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Sensitivity of left ventricular mechanics to myofiber architecture: A finite element study

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Abstract

The goal of this study was to investigate the sensitivity of computational models of the heart to their incorporated myofiber architecture during diastole. This architecture plays a critical role in the mechanical and electrical function of the heart and changes after myocardial tissue remodeling, which is associated with some of the most common heart diseases. In this study, a left ventricular finite element model of the porcine heart was created using magnetic resonance imaging, which represents the in vivo geometry. Various myofiber architectures were assigned to the finite element mesh, in the form of fiber and sheet angles. A structural-based material law was used to model the behavior of passive myocardium and its parameters were estimated using measured in vivo strains and cavity volume from magnetic resonance imaging. The final results showed noticeable sensitivity of the stress distribution to both the fiber and sheet angle distributions. This implies that a structural-based material law that takes into account the effect of both fiber and sheet angle distributions should be used. The results also show that although the simulation results improve using available data from histological studies of myocardial structure, the need for individualized myofiber architecture data is crucial.

Keywords

Myofiber architecture; numerical modeling; stress distribution; passive myocardium

Introduction

The myocardium of the left ventricle (LV) is predominantly composed of bundles of myofibers, which have a significant effect on both the mechanical and electrical function of the heart. The architecture of these myofibers has orientation angles that vary transmurally, which enables the heart to eject blood in the most efficient manner as it deforms.¹ Some of

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the first quantitative measurements of myofiber orientations were collected from canine ventricles.² Subsequent investigations showed that myocardial microstructure is composed of discrete layers referred to as sheets, which run transmurally across the ventricular wall.^{3,4} LeGrice et al.⁵ provided a more detailed and systematic account of the architecture of these sheets. Finite element (FE) models of the heart incorporate constitutive laws that simulate the anisotropic and nonlinear behavior of the myocardium, which rely on a description of myofiber architecture (i.e. the distribution of fiber and sheet orientation angles).¹

A common approach to incorporate anisotropy of myocardium in FE models of the heart is to assume a uniform distribution of fiber and sheet angles based on the information obtained from histological studies.^{6,7} In order to create more realistic FE models of the heart, it is crucial to investigate the sensitivity of these models to myofiber architecture. Previously, Wang et al.⁸ studied the sensitivity of a human LV model to changes in myofiber architecture. The FE model incorporated a structural-based material law,¹ which employed a set of material parameters that were taken from simple shear tests on specimens of excised pig heart previously reported by Dokos et al.⁹ The results of that study imply that the transmural distribution of myofiber stress and strain is highly sensitive to fiber angle distributions but insensitive to sheet angles. However, those results were taken from a single longitudinal region. In this work, a comprehensive animal-specific model is constructed to conduct a similar sensitivity study. Here, the same constitutive law used in Wang et al.⁸ was used to model healthy LV myocardium of a porcine heart in diastole. In order to use realistic animal-specific material parameters in the constitutive model, threedimensional (3D) in vivo strains were measured from magnetic resonance imaging (MRI) and used for parameter estimation of the material law. A FE model was created from the in vivo images of the LV and was assigned different combinations of fiber and sheet angles. Parameter estimation was performed by minimizing the difference between MRI measured and FE predicted strains and cavity volumes. Both were assessed at the same end-diastolic pressure, which was measured via catheterization.

Methods

Animal data

In this study, a healthy adult male pig weighing approximately 40 kg was used in order to assess in vivo cardiac function. The animal used in this work received care in compliance with the protocols approved by the Institutional Animal Care and Use Committee at the University of Pennsylvania in accordance with the guidelines for humane care (National Institutes of Health Publication 85-23, revised 1996). The data used in this study are from the same animal cohort that was used in previous studies,¹⁰ in which many of the experimental details can be found. Briefly, 3D spatial modulation of magnetization (SPAMM) MRI was conducted. The endocardium and epicardium of the LV were contoured from the images and fit with 3D surface geometry. All six components of the 3D strain tensor were calculated at end-diastole from the images using a custom optical flow plug-in for ImageJ.¹¹ An MRI-compatible pressure transduction catheter (Millar Instruments, Houston, TX) was used to measure LV pressure.

FE model

Many of the details regarding the FE model can be found in Nikou et al.¹² Briefly, each mesh was generated with approximately 1500 trilinear hexahedral elements, which were bounded by the endo- and epicardial surface geometries. A homogeneous linear distribution of the myofiber and myocyte sheet orientation angles was assigned to each element (Figure 1). The base of the LV model was constrained to deform only in the horizontal plane, except for the epicardial edge that was fixed, and the measured end-diastolic pressure (6.8mmHg) was used as a loading boundary condition in the model. The constitutive model outlined in section “Constitutive law and parameter estimation” was coded as a user-defined material subroutine that was implemented in the nonlinear FE solver LS-DYNA (Livermore Software Technology Corporation, Livermore, CA, USA). In this study, an explicit time integration scheme was used.

Constitutive law and parameter estimation

A structural-based constitutive law for passive myocardium was used to model material properties of the LV myocardium.¹ In this model, the myocardium is treated as a non-homogeneous, orthotropic, and nonlinearly elastic material and takes into account the myofiber, myocyte sheet, and sheet normal directions. The strain energy function per unit reference volume is as follows

$$\begin{aligned} \psi = & \frac{a}{2b} \{ \exp[b(I_1 - 3)] - 1 \} \\ & + \sum_{i=f,s} \frac{a_i}{2b_i} \{ \exp[b_i(I_{4i} - 1)^2] - 1 \} \\ & + \frac{a_{fs}}{2b_{fs}} \{ \exp(b_{fs}I_{8fs}^2) - 1 \} \end{aligned} \quad (1)$$

where a , b , a_f , b_f , a_s , b_s , a_{fs} , and b_{fs} are the eight positive material parameters (a parameters have dimensions of stress, while b parameters are dimensionless). The four invariants used in the strain energy function are defined as follows

$$\begin{aligned} I_1 &= \text{tr}(\mathbf{C}), & I_{4f} &= \mathbf{f}_0 \cdot (\mathbf{C}\mathbf{f}_0), \\ I_{4s} &= \mathbf{s}_0 \cdot (\mathbf{C}\mathbf{s}_0), & I_{8fs} &= \mathbf{f}_0 \cdot (\mathbf{C}\mathbf{s}_0) \end{aligned} \quad (2)$$

where $\mathbf{f}_0$ and $\mathbf{s}_0$ are unit vectors that define the myofiber direction and myocyte sheet direction, respectively, and $\mathbf{C}$ is the right Cauchy-Green deformation tensor defined as follows

$$\mathbf{C} = \mathbf{F}^T \mathbf{F} \quad (3)$$

where $\mathbf{F}$ is the deformation gradient tensor.

Estimation of the animal-specific material parameters has been described previously in Nikou et al.¹² Briefly, optimization was performed by minimizing the mean squared error (MSE) defined as follows

$$\text{MSE} = \sum_{n=1}^N \sum_{i,j=1,2,3} (E_{ij,n} - \bar{E}_{ij,n})^2 + \left(\frac{V - \bar{V}}{\bar{V}} \right)^2 \quad (4)$$

In this definition, $N = 252$ is the total number of points (centroids of mid-wall elements) where strains were compared to the nearest LV points from the MRI data, n is the strain point within the myocardium, $E_{ij,n}$ and $\bar{V}$ are the FE predicted end-diastolic strain components and end-diastolic LV cavity volume, respectively, and the corresponding over bar variables represent in vivo MRI measured values. A genetic algorithm (GA) technique was chosen for the optimization and was performed using the software LS-OPT (Livermore Software Technology Corporation).

Myofiber architecture

Previously, Lee et al.¹³ measured myofiber orientation angles in five in vitro porcine hearts and reported the transmural change of average myofiber angle with respect to the circumferential direction from -40° (at epicardium) to 80° (at endocardium). Myocyte sheet angles following the study of LeGrice et al.⁵ on canine hearts varied from -45° (at epicardium) to $+45^\circ$ (at endocardium) with respect to radial direction. In this study, a custom MATLAB code was used to assign a linear distribution of myofiber and myocyte sheet orientation angles to each hexahedral element. It has been shown that a linear distribution of myofiber angles across the myocardium provides a relatively close match to diffusion tensor magnetic resonance imaging (DT-MRI) data.⁷ In order to investigate the sensitivity of LV response to changes of myofiber architecture, we assumed seven different transmural distributions of myofiber and sheet angles. Each set of angles was assigned to an identical FE model of a porcine LV (Table 1).

Results

Parameters of the material law were estimated for each one of the FE models using the procedure described in section “Constitutive law and parameter estimation” (a total of seven optimization problems, eight parameters estimated in each). The final MSE values are listed in Table 1 and the resulting parameters of each optimization are listed in Table 2. It can be seen that there is little variation between the parameters in cases 3 and 4, since the angles are fairly close, but there is quite a bit of variability when the fiber or sheet angles deviate from these values. Upon inspection of the MSE values obtained from the structural-based material law, it is clear that the MSE values vary when identical FE models with different myofiber architecture were used during the parameter estimation. The best fit was obtained when a distribution of -45° to 90° for the myofiber angle and a distribution of -45° to $+45^\circ$ for the sheet angle were used. Considering the variability between animals used in different studies, this result is consistent with the results of previous histological studies.^{5,13} In order to study the sensitivity of the stress distribution to myofiber architecture, the estimated parameters of

the material law were used in FE models which were loaded to the same end-diastolic pressure. Figure 2(a)-(c) shows the results of these FE simulations in the form of the circumferential distribution of myofiber stress at three regions of the LV model, that is, near the base, mid-ventricle, and apex. The stresses in these figures are the average of the three neighboring transmural elements (transmural average). It can be seen in these figures that the stress distributions are sensitive to both fiber and sheet angle variations in all regions of the LV model.

Discussion

Based on the results of this study (Figure 2(a)-(c)), the myofiber stress distribution is sensitive to both fiber and sheet angle distributions in several regions of the FE model of the in vivo LV. Although the stresses are more affected by fiber angles compared to sheet angles, their dependence to sheet angles is not negligible. Notably, Wang et al.⁸ did not observe sensitivity of stresses to sheet angles in their study with FE models of a human LV. This could be due to the fact that in that study, myofiber stress was only assessed at one longitudinal section of the LV model, that is, the circumferential myofiber stress distribution was not assessed. In this study, it can be seen that in multiple circumferential locations the fiber stress varies when the sheet angle distribution changes (where dashed lines in Figure 2(a)-(c) deviate). The contribution of sheet angles on the myofiber stress distribution is due to terms in equation (1) that contain $\bar{T}_{4s}$ and $\bar{T}_{8fs}$ (sheet and fiber-sheet coupling invariants).

In contrast, constitutive laws that treat the myocardium as transversely isotropic relative to the local myofiber direction (see, for example, Guccione et al.¹⁴) cannot capture the effect of variations of local myocyte sheet directions.

Conclusion

The results of this study show that the in vivo stress distributions of the LV during diastole are sensitive to both fiber and sheet angle distributions. Therefore, precise patient-specific descriptions of myofiber architecture should be an essential part of a realistic computational model of the heart. The results of this study also imply that in order to have a more realistic computational simulation of myocardial mechanics, structural-based material law that takes into account the effect of both myofiber and sheet angle distributions should be used.

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Figure 1.

(a) The FE model of the LV used in this study. The local myofiber, sheet, and normal angles incorporated in the structural-based material law are shown in a representative element. (b) Short axis view of the FE model. Numbers indicate the circumferential location around the LV, where 1 is the septal region, 9 is the anterior region, 18 is the free wall region, and 27 is the posterior region.

Figure 2.

Circumferential distribution of myofiber stress (a) near base region, (b) mid-ventricle region, and (c) near apex region. Stress was calculated as the average of three elements in the same circumferential location. Solid lines represent results of FE models in which only fiber angle distributions were deviated from measured experimental values and dashed lines represent results of FE models in which only sheet angle distributions were deviated from measured experimental values. The black line represents the average and standard deviation of the seven cases.

Table 1.

Seven variations of myofiber orientation and myocyte sheet angles assigned to the FE model (angles in degrees), as well as the resulting MSE values from the material parameter optimization.

	Fiber angle at epicardium	Fiber angle at endocardium	Sheet angle at epicardium	Sheet angle at endocardium	MSE values
1	-20	40	-45	45	7.283
2	-30	60	-45	45	7.166
3	-40	80	-45	45	7.033
4	-45	90	-45	45	6.984
5	-70	90	-45	45	7.017
6	-40	80	-30	30	7.242
7	-40	80	-60	60	6.999

MSE: mean squared error.

Shaded cells represent average measured values from LeGrice et al.⁵ and Lee et al.¹³

Material parameters determined from the optimization routine for each of the seven variations of myofiber orientation and myocyte sheet angles assigned to the FE model.

Table 2.

	a (kPa)	b	a_f (kPa)	b_f	a_s (kPa)	b_s	a_{fs} (kPa)	b_{fs}
1	1.51	1.22	3.21	0.28	0.54	61.38	3.26	3.75
2	0.89	7.80	2.71	3.04	0.13	85.27	0.61	89.67
3	0.91	8.60	3.25	27.07	0.30	26.12	0.37	96.19
4	0.83	9.59	4.47	5.53	0.29	24.74	0.35	95.10
5	0.79	8.57	5.41	1.27	0.35	26.76	0.93	52.07
6	1.09	6.12	3.26	1.27	0.30	74.14	0.47	92.90
7	0.68	9.81	3.94	21.27	1.06	4.18	0.83	56.28