in the context of tensor based morphometry, has been previously used in brain research [6,7]. These methods are based on using deformation fields that maps a template to each individual images in the time series to identify regions of shape difference. A necessary step for statistical analysis of deformation fields across subject is to transfer these fields to a common template. While this can be achieved by mapping all images onto the common template, the resulting transformations contain both the within subject and across subject shape variations. This could potentially mask subtle shape alterations that occur in the time series. Parallel transport offers a solution by transferring within subject deformation to a global template without incorporating across subject deformations. Hence, parallel transport is a

promising technique to analyze motion variation across subjects and can be potentially used to quantify the progress of pathology or response to treatment.

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Fig. 1.

This figure depicts different steps of parallel transport. For each subject, ED LV images were defined as baseline and were mapped to the global template (cross-subject matching). Next, for each subject LV images at ES were mapped to corresponding ED. In the final stage, parallel transport technique was used to translate the cross-subject ES-ED deformation in the global coordinate system

Fig. 2.

Illustration of parallel transport for a sample subject. Top panel: Long axis view of LV in ED (right) and ES (left) at the subject's coordinate. Bottom panel: Long axis view of LV in ED (right) and ES (left) at the global template's coordinate. Notice that parallel transport method has successfully translated the ED to ES relationship in the subject coordinate to the global coordinate.

Fig. 3.
Illustration of average parallel transported ES images for ICM and NICM groups.