Open-Source Routines for Building Personalized Left Ventricular Models From Cardiac Magnetic Resonance Imaging Data

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Creating patient-specific models of the heart is a promising approach for predicting outcomes in response to congenital malformations, injury, or disease, as well as an important tool for developing and customizing therapies. However, integrating multimodal imaging data to construct patient-specific models is a nontrivial task. Here, we propose an approach that employs a prolate spheroidal coordinate system to interpolate information from multiple imaging datasets and map those data onto a single geometric model of the left ventricle (LV). We demonstrate the mapping of the location and transmural extent of postinfarction scar segmented from late gadolinium enhancement (LGE) magnetic resonance imaging (MRI), as well as mechanical activation calculated from displacement encoding with stimulated echoes (DENSE) MRI. As a supplement to this paper, we provide MATLAB and Python versions of the routines employed here for download from SimTK. [DOI: 10.1115/1.4043876]

Keywords: cardiac biomechanics, finite element models, patient-specific modeling, image registration, data fusion

Introduction

Creating patient-specific models has become an important step in simulating cardiovascular injuries and predicting therapeutic outcomes [1–6]. A range of cardiac imaging modalities now enable noninvasive collection of data on geometry, motion, perfusion, electrical activation, and even tissue properties such as fibrosis. Each of these pieces of information could be important for defining local tissue properties in a model or for validating local predictions of that model for a particular application. However, integrating these data across multiple modalities or scans to

construct a coherent patient-specific model is a nontrivial task. Different modalities typically employ different coordinate systems, produce images with different spatial and temporal resolution, and store and display that information in different formats (e.g., a series of two-dimensional slices versus a three-dimensional (3D) surface map). Thus, standardization and sharing of methods for integrating multimodal imaging data has the potential to enhance reproducibility within and across research groups [7].

Here, we propose a method for constructing a three-dimensional model of the left ventricle (LV) from multiple magnetic resonance imaging (MRI) protocols. We use short- and long-axis cine MRI to construct the LV geometry by fitting the endocardial and epicardial surfaces in prolate spheroidal coordinates. We then interpolate and map data from other MRI sequences onto the personalized geometry. We focus here on the mapping of scar determined by myocardial late gadolinium enhancement (LGE) MRI and mechanical activation from displacement encoding with stimulated echoes (DENSE) MRI. The MATLAB code employed here and a Python version are both available for download from SimTK.² The data fusion routine uses the freely available, MATLAB-based software SEGMENT for MRI segmentation³ [8] and generates geometries that port easily to FEBio for finite element (FE) simulations [9]. The dataset used here is obtained from a canine myocardial infarction experiment performed previously by our group. While this paper uses canine data to illustrate the method, we are currently employing the same data fusion routines to create human, rat, and mouse models in our laboratory.

Methods

Overview of Approach. The goal of our method is to combine personalized information from different MRI protocols and/or different imaging modalities to build a model representation of a patient's LV. Combining different MRI imaging sequences acquired during the same exam has the advantage that all data are recorded in the same coordinate system. However, even in this case, challenges arise due to differences in image resolution and physiologic state of the patient. For example, while cine MRI provides high spatial and temporal resolution of the heart geometry during the cardiac cycle, LGE MRI provides the geometry of the LV and scar at a lower resolution at end diastole. We resolve these differences by mapping the patient information at a matched cardiac phase (end diastole) to the epicardial surfaces fit from each imaging modality. The epicardial surface was chosen as the platform for information exchange because it is smoother than the endocardial surface, and in our experience, simpler to register across protocols, exams, and imaging modalities. The geometries fit from different imaging modalities are rotated into a common cardiac coordinate system based on landmark locations on the LV. The data are then projected onto a common visualization created from the high-resolution cine MRI geometry, which is used to create a FE model of the LV.

Constructing the Left Ventricle Finite Element Geometry.

The patient-specific FE geometry of the left ventricle was generated from multiple short-axis cine MRI slices taken at end diastole. Fitting of the segmented MRI contours to create a finite element mesh was previously described by our group [10]. Briefly, the epicardial and endocardial surfaces were segmented using software SEGMENT v2.0 R5430 [8].³ Landmark pinpoints were placed at the right ventricle insertions in the most basal short-axis slice and at the base and apex in the two-chamber long-axis view to define the cardiac coordinate system (Fig. 1(a)). The segmentations were registered in three dimensions in cardiac coordinates with the *x*-axis oriented from LV base to apex, the *y*-axis oriented from lateral to septal wall, and the *z*-axis oriented

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²<https://simtk.org/projects/lvdatamap>

³<http://segment.heiberg.se>

Fig. 1 (a) Long- and short-axis cine MRI were segmented and landmarked at the right ventricular insertions, base, and apex points. (b) The segmentations were registered in three dimensions. (c) The endocardial and epicardial surfaces were fit independently using two-dimensional bicubic Hermite elements.

from anterior to posterior wall. The endocardial and epicardial surfaces were independently fit using bicubic Hermite elements (eight circumferential by four longitudinal) in a prolate spheroidal coordinate system (Fig. 1) [10–12]. In this coordinate system, μ describes an angle spanning from apex to base of the LV, θ describes an angle measured circumferentially around the LV from midseptum, and λ describes a term similar to a radius extending from the origin. The wall mass between the two surface fits was filled with 3600 linear, hexahedral elements with a resolution of 24 longitudinal by 30 circumferential by 5 radial elements. Interior nodes between the endocardial and epicardial surfaces were created at equally spaced intervals in λ along lines of constant angular (μ, θ) coordinates. The nodes on the epicardial surface were used as the points onto which patient-specific data were projected and exchanged.

Extracting and Registering Scar Location Data. Epicardial, endocardial, and scar boundaries were segmented from short-axis and long-axis LGE MRI using semi-automated methods in SEGMENT [13]. Segmentations were registered to map data onto the epicardial surface through the process shown in Fig. 2. Scar extent was quantified using two metrics: transmural depth from the epicardium, both expressed as fractions of wall thickness. Scar metrics were computed in individual image slices for 50 evenly spaced bins ranging from 0 deg to 360 deg in θ in short-axis slices and 100 evenly spaced bins ranging from 0 deg to 120 deg in μ in long-axis slices. These two metrics allowed us to effectively project all information needed to recreate the scar geometry onto the epicardial surface of the ventricle. Landmark points described in the Constructing the Left Ventricle Finite Element Geometry section were selected and used to express segmented scar, endocardial, and epicardial data from the LGE MRI in the same cardiac coordinate system employed to generate the FE geometry. The registered coordinates were converted to a prolate spheroidal coordinate system as detailed earlier. The (μ, θ) location of each resulting scar data point on the epicardial surface is displayed as circles in Figs. 3(b) and 3(c).

Mapping Scar Data Onto the Model Geometry. Once scar data were projected onto the epicardial surface from the LGE image slices, the next step was to interpolate and transfer the scar information to the FE model. Defining the prolate spheroidal coordinate system for the geometric fits and the LGE analysis using the same anatomic landmarks allowed us to simply overlay the

scar data onto a (μ, θ) grid representing the epicardial surface in the geometric model (Fig. 3). The scar transmural depth and measures were transferred using a scattered, linear interpolation function with nearest neighbor extrapolation in MATLAB. The epicardial nodal points from the FE geometry were used as sample points and the epicardial points containing scar data from LGE as the data points (Fig. 3). In order to decide which elements in the finite element mesh would be considered to be scar, the data at the four nodes of each epicardial element face were averaged to get a single transmural depth and depth per transmural stack of elements. The depth value defined the starting scar element from the epicardium in each transmural stack of elements, and the transmural metric described the number of elements through each transmural stack that were defined to be scar. Each metric was multiplied by the number of radial elements and rounded to the nearest whole number to determine which elements in a transmural column are scar. For example, given a resolution of five elements from epicardium to endocardium through the wall, a scar starting at depth of 9% with transmural depth of 57% would be represented as scar starting at the first epicardial element and spanning three elements (Fig. 4).

Mapping Mechanical Activation Data Onto the Model Geometry. In principle, these same methods can be used to fuse any information that can be expressed as one or more numerical values associated with epicardial surface points. As a second illustration, we mapped mechanical activation time calculated from DENSE MRI short-axis slices onto the finite element mesh (Fig. 5) [14]. Since these data already consisted of a single number (activation time) associated with each of 18 segments per short-axis DENSE slice, we were able to transfer this information using a single interpolation scheme. We used linear interpolation between the short-axis slices and the nearest neighbor extrapolation above and below the most basal and apical short-axis slices.

Results

Validation of Scar Mapping. In order to assess the ability of the entire pipeline to accurately map LGE scar data onto a geometric model, we created plane cuts through the final FE model that approximated the MRI planes used for LGE MRI acquisition and compared the resulting images side-by-side (Fig. 6). Although the FE model geometry was created from a separate cine MRI sequence rather than the LGE images shown in the comparison,

Fig. 2 Long- and short-axis LGE MRI were segmented (a) and registered (b) into their common imaging coordinate system. Transmurality of the segmented scar was calculated and projected onto the epicardial surface of the heart in each image (c). The scar transmurality data from all images were projected onto the epicardial surface (wireframe) fitted to the segmented epicardial contours (d).

the dimensions and shape of the LV appeared similar, with some loss of detail around the papillary muscles due to smoothing apparent in short-axis cuts of the model. Long- and short-axis views showed comparable scar location and transmurality to the segmented LGE MRI.

Discussion

We have presented a method for mapping MRI-derived data on scar location or mechanical activation onto a patient-specific finite element geometry using prolate spheroidal coordinates. The data fusion routine relies on identifying landmark locations in the LV anatomy in each image set to register the information. The use of prolate spheroidal coordinates allowed us to simplify the mapping of LGE or DENSE data into a two-dimensional interpolation problem along the epicardial surface of the heart (Fig. 3). The projection onto the epicardium requires parameterizing the quantities of interest using metrics that can represent an entire transmural column; thus, mapping nontransmural scar presented an interesting challenge. To maintain information on both transmural extent and transmural location, we created separate variables that quantified these two features. The transmurality metric tracked what percentage of the wall was scar, and the depth metric tracked the distance below the epicardium at which the scar began (Fig. 4(c)).

These two parameters allowed for reconstruction of the scar in the finite element model (Fig. 4(b)).

Because of the relatively low resolution of finite elements through the wall (five elements from epicardium to endocardium) used here, the representation of scar was discretized to 20% of wall depth bins. Therefore, locations with less than 10% scar transmurality were marked as having no scar due to rounding. This likely accounted for some differences in the observed scar map in comparison to the raw MRI images (Fig. 6). However, greater resolution in representing the scar geometry could be achieved either by increasing the number of elements in the finite element mesh or by employing a mixture formulation for the material properties so that individual elements could be partially composed of scar. Employing a mixture formulation or adding transitional border zone elements with material properties that are intermediate between scar and muscle could also smooth any stress concentrations that might arise at the infarct border.

The fact that MRI data on scar location are typically available only at discrete slice locations rather than continuously in 3D space also presents a challenge when mapping to a three-dimensional finite element mesh. Here, we used interpolation to integrate all available data from both long- and short-axis slices in the LGE MRI dataset, but the accuracy of this approach depends heavily on the number of image slices. We also demonstrated that

Fig. 3 Fusion of geometric data from cine MRI and scar location data from LGE MRI. (a) Diagram of the prolate spheroid coordinate system with arrows showing the two angular coordinates that describe the location of any point on the epicardial surface. (b) After expressing both the fitted epicardial nodes and the scar data on the same coordinate system and registering them, information about scar transmurality calculated from different LGE MRI imaging planes (closed circles) was transferred to the epicardial nodes (squares) of the finite element mesh by interpolation. (c) The same interpolation procedure was also used to transfer information on scar starting depth.

the mapping techniques presented here can be used for sparser data sets, such as mechanical activation times determined from DENSE MRI (Fig. 5) [15]. However, in this case, estimating mechanical activation values for the entire LV required extrapolation, so the results should be interpreted cautiously in locations beyond the image slices used to generate the original data.

We chose to demonstrate the methods presented here on datasets from multiple different MRI sequences, which had the advantage that all the data were recorded in the same coordinate system. However, in general, the process required to fuse these datasets was the same as would be required to integrate data from another imaging modality with MRI-derived geometry. Each set of images had different voxel resolutions and gap distances

Fig. 4 (a) Scar transmurality is represented as a heat map on the epicardial surface of the finite element mesh and shown in an anterior view (anterior wall of LV in front). (b) The reconstructed scar location is visualized in a lateral view to display the variable depth and transmural extent. The meshes show the epicardial and endocardial surfaces of the finite element mesh, and the boxes indicate elements designated as scar. (c) A single transmural column of elements is shown with the interpolated scar transmurality and depth at the corresponding μ and θ values.

between imaging planes, which we addressed by separately mapping each dataset to the epicardial surface before fusing with the geometry. The sequences provided information at differing numbers of time points during the cardiac cycle, requiring selection of data from similar time points (in this case end diastole) prior to fusion. Furthermore, given the potential for subject motion between sequences and the fact that the anatomy is not identical in the three datasets (due to the differing resolution and slice locations), we also performed a rigid registration step using anatomical landmarks, just as we would employ when integrating data from another imaging system.

While many previous papers have employed imaging data to generate patient-specific heart models, few have utilized methods

Fig. 5 (a) Mechanical activation was calculated from DENSE MRI for each of 18 segments in five short-axis slices and registered with the fitted finite element geometry (closed circles). The epicardial nodes of the finite element mesh were used as sample points (squares), and mechanical activation times estimated at each using a combination of interpolation and extrapolation. (b) Mechanical activation is shown as a heat map on the epicardial surface of the geometry.

Fig. 6 Segmented long ((a)–(c)) and short (d) axis LGE MRI planes are shown with their corresponding cut in the finite element scar model. All voxels enclosed by the scar segmentation outline is marked as scar. The scar location and volumes in each frame show good agreement with the corresponding MRI image. Note that, in general, the spatial resolution of the LGE images is lower than that of the cine MRI images used to generate the finite element geometry.

that extend easily to fusion of data from multiple MRI sequences or imaging modalities. The most common approach for mapping the location and extent of an infarct onto a model is to identify the infarct using information (such as local wall thickness) segmented from the same images used to construct the model geometry [16–22]. This approach ensures that all information is both represented in the same coordinate system and correctly aligned, avoiding the need for landmark-based registration. In situations where registration is required in order to combine information from different imaging modalities, most groups have placed physical markers such as beads or wire sutures that are visible in multiple

imaging modalities [23–28]. For example, Mazhari and coworkers quantified regional strain using radiopaque markers imaged by high-speed X-ray, then used the marker locations to register the mechanics to LV geometry and perfusion boundaries mapped by a 3D manual digitizing probe [25,26]. Another related approach is to register information from different images by identifying physical landmarks that can be aligned using rigid body rotation or probabilistic atlases [29–31]. A small number of papers in this area have used commercial or open-source software packages such as CONTINUITY, CARDIOVIZ3D, and ITK-SNAP, making their methods easier for other interested groups to reproduce [2–4,32].

However, to our knowledge, the routines presented here represent the simplest available open-source method for fusing information from multiple imaging sequences or techniques onto a cardiac model geometry.

Starting with raw images, the fusion and mapping process outlined here can be completed in less than half an hour by a single, trained operator. The main limitation is the time required to segment the cine and LGE MRI. While the full FE mesh is important for simulating mechanical models, a simpler visualization can be created from the epicardial surface alone (Fig. 5(b)). The simple visualization extends the use of this registration routine from building patient-specific computational models to creating a clinical tool that can superimpose LV data from multiple imaging modalities, which we are currently testing in a randomized, clinical trial.⁴

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⁴<https://clinicaltrials.gov/ct2/show/NCT03398369>