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An Ultrasound-Driven Kinematic Model for Deformation of the Infarcted Mouse Left Ventricle Incorporating A Near-Incompressibility Constraint

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Abstract

Mathematical models of varying complexity have proved useful in fitting and interpreting regional cardiac displacements obtained from imaging methods such as ultrasound speckle tracking or MRI tagging. Simpler models, such as the classic thick-walled cylinder model of the left ventricle (LV), solve quickly and are easy to implement, but they ignore regional geometric variations and are difficult to adapt to the study of regional pathologies such as myocardial infarction. Complex, anatomically accurate finite-element models work well but are computationally intensive and require specialized expertise to implement. We developed a kinematic model that offers a compromise between these two traditional approaches, assuming only that displacements in the left ventricle are polynomial functions of initial position and that the myocardium is nearly incompressible, while allowing myocardial motion to vary spatially as would be expected in an ischemic or dyssynchronous left ventricle. Model parameters were determined using an objective function with adjustable weights to account for confidence in individual displacement components and desired strength of the incompressibility constraint. The model accurately represented the motion of both normal and infarcted mouse left ventricles during the cardiac cycle, with normalized root mean square errors in predicted deformed positions of $8.2 \pm 2.3\%$ and $7.4 \pm 2.1\%$ for normal and infarcted hearts, respectively.

Keywords

Kinematic model; myocardial infarction; incompressibility; polynomial function; high frequency ultrasound

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INTRODUCTION

Despite significant achievements being made in diagnosing and treating cardiovascular disease (CVD), it remains a major global health concern. In the United States, heart disease is the leading cause of death, accounting for 32.3% of all deaths in 2009 (Roger 2013). Ultrasound is routinely used to diagnose patients with suspected heart disease, including Doppler-based ultrasound such as Tissue Doppler Imaging assessing cardiac function based on myocardial velocities (Sutherland 1994; Sebag 2005), and M-mode echocardiography to analyze the time delay between septal and posterior wall motion (Pizalis 2005). Post image formation techniques, using B-mode ultrasound images, such as speckle tracking, can assess myocardial mechanics by tracking tissue motion (Li 2007; Nesser 2009). These measurements are important to the understanding of normal heart function and CVD. Recent advances in high frequency ultrasound have made it possible to study myocardial mechanics in transgenic mouse models by capturing high frame rate cines with spatial resolutions of approximately 50 μ m axial and 110 μ m lateral resolutions (Foster 2009). However, motion estimates using speckle tracking techniques are often noisy (Bansal 2008; Hjertaas 2013). For example, in mouse heart imaging, high heart rate (400 – 600 beats per minute), consequent limited number of image frames per cardiac cycle, and out of plane motion can result in significant decorrelation between frames. Additionally, signal dropout, attenuation and anatomical related artifacts (e.g. sternum, rib or lung related multipath reverberation or shadowing) can degrade image quality. To partially compensate for these artifacts, several groups have developed image processing techniques that include clutter and artifact reduction using finite impulse response (FIR) filters (Lediju 2009) and principal component analysis (Gallippi 2002; Mauldin 2011).

Another approach to compensate for artifacts in cardiac motion estimation is the use of mathematical models. Using this approach, mathematical models can operate as filters by imposing geometric constraints on allowed myocardial motion to discard and correct improbable motion estimates derived from motion tracking techniques. These constraints might include requiring strains or displacements to be locally smooth or to vary spatially in ways determined by the geometry of the heart. One particularly useful constraint arises from the fact that myocardium is composed primarily of water, and movement of blood in and out of the coronary vessels over a cardiac cycle produces volume changes of less than 4% (Judd 1991). As a result, myocardium is nearly incompressible; that is, the total volume of any region is nearly constant throughout the cardiac cycle. This is a particularly attractive constraint because it holds locally and requires no assumptions about heart geometry, material properties, or loading. For example, models using tissue incompressibility as a constraint have been used to improve both automated segmentation (Hansegard 2007; Garson 2008; Zhu 2007; Zhu 2010) and motion estimation (Bistoquet 2008; Mansi 2010; Touil 2010; Wang 2010).

Models using simple geometric shapes appropriate to the LV have been influential in studying cardiac mechanics. Cylindrical models have been used to predict distributions of stress and strain around the myocardium (Humphrey 1989; Costa 1996), and to estimate material properties of the myocardium (Guccione 1991). While these models have been instrumental in understanding ventricular mechanics, they are generally taken to represent

only a mid-ventricular section of the LV and are inadequate in modeling regions near the apex. In addition, they frequently assume that deformation is axisymmetric, limiting their application in settings such as myocardial infarction (MI), where ventricular remodeling and dyssynchrony give rise to substantial regional variation in cardiac deformation. Other models using prolate spheroidal and realistic heart geometries have had better success in describing motion near the apex as well as regional ischemia and dyssynchrony (Arts 1992; Kerckhoffs 2009). However, increasing anatomic fidelity in such models comes at the cost of steeply increasing computation time and the need to utilize highly specialized modeling software, limiting their routine use in fitting and interpreting imaging data. In this paper, we derive a kinematic model in cylindrical polar coordinates. The models allows radial (r), circumferential (θ) and longitudinal (z) displacements to vary as polynomial functions of initial position R , Θ , and Z within a realistic initial geometry, incorporating the additional constraint of near incompressibility within the myocardium. This formulation allows more freedom in describing cardiac motion while retaining the advantages of enforcing incompressibility in enhancing physical consistency of the reported displacements.

MATERIALS AND METHODS

Mouse Heart Imaging and Motion Estimates

Our mathematical heart model was validated using *in vivo* ultrasound mouse data. The animal experiments in this study followed a protocol approved by the University of Virginia Animal Care and Use Committee. Short-axis (SA) and long-axis (LA) cine B-mode images of 6 healthy male C57BL/6 mice (10- to 12-wk old, 24 to 26 g) were acquired using a VisualSonics Vevo 2100 scanner (Toronto, Ontario, Canada) with a MS400 transducer operating at 30 MHz, with 50 μ m axial and 110 μ m lateral resolutions (Foster 2009). Imaging frame rate was approximately 350 fps, and the average heart rate of mice under anesthesia was 462 ± 14 bpm. To achieve this frame rate, the field of view (FOV) was approximately 7mm $\times$ 7mm with standard line density and a single focal zone centered at the mouse left ventricle. During scanning, the mouse was carefully maintained under anesthesia using isoflurane at approximately 1.5 – 1.8% mixed with atmospheric air. Body temperature was maintained at $37 \pm 0.2^\circ\text{C}$ by a heated platform under the animal and an incandescent lamp, and the body temperature monitored with the aid of a digital thermometer. ECG signals were obtained using ECG electrodes integrated into the heating platform. A constant body temperature was important in maintaining a consistent heart rate. A stack of serial SA images was acquired at 0.5 mm intervals, with 10 to 12 slices from base to apex. An orthogonal stack of 6 to 8 LA images, also using 0.5 mm intervals, was acquired across the LV of each mouse. All mice underwent myocardial infarction (MI) via 1-hour occlusion of the left anterior descending (LAD) coronary artery followed by reperfusion (Yang 2002). Post-infarct mice were assessed using ultrasound 28 days after MI with the same acquisition parameters (1 mouse died after surgery, and another mouse was excluded due to poor ultrasound data). Average heart rate for MI mice was 561 ± 54 bpm. Displacement fields across the myocardium were determined by speckle tracking with approximately 0.2 mm $\times$ 0.2 mm pixel block size using a minimum sum absolute difference (MSAD) algorithm and parabolic fit derived sub-pixel resolution (Li 2007). The MSAD algorithm provides approximately equivalent performance to more computationally intensive tracking

algorithms (e.g. normalized cross correlation) in representative B-Mode images possessing adequate SNR (Friemel 1995).

Myocardial Incompressibility

The myocardium is generally assumed to be nearly incompressible, since it is composed of 80% water (Aliev 2002; Vinnakota 2004). This assumption is supported by studies showing that changes in cardiac muscle volume due to movement of blood into and out of the coronary blood vessels during the cardiac cycle are less than 4% (Judd 1991). The change in volume is even smaller in ischemic regions of the heart, since blood perfusion and motion in these regions are limited. We considered two different approaches to enforcing incompressibility: a simple model for normal hearts in which incompressibility is assumed in order to derive an analytic expression for radial deformation as a function of circumferential and axial deformation; and a more general approach where the incompressibility constraint is weighted against measured displacements to achieve a balance between enforcing incompressibility and matching measured deformation.

General Model Formulation

We began with a general description of deformation of the heart from end systole (ES) to end diastole (ED) in cylindrical coordinates as expressed in Equation (1), where (R, Θ, Z) are (radial, circumferential, longitudinal) undeformed myocardial positions at ES, and (r, θ, z) are deformed myocardial positions at ED (Adkins 1955).

$$r=r(R, \Theta, Z), \theta=\theta(R, \Theta, Z), \text{ and } z=z(R, \Theta, Z) \quad (1)$$

In cylindrical polar coordinates, the deformation gradient matrix, F , describing deformation from ES to ED is then (Spencer 1980):

$$F = \begin{bmatrix} \frac{\partial r}{\partial R} & \frac{1}{R} \frac{\partial r}{\partial \Theta} & \frac{\partial r}{\partial Z} \\ r \frac{\partial \theta}{\partial R} & r \frac{\partial \theta}{\partial \Theta} & r \frac{\partial \theta}{\partial Z} \\ \frac{\partial z}{\partial R} & \frac{1}{R} \frac{\partial z}{\partial \Theta} & \frac{\partial z}{\partial Z} \end{bmatrix} \quad (2)$$

For an incompressible material the determinant of the deformation gradient matrix is equal to unity:

$$\frac{r}{R} \left[\begin{aligned} & \left(\frac{\partial r}{\partial R} \frac{\partial \theta}{\partial \Theta} \frac{\partial z}{\partial Z} \right) + \left(\frac{\partial r}{\partial \Theta} \frac{\partial \theta}{\partial Z} \frac{\partial z}{\partial R} \right) + \left(\frac{\partial r}{\partial Z} \frac{\partial \theta}{\partial R} \frac{\partial z}{\partial \Theta} \right) \\ & - \left(\frac{\partial r}{\partial R} \frac{\partial \theta}{\partial Z} \frac{\partial z}{\partial \Theta} \right) - \left(\frac{\partial r}{\partial \Theta} \frac{\partial \theta}{\partial R} \frac{\partial z}{\partial Z} \right) - \left(\frac{\partial r}{\partial Z} \frac{\partial \theta}{\partial \Theta} \frac{\partial z}{\partial R} \right) \end{aligned} \right] = v = 1 \quad (3)$$

Cylindrical models of the left ventricle generally assume an axisymmetric initial geometry and a simple form for the functions r , θ , and z in Equation (1), such that most of the partial derivatives in the deformation gradient matrix are either zero or constant. Seeking a more general formulation, we plotted measured deformed versus undeformed positions from the mouse hearts we studied and sought the simplest polynomial functions that adequately described regional variations in deformation in both control and infarcted hearts.

Linear Model of Deformation in the Normal Mouse Heart

For normal mouse hearts, deformed longitudinal position z was a linear function of undeformed longitudinal position Z but independent of R or Θ (Figure 1A). Deformed circumferential position θ was a nearly linear function of undeformed circumferential position Θ and independent of R , but did vary with undeformed longitudinal position Z (Figure 1B). Accordingly, we used the following first-order polynomial functions to describe circumferential and longitudinal motion, respectively:

$$\theta(\Theta, Z) = a\Theta + \tau Z + b, \text{ and } z(Z) = cZ + d \quad (4)$$

Since the derivatives of θ and z are independent of R and Θ , respectively, we can simplify the deformation matrix in (2) to (5):

$$F = \begin{bmatrix} \frac{\partial r}{\partial R} & \frac{1}{R} \frac{\partial r}{\partial \Theta} & \frac{\partial r}{\partial Z} \\ r \frac{\partial \theta}{\partial R} & \frac{r}{R} \frac{\partial \theta}{\partial \Theta} & r \frac{\partial \theta}{\partial Z} \\ \frac{\partial z}{\partial R} & \frac{1}{R} \frac{\partial z}{\partial \Theta} & \frac{\partial z}{\partial Z} \end{bmatrix} = \begin{bmatrix} \frac{\partial r}{\partial R} & \frac{1}{R} \frac{\partial r}{\partial \Theta} & \frac{\partial r}{\partial Z} \\ 0 & \frac{r}{R} \frac{\partial \theta}{\partial \Theta} & r \frac{\partial \theta}{\partial Z} \\ 0 & 0 & \frac{\partial z}{\partial Z} \end{bmatrix} \quad (5)$$

Similarly, Equation (3) can be simplified to (6):

$$\det(F) = \left(\frac{\partial r}{\partial R} \right) \left(\frac{r}{R} \frac{\partial \theta}{\partial \Theta} \right) \left(\frac{\partial z}{\partial Z} \right) = 1 \quad (6)$$

By integrating Equation (6) we arrive at an expression for the deformed radius at any point:

$$r(R, \Theta, Z) = \sqrt{\frac{R^2 - R_0^2}{f(\Theta, Z)}} + r_0^2, f(\Theta, Z) = \left(\frac{\partial \theta}{\partial \Theta} \right) \left(\frac{\partial z}{\partial Z} \right) = ac \quad (7)$$

where R_0 is the undeformed endocardial radius and r_0 the deformed endocardial radius.

To optimize these constants, the normalized root mean square error (NRMSE) between observed, (r_i, θ_i, z_i) , and predicted, $(\hat{r}_i, \hat{\theta}_i, \hat{z}_i)$, positions after deformation is calculated, where i denotes the i^{th} observation:

$$NRMSE = \frac{1}{3\sqrt{n}} \sum_{t \in (r, \theta, z)} \frac{\sqrt{\sum_i^n (t_i - \hat{t}_i)^2}}{t_{\max} - t_{\min}} \quad (8)$$

The combination of parameter values that yields the minimum NRMSE are considered optimal:

$$(a, b, c, d, \tau) = \arg \min(NRMSE(a, b, c, d, \tau)) \quad (9)$$

Polynomial Model of Deformation in Normal and Infarcted Mouse Hearts

Not surprisingly, given the regional nature of the insult, in infarcted mouse hearts we found substantial regional variations in displacements: radial and circumferential motion varied with radial, circumferential, and longitudinal position in the heart wall (Figure 2), while

longitudinal motion varied significantly in the circumferential and longitudinal directions only. Therefore, the deformation matrix in (2) could be simplified only slightly to (10), with the determinant expressed in (11):

$$F = \begin{pmatrix} \frac{\partial r}{\partial R} & \frac{1}{R} \frac{\partial r}{\partial \Theta} & \frac{\partial r}{\partial Z} \\ r \frac{\partial \theta}{\partial R} & \frac{r}{R} \frac{\partial \theta}{\partial \Theta} & r \frac{\partial \theta}{\partial Z} \\ \frac{\partial z}{\partial R} & \frac{1}{R} \frac{\partial z}{\partial \Theta} & \frac{\partial z}{\partial Z} \end{pmatrix} = \begin{pmatrix} \frac{\partial r}{\partial R} & \frac{1}{R} \frac{\partial r}{\partial \Theta} & \frac{\partial r}{\partial Z} \\ r \frac{\partial \theta}{\partial R} & \frac{r}{R} \frac{\partial \theta}{\partial \Theta} & r \frac{\partial \theta}{\partial Z} \\ 0 & \frac{1}{R} \frac{\partial z}{\partial \Theta} & \frac{\partial z}{\partial Z} \end{pmatrix} \quad (10)$$

$$\frac{r}{R} \left[\left(\frac{\partial r}{\partial R} \frac{\partial \theta}{\partial \Theta} \frac{\partial z}{\partial Z} \right) - \left(\frac{\partial r}{\partial R} \frac{\partial \theta}{\partial Z} \frac{\partial z}{\partial \Theta} \right) - \left(\frac{\partial r}{\partial \Theta} \frac{\partial \theta}{\partial R} \frac{\partial z}{\partial Z} \right) + \left(\frac{\partial r}{\partial Z} \frac{\partial \theta}{\partial R} \frac{\partial z}{\partial \Theta} \right) \right] = v = 1 \quad (11)$$

We selected polynomials containing terms that captured the nature and polynomial order of observed variations:

$$\begin{aligned} r(R, \Theta, Z) &= R_c + \sum_{i=1}^m g_i R^i + \sum_{i=1}^n h_i \Theta^i + x_1 R \Theta + x_2 R^2 \Theta + x_3 R \Theta^2 + x_4 R^2 \Theta^2 + v_1 Z + v_2 \Theta Z \\ \theta(R, \Theta, Z) &= \Theta_c + \sum_{i=1}^m s_i R^i + \sum_{i=1}^n t_i \Theta^i + y_1 R \Theta + y_2 R^2 \Theta + y_3 R \Theta^2 + y_4 R^2 \Theta^2 + w_1 Z + w_2 \Theta Z \\ z(\Theta, Z) &= Z_c + u_1 \Theta + u_2 Z + u_3 \Theta Z \end{aligned} \quad (12)$$

For this more complicated model, we could not simply integrate to determine radial deformation as for the linear model. Instead, we obtained coefficients for Equation (12) for both control and infarcted hearts by minimizing mean square error (MSE) between measured and model deformations:

$$MSE = \frac{1}{n} \sum_{i=1}^n \left[w_r (r_i - \hat{r}_i)^2 + w_\theta (\theta_i - \hat{\theta}_i)^2 + w_z (z_i - \hat{z}_i)^2 + w_v (1 - \hat{v}_i)^2 \right] \quad (13)$$

where w_r , w_θ , w_z , and w_v are weighting factors for radial, circumferential, longitudinal and the incompressibility constraint, respectively. The weights sum to unity, and can be chosen based on the confidence of tracking accuracy in each direction, and the desired level of incompressibility (i.e. tolerance for volume change during contraction). (r_i, θ_i, z_i) are the actual displacement data and $(\hat{r}_i, \hat{\theta}_i, \hat{z}_i)$ are the polynomial model-predicted values.

RESULTS

Linear Model of Deformation in the Normal Mouse Heart

Longitudinal motion was obtained using lateral displacement data derived from tracking LA cine loops. The 0 mm-position was defined at the apex at ES. As shown in Figure 1A, tissues at the basal level moved upward relative to the apex, resulting in LV extension (slope of fitted line > 1.0). Circumferential motion is illustrated in Figure 1B. The 0-rad reference was defined at the section between the papillary muscles, increasing in the counterclockwise direction. A shift in the $\theta(\Theta)$ curve was observed at different levels of the LV. Using the midventricular layer as a reference, the basal and apical layers were observed to rotate in opposite directions, reflecting LV torsion. The small differences between deformation at the different axial levels shown in Figure 1B are more readily apparent when plotting predicted

versus observed circumferential displacements (Figure 1C), as are small local variations about the linear fits within each short-axis section.

The slope of the regression lines shown in Figure 1 provided an initial estimate of the coefficients a and c in the linear deformation model (Equations 4,7). We then simulated a range of values in the neighborhood of the regression coefficients a and c , and determined the combination that minimized NRMSE (Figure 3). We determined the remaining coefficients b , d , and τ , which do not affect model-predicted radius, from a best fit to the data using Equations (4) and optimized values for a and c . All coefficients were determined individually for each mouse. A statistical summary of the mean and standard deviation of the values for these coefficients is reported in Table 1.

The NRMSE of the optimized models was $4.4 \pm 1.2\%$, represented by the minimum value of the surface in Figure 3. Figure 4 shows predicted radial motion at different levels of the LV. The fact that the model captures radial motion throughout the normal mouse LV with a single choice of parameters for θ/Θ and z/Z suggests that most of the variation in radial motion in the normal mouse heart arises from spatial variation in geometry (R_0 and r_0 in Equation (7)). As shown in Figure 4C, the apical section contributes most of the error; this error near the apex is largely due to tracking error arising from partial volume effects and out of plane motion.

Polynomial Model of Deformation in Normal and Infarcted Mouse Hearts

LAD occlusion created a myocardial infarction (MI) in the apical antero-lateral region of the LV. Speckle tracking for a typical SA cine is shown in Figure 2E; the infarct region is located in the enclosed red contour. Compared to normal hearts, there was higher regional variability in both radial and circumferential motion in the infarcted heart (Figures 2A–D). Equal weighting factors for longitudinal, circumferential and radial components were chosen for the objective function, and the weighting factor for the incompressibility constraint was 4 times greater. Reflecting the greater regional variation in the presence of infarction, coefficient values in Table 2 show larger contributions from coupling and higher order terms in infarcted hearts than in normal hearts. Normalized MSE for predicted motion in the polynomial model was $7.4 \pm 2.1\%$ for infarcted hearts, and $8.2 \pm 2.3\%$ for normal mouse hearts.

Impact of the Incompressibility Constraint

Figure 5 shows the effects of tolerating different levels of myocardial volume change on the match between model-predicted and measured deformations using the generalized model. As expected, increasing the weight for the incompressibility constraint in the objective function reduced volume changes while increasing the mismatch between measured and predicted deformed positions. Increasing the weight for the incompressibility constraint had more effect on predicted longitudinal and circumferential motion than on radial motion. This trade-off between incompressibility and measured deformation may be particularly useful in the presence of locally incompatible deformations due to acquisition artifacts or limitations of speckle tracking algorithms. Figure 6 shows an SA image where myocardial displacement from end-diastole to end-systole were derived using MSAD speckle tracking. In Figure 6A,

improbable displacements are observed in the septal and posterior regions of the endocardial wall (outlined by white circles), where initially square elements appear to collapse or overlap in the deformed state. By incorporating a near incompressibility constraint using our kinematic polynomial model, improbable displacements are corrected as shown in Figure 6B.

DISCUSSION AND CONCLUSIONS

Ultrasound imaging is commonly used to image myocardial motion in patients and in animal models of heart disease. Techniques, such as speckle tracking, provide valuable information about deformation throughout the myocardium, which can be particularly valuable in diagnosing regional abnormalities such as ischemia or infarction. However, motion estimates from techniques, including speckle tracking, are also susceptible to noise and artifacts, particularly at the rapid heart rates present in small animals. Mathematical models that incorporate other known information about myocardial deformation can be used as a filter to correct errors in raw displacement or deformation data. In this paper, we present a simple kinematic model that incorporates three important aspects of myocardial deformation: the fact that myocardium is nearly incompressible; the fact that adjacent pieces of myocardium are physically connected, so that deformed positions vary smoothly in space; and regional variation in undeformed geometry. We found that a model based on relatively simple polynomial functions could capture deformation even in the setting of severe regional dysfunction due to myocardial infarction, matching measured deformations from speckle tracking well overall while correcting locally incompatible deformations that clearly reflected errors in the underlying data.

The incompressibility constraint has been widely used in cardiac image processing to improve segmentation and motion tracking (Bistoquet 2008; Garson 2008; Mansi 2010; Wang 2010; Zhu 2010). Geometric models of the left ventricle inherently incorporate both incompressibility and local smoothness of deformation, in addition to other prior information, but have been less widely used in image processing. At the simplest extreme, models that treat the equatorial region of the left ventricle (LV) as an axisymmetric, thick-walled cylinder are easy to implement, solve quickly, and have provided important insights into aspects of heart mechanics such as the impact of material properties on deformation and the genesis of LV torsion (Humphrey 1989; Guccione 1991; Costa 1996). Unfortunately, assumptions such as axisymmetry have limited the utility of these simpler models in real-world medical imaging settings. By contrast, sophisticated finite-element models that incorporate not only incompressibility and smoothness of deformation but also realistic geometries, fiber anatomy, activation patterns, etc. have proven very useful in extracting 3D displacement fields from tagged MRI image sequences (Young 1995; Young 1999; Aelen 1999). The primary limitation of these more sophisticated models is that they are time-consuming to construct and run. The kinematic approach proposed here attempts to strike a balance – incorporating incompressibility through a penalty in the objective function and local smoothness and geometric variations in undeformed geometry through the chosen polynomial functions – while limiting computational costs of fitting the model to each dataset. Our approach required less than 2 hours per animal to fit displacements to Equation 12 on an Intel Core i7 2.66 GHz processor, compared to several days typically required to

customize a finite-element model to match the geometry and deformation of an individual heart. One of the most surprising findings of this study was that deformation throughout the normal mouse heart can be so accurately described with a very simple linear model (Equations 4,7) that assumes that most components of the deformation gradient tensor are constant everywhere. In fact, while the nonzero components of the deformation gradient tensor identified from plotting displacement data here are not the same as those typically assumed in cylindrical models, the expression for radial deformation in Equation 7 turned out to be identical to that used by Guccione et al. in their classic cylindrical model of LV deformation (Guccione 1991). The success of this model in our study suggests that much of the regional variation in deformation in a normal heart must be due to regional variation in anatomy (R_0 and r_0 in Equation 7). This finding may explain in part why cylindrical models have provided so much insight into normal heart mechanics despite their obvious geometric limitations.

We introduced an objective function that allows the weight of the incompressibility constraint to be varied relative to measured deformations. As we increased the weight for the incompressibility constraint relative to the deformations (Figure 5), we found that the MSE in the incompressibility term converged to 4%, reflecting an overall change in myocardial volume of 4%. While consistent with previous studies (Judd 1991), this number also accounts for roughly half the overall NRMSE in the fitted data, which could be reduced by using a different target value for the determinant of the deformation gradient tensor. Our objective function also allowed individual deformation components to be weighted differently according to confidence in their measurement, a capability we did not utilize in this study. However, this formulation could be particularly attractive in situations where confidence in measurements of individual deformation components varies. For example, if deformation information at a point in the heart wall were derived from two intersecting views, one of which had an artifact or speckle tracking error that could be recognized by a quality metric, then de-weighting the flawed deformation information would allow the model to locally replace the missing component based on the high-quality components in the perpendicular view and the incompressibility constraint. In the case of MSAD, the actual minimum difference, versus the mean difference across all search observations, provides a convenient quality metric that is applicable in conditions appropriate for MSAD – i.e. all but very low SNR imaging.

One limitation of the modeling approach presented here is that weights for all deformation components and locations were not exactly equal. We did choose units that gave approximately equal numerical ranges for each variable (approximately 0–3 mm for radius, 0–5 mm for axial position, 0–6 radians for circumferential position). However, additional scaling of individual deformation measures in the objective functions could further improve the method, such as introducing weighting schemes that vary by component or by region. In situations where the infarct location is known, displacement functions constructed to specifically anticipate different displacements in the infarct might improve the fit to measured displacements and/or reduce the number of coefficients required to capture the spatial variability in measured displacements. We also note that we modeled deformation from end systole to end diastole, when the LV is expanding and extending, while most

models use end diastole as a reference state and examine deformations between end diastole and end systole. These two approaches provide equivalent deformation information, and can be inter-converted by taking the inverse of the deformation gradient tensor F .

In summary, we developed a kinematic model intended to offer a compromise between incorporating prior information about left ventricular deformation and limiting computational expense, assuming only that displacements in the left ventricle are polynomial functions of initial position and that the myocardium is nearly incompressible, while allowing myocardial motion to vary spatially as would be expected in an ischemic or dyssynchronous left ventricle. This model accurately represented the motion of both normal and infarcted mouse left ventricles during the cardiac cycle, with normalized root mean square errors in predicted deformed positions of only $8.2 \pm 2.3\%$ and $7.4 \pm 2.1\%$ for normal and infarcted hearts, while correcting physically unrealistic local deformation components arising from errors in speckle tracking.

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Fig. 1.

Linear regression of LV deformed longitudinal (A) and circumferential (B) positions and circumferential displacement (C) in a representative normal mouse heart. LV extension (slope > 1.0 in panel A) and torsion (different signs of mean circumferential displacement in panel C) are apparent in both raw and fitted data.

Fig. 2.

Radial (panels A and B) and circumferential (panels C and D) observed (circles) and polynomial model predicted (triangles) displacement of points throughout the myocardium as derived from speckle tracking using SA B-mode images for infarcted (panels A and C) and normal (panels B and D) hearts. X-axes in panels A and B are myocardial position in SA view as defined in panel E. Region in the enclosed red contour is the infarcted zone, with minimal radial displacement and clockwise circumferential motion.

Fig. 3. Linear model simulations for normal hearts using different combinations of a and c . The NRMSE is calculated for each simulation and the combination with the minimum NRMSE (arrow) represents the optimal parameter values.

Fig. 4. Observed and linear model-predicted radial motion at the basal (A), midventricular (B) and apical (C) levels of a normal LV.

Fig. 5.

Mean Squared Error (MSE) in the polynomial model for each component of the optimization Equation (13) for a representative infarcted heart. Higher incompressibility weights push the determinant value closer to 1, decreasing incompressibility error (blue curve). The tradeoff for increasing incompressibility weights is the increase in error in the longitudinal (black curve) and radial (red curve) deformation components.

Fig. 6. Color map of myocardial displacement derived from using MSAD speckle tracking only (A), and corrected displacement map using the polynomial kinematic model (B). Color represents relative magnitude of displacement. In (A), improbable displacements are observed where myocardial regions appear to collapse or overlap as shown inside the white circle.

Table 1

Optimized values for linear model parameters:

Parameter	Value
a	1.03 ± 0.12
b	-0.09 ± 0.04 rad
c	1.12 ± 0.08
d	-0.18 ± 0.03 mm
r	-0.01 ± 0.004 rad/mm

Table 2

Normalized coefficient values for polynomial model:

Parameter	Normal Heart	Infarcted Heart
$r(R)$	R_c	-0.53 ± 0.12
	g_i	1.35 ± 0.19
	h_i	0.91 ± 0.18
		-4.15 ± 1.35
		10.29 ± 5.21
		-28.21 ± 6.61
		5.41 ± 2.17
$r(R, \Theta)$	x_1	-1.42 ± 0.21
	x_2	0.06 ± 0.02
	x_3	1.25 ± 0.31
	x_4	0.02 ± 0.12
$r(\Theta, Z)$	v_1	0.26 ± 0.07
	v_2	0.01 ± 0.12
$\theta(\Theta)$	Θ_c	$.09 \pm 0.05$
	s_i	-0.24 ± 0.11
	t_i	0.76 ± 0.18
		2.42 ± 0.91
		-9.81 ± 3.26
		12.59 ± 6.27
		-7.48 ± 3.46
$\theta(R, \Theta)$	y_1	-0.11 ± 0.05
	y_2	0.45 ± 0.13
	y_3	0.14 ± 0.08
	y_4	-0.03 ± 0.12
$\theta(\Theta, Z)$	w_1	0.11 ± 0.14
	w_2	-0.09 ± 0.10
$z(\Theta, Z)$	Z_c	-0.14 ± 0.05
	u_1	0.04 ± 0.02
	u_2	1.15 ± 0.06
	u_3	-0.01 ± 0.06