Akinetic myocardial infarcts must contain contracting myocytes: finite-element model study

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Dang, Alan B. C., Julius M. Guccione, Jacob M. Mishell, Peng Zhang, Arthur W. Wallace, Robert C. Gorman, Joseph H. Gorman III, and Mark B. Ratcliffe. Akinetic myocardial infarcts must contain contracting myocytes: finite-element model study. Am J Physiol Heart Circ Physiol 288: H1844–H1850, 2005. First published December 16, 2004; doi:10.1152/ajpheart.00961.2003.—Infarcted segments of myocardium demonstrate functional impairment ranging in severity from hypokinesis to dyskinesis. We sought to better define the contributions of passive material properties (stiffness) and active properties (contracting myocytes) to infarct thickening. Using a finite-element (FE) model, we tested the hypothesis that infarcted myocardium must contain contracting myocytes to be akinetic and not dyskinetic. A three-dimensional FE mesh of the left ventricle was developed with echocardiographs from a reperfused ovine anterolateral infarct. The nonlinear stress-strain relationship for the diastolic myocardium was anisotropic with respect to the local muscle fiber direction, and an elastance model for active fiber stress was incorporated. The diastolic stiffness ($C$) and systolic material property (isometric tension at longest sarcomere length and peak intracellular calcium concentration, $T_{\text{max}}$) of the uninfarcted remote myocardium were assumed to be normal ($C = 0.876 \text{kPa}$, $T_{\text{max}} = 135.7 \text{kPa}$). Diastolic and systolic properties of the infarct necessary to produce akinosis, defined as an average radial strain between −0.01 and 0.01, were determined by assigning a range of diastolic stiffnesses and scaling infarct $T_{\text{max}}$ to represent the percentage of contracting myocytes between 0% and 100%. As $C$ was increased to 11 times normal ($C = 10 \text{kPa}$) the percentage of $T_{\text{max}}$ necessary for akinosis increased from 20% to 50%. Without contracting myocytes, $C = 250 \text{kPa}$ was necessary to achieve akinosis. If infarct stiffness is < 285 times normal, contracting myocytes are required to prevent dyskinetic infarct wall motion.

Despite advances in the understanding of the pathophysiology of ischemic and infarcted myocardium at the tissue, cellular, and molecular levels, it is unknown what determines the ultimate degree of functional impairment. Possible reasons for the range of observed outcomes include size of the area, location, magnitude and direction of regional stress and strain, percentage of surviving contractile myocytes, degree of ischemic preconditioning, and the characteristics of the surrounding border zone (BZ) tissue. The systolic and diastolic function of an infarcted segment is likely a complex interaction of a multitude of internal and external factors.

We sought to better define the effects of passive material properties (stiffness) and active properties (contracting myocytes) on infarct thickening. For instance, although myocardial material properties are nonlinear (7), large-deformation analysis using linear material properties suggests that the resistance of a plate to bending is a function of material stiffness and plate thickness (8). Akinetic behavior might, therefore, be due to increased infarct thickness and material stiffness. Alternatively, akinetic regions often show contractile reserve with dobutamine stimulation, a phenomenon attributed to the presence of viable myocytes (17).

We previously simulated (11) the BZ of an ovine anterolateral infarct with a large deformation finite-element (FE) model of the LV incorporating nonlinear diastolic and systolic material properties (function) linked to myocyte fiber architecture. Although BZ systolic function was thought to be normal and altered BZ systolic motion the result of high stress (17, 23), we were able to show that BZ systolic function must be reduced by 50% for the BZ to stretch during isovolumic systole (11). Given that such FE simulations can calculate regional deformation and stress from the unloaded structural geometry (LV at early diastolic filling), external loads (LV cavity pressure), and material properties, the FE method is inherently suited to determine the contribution of contracting myocytes in akinetic vs. dyskinetic segments.

We developed a FE simulation based on an ovine model of ischemia and reperfusion. Of note, reperfusion of an anterolateral sheep infarct after 1 h produced an akinetic infarct as well as significant LV remodeling at 12 wk (infarct thickness 5.1 ± 0.3 mm; LV volume at end systole 33 ± 6 ml) (4). We used that FE simulation to address two questions: 1) Can akinetic myocardium be modeled as a stiff region of dense fibrosis and noncontractile muscle? and 2) What is the relationship between...
the number of contracting myocytes and the diastolic stiffness in akinesia? We tested the hypothesis that akinetic myocardium contains contracting myocytes.

**MATERIALS AND METHODS**

The three-dimensional (3D) FE method of Costa et al. (6) for large elastic deformations of ventricular myocardium was used, together with the mathematical descriptions for normal diastolic and systolic myocardial material properties (stress-strain relations) of Guccione et al. (9). FE modeling and analysis were performed on a UNIX workstation (Octane2; SGI, Mountain View, CA).

**Sheep Reperfused Infarct and Echocardiography**

All animal procedures conformed to the “Guiding Principles for Research Involving Animals and Human Beings” of the American Physiological Society. A single sheep from a group previously reported by Bowen et al. (4) underwent anteroapical ischemia and reperfusion after 1 h. Subdiaphragmatic two-dimensional (2D) long-axis echocardiographs were obtained through a sterile midline laparotomy (1.8- to 4.2-MHz probe; SONOS 5500, Agilent Technologies, Andover, MA) 12 wk after infarction. Long-axis images were recorded on VHS videotape at 30 Hz (Panasonic AG-6300; Matsushita Electric). Echocardiographs at early diastolic filling (Fig. 1A), end diastole, and end systole were digitized (WinTV USB; Hauppauge Computer Works, Hauppauge, NY) and analyzed (Findtags; Medical Imaging Lab at Johns Hopkins University School of Medicine, Baltimore, MD). End diastole was defined as the interval immediately preceding the onset of the QRS segment of the electrocardiogram. Early diastolic filling was defined by opening of the mitral valve. End systole was defined as the smallest LV cavity cross-sectional area after the QRS complex. The early diastolic filling state was our stress-free reference state for FE simulations of end-diastolic and end-systolic ventricular mechanics. Epicardial and endocardial contours were hand traced, and the border between the akinetic and kinetic regions was visually identified, using the video as a guide.

**FE Mesh and Boundary Conditions**

A 2D prolate spheroidal mesh of the LV (Fig. 2A) was constructed from 32 points on each of the endocardial and epicardial contours. With the use of a 25.0-mm focal length, the FE software (Continuity; Cardiac Mechanics Research Group at the University of California, San Diego, CA) generated an interpolated 3D model. Further subdivision of the mesh into 8 elements circumferentially and 3 elements transmurally produced a 192-element model of the LV (Fig. 2B). This low-order FE mesh in curvilinear coordinates allows fewer nodes to represent LV geometry than would be necessary with a Cartesian coordinate system. The subdivision allowed regional, nonsymmetrical variation of the ventricular wall. Longitudinal displacement of nodes at the apex and base and circumferential displacement of the epicardial node at the base were constrained.

Muscle fiber orientation was assumed to vary linearly in the transmural direction from 60° clockwise at the endocardium to 60° counterclockwise at the epicardium, based on experimental measurements by Streeter et al. (32) in canine hearts, in the absence of human data. The sarcomere length throughout the LV was 1.845 μm, following the suggestion of Kresh and Wechsler (20) that a dilated, volume-overloaded heart is devoid of residual stress and the stress-free sarcomere length measured in rats by Rodriguez et al. (30).

**Material Properties**

**Diastolic material properties.** Diastolic and systolic material properties of the LV wall were assumed to be homogeneous and anisotropic. Diastolic material properties were described by the strain energy potential (W) developed by Guccione et al. (9) to describe myocardium as a nonlinear material that is anisotropic (transversely isotropic) with respect to the local muscle fiber direction:

\[ W = \frac{C}{2} \left\{ \exp[b_1E_{11}^2 + b_2(E_{22}^2 + E_{33}^2 + E_{23}^2 + E_{13}^2)] - 1 \right\}, \]

where \( E_{11} \) is fiber strain, \( E_{22} \) is cross-fiber in-plane strain, \( E_{33} \) is radial strain, \( E_{23} \) is shear in the transverse plane, and \( E_{12} \) and \( E_{13} \) are shear strains.

**Systolic material properties.** Systolic material properties were described by the strain energy potential (W) developed by Streeter et al. (32) in canine hearts, in the absence of human data. The sarcomere length throughout the LV was 1.845 μm, following the suggestion of Kresh and Wechsler (20) that a dilated, volume-overloaded heart is devoid of residual stress and the stress-free sarcomere length measured in rats by Rodriguez et al. (30).
strain in the fiber-cross fiber and fiber-radial coordinate planes, respectively. Guccione et al. (10) found that the material constants of stiffness \( (C) = 0.876 \text{kPa}, b_h = 18.48, b_l = 3.58, \) and \( b_w = 1.627, \) where the subscripts fst, and fs are fiber, transverse, and fiber shear, respectively, allowed a cylindrical model of the LV to match epicardial strains measured in an intact canine heart during passive LV filling. Solutions were obtained at a range of diastolic \((0–40 \text{mmHg})\) LV pressures.

Systolic material properties. Systolic contraction was modeled by defining the (second Piola-Kirchhoff) stress tensor referred to fiber \( v^n \)-coordinates in the undeformed body as the sum of the passive 3D stress derived from \( W \) and an active fiber-directed component, \( T_0, \) which was a function of time \( (t), \) peak intracellular calcium concentration \( (C_{a0}), \) and sarcomere length \( (l) \) (14)

\[
\tau^{ab} = \frac{1}{2} \left( \frac{\partial W}{\partial E_{ab}} + \frac{\partial W}{\partial E_{ba}} \right) - \rho g^{ab} + T_0(t,C_{a0})\delta_1^{ab},
\]

(2)

where the contravariant metric tensor refers to fiber coordinates \( g^{ab} = (\partial x^a/\partial x^b) \) \( \delta_1^{ab} \) is the Kronecker delta; its value is unity if \( \alpha = \beta \) (i.e., \( \delta_1^{11} = \delta_1^{22} = \delta_1^{33} = 1 \)) and its value is zero if \( \alpha \neq \beta \). Thus, only the case in which \( \delta_1^{11} \) is not equal to zero is when \( \alpha = 1 \) (fiber-directed component). \( x^a \) is rectangular Cartesian coordinates in the deformed state, and \( v^n \) \( \delta_1^{ab} \) are fiber coordinates in the undeformed state. We introduced the hydrostatic pressure \( p \) as the Lagrange multiplier needed to enforce the kinematic constraint that the third principal strain invariant \( (I_3) \) equals 1. The FE stress analysis of Guccione and colleagues (9) suggested that at end systole

\[
T_0 = T_{\text{max}} \frac{C_{a0}}{C_{a0} + E C_{a0}},
\]

(3)

where \( T_{\text{max}} \) is the isometric tension achieved at the longest sarcomere length and peak \( C_{a0} \) [(\( C_{a0}\)max)]. The length-dependent calcium sensitivity and the internal variable are given by

\[
E C_{a0} = \frac{(C_{a0})_{\text{max}}}{\exp[B(l - l_0)] - 1}
\]

(4)

and

\[
C_l = \frac{1}{2} (1 - \cos \omega),
\]

(5)

where \( B \) is a constant, \( l_0 \) is the sarcomere length at which no active tension develops, and

\[
\omega = \pi \left( \frac{0.25 + t_c}{t_c} \right)
\]

(6)

In Eq. 6, the duration of relaxation \( (t_c) \) is a linear function of sarcomere length

\[
t_c = m l + b,
\]

(7)

where \( m \) and \( b \) are constants. Because material properties for sheep are not well defined, canine material properties were used (11). Previously, we found (9) that the values \( T_{\text{max}} = 135.7 \text{kPa}, C_{a0} = 4.35 \mu \text{M}, (C_{a0})_{\text{max}} = 4.35 \mu \text{M}, B = 4.75 \mu \text{m}^{-1}, l_0 = 1.58 \mu \text{m}, m = 1.0489 \mu \text{m} \mu \text{m}, \) and \( b = -1.429 \) allowed an FE model of the beating dog heart to predict end-systolic in-plane normal and shear-strain distributions from a midventricular region of the anterior LV free wall consistent with experimental measurements (33, 35).

A sharp boundary was assumed between the infarcted and uninfarcted regions, and diastolic and end-systolic material properties of the remote uninfarcted myocardium were assumed to be normal \( (C = 0.876 \text{kPa}, T_{\text{max}} = 135.7 \text{kPa}) \). Scaling the parameter \( T_{\text{max}} \) by a “percentage of contracting myocytes” between 100% and 0% reduced the ability of the infarcted region to develop active stress. This approach [as opposed to altering \( (C_{a0})_{\text{max}} \) (10) does not change the shape of the relationship between active stress and sarcomere length. Of note, \( T_{\text{max}} \) represents the percentage of surviving infarct myocytes; all are assumed to have normal contractility. In each case the end-systolic elastance \( (E_{\text{es}}) \) is obtained by \( I \) incrementally increasing \( T_{\text{max}} \) in both the remote and infarct regions and load to 120 mmHg and then \( 2 \) reducing load to 0 mmHg.

Quantification of Akinesis

Echocardiography. Regional function was calculated with the center line method (31).

FE models. The change in wall thickness between end diastole and end systole was measured with the average radial strain \( (RS) \) which describes the fractional change of wall thickness. Negative RS indicates thinning of the myocardial wall during systole (dyskinesis). Positive values indicate wall thickening (contraction). RS was measured at 24 locations distributed throughout the akinetic region. These represent all the locations where RS can be directly calculated in our model. Akinesis was defined as an average RS between \(-0.01 \) and \( 0.01 \).

At a given diastolic stiffness, the percentage of surviving myocytes was modified until akinesia was observed. \( T_{\text{max}} \) was increased when the RS indicated a dyskinetic heart and decreased when the result was hypokinesis until akinesia was obtained.

Finally, to determine the amount of diastolic stiffness required for akinesia in a region with no contracting myocytes, we ran an initial simulation with diastolic stiffness \( C = 0.876 \text{kPa} \) (“normal diastolic stiffness”) and no contractility. These conditions produced a dyskinetic LV. Subsequent simulations increased diastolic stiffness in the abnormal region until akinesia was reached.

Statistical analysis. All values are expressed as means ± SD. RS from different infarct areas (apex, midinfarct, BZ) and groups (hypokinetic, akinetic, dyskinetic) were compared with ANOVA, and individual comparisons were adjusted with the Bonferroni correction (Prism 3.0, GraphPad, San Diego, CA).

RESULTS

Echocardiography

Center-line measurement of regional function on echocardiographs documented akinesis (Fig. 1B).

FE Output

Figure 3A shows the model configuration obtained for an end-diastolic LV chamber pressure of 2.67 kPa (20 mmHg) and normal diastolic stiffness. Figure 3B shows the akinetic model at end systole, with a LV chamber pressure of 13.33 kPa (100 mmHg). The superimposed image of the endocardial surface at end diastole and end systole is shown in Fig. 3C.

Contractile infarct. When the infarct was assigned a normal diastolic stiffness, 20% of the myocytes \( (T_{\text{max}} = 27.1 \text{kPa}) \) needed to contract to produce akinesis (average RS = 0.0033). Reducing the number of contracting myocytes (“percent contractility”) to 10% \( (T_{\text{max}} = 13.6 \text{kPa}) \) produced dyskinetic infarct (average RS = −0.0381) and a hypokinetic infarct (average RS = 0.0787) at 35% \( (T_{\text{max}} = 47.5 \text{kPa}) \). The difference in RS between groups (hypokinetic vs. akinetic vs. dyskinetic) was statistically significant \( (P < 0.0001) \).

Figure 4 shows the RS of these models plotted against the position of the infarct. Notably, the region of the infarct closest to the BZ had the greatest variability in RS. In the akinetic and dyskinetic model, there is an increase in RS, whereas the hypokinetic model has reduced RS at the region closest to the BZ. The statistically significant difference in RS between
groups ($P < 0.0001$) and pattern of akinesis flanked by dyskinesis and hypokinesis was seen in all diastolic stiffness parameters tested (Fig. 5). Table 1 summarizes these results.

**Noncontractile infarct.** Our simulations demonstrate that akinesis in a region void of contracting myocytes must be 285 times stiffer than normal myocardium. For instance, increasing diastolic stiffness to 100 or even 200 was insufficient for akinesia (average RS of $0.0233$ and $0.0121$, respectively). The LV remained dyskinetic until the segments were made 285 times stiffer than normal myocardium (average RS of $0.0098$). In the physiological stiffness range of 0.876 to 10 kPa, the models with no contractility demonstrated significant dyskinesia, with average RS ranging from $0.08$ to $0.07$. Figure 6 provides a complete summary of results.

**DISCUSSION**

Our simulations demonstrate that akinesis in a region void of contracting myocytes must be 285 times stiffer than normal myocardium. If infarct stiffness is $285$ times normal, contracting myocytes are required to prevent dyskinetic infarct wall motion. It is not merely possible for normal myocytes to survive in a region of akinesia: contracting myocytes are obligatory.

**Number and Function of Surviving Infarct Myocytes**

Although muscle content in akinetic segments can range from $<25\%$ to $70\%$ (2), there are no published data addressing the number of myocytes in akinetic infarcts that contract. Of note, colorimetric analysis of infarct histology from the sheep model on which the current FE simulations are based (4) shows that $28\%$ of the infarct is surviving muscle. The amount of fibrosis in akinetic segments is also highly variable and can vary between $17\%$ to $>50\%$ (2, 24).

Our simulations assume that all surviving infarct myocytes have normal contractility. This is unlikely. Studies performed on skeletal muscle preparations demonstrate reduced myocyte contractility in a hypoxia-reperfusion injury model (19). However, others did not find reduced contractility of individual cardiomyocytes exposed to ischemic conditions (5). In future studies, we will model the effect of both reduced numbers of
infarct myocytes and reduced infarct myocyte function. Although this will improve the precision of the model, it will not affect the final results we report here.

**Measurement of Infarct Material Properties**

A range of diastolic and end-systolic material properties was able to produce akinesis. Specifically, for each value of diastolic stiffness, a unique number of contracting myocytes necessary to prevent dyskinesis can be calculated. Conversely, knowing diastolic infarct stiffness should allow the calculation of end-systolic infarct stiffness. For instance, if biaxial testing shows the passive stiffness of akinetic infarct to be 5 kPa, our methodology would estimate the number of contracting myocytes to be 35% of preinfarct values.

Biaxial mechanical stretch testing can directly measure the stiffness properties of ventricular aneurysm (15) but may be problematic in akinesis: the increased thickness and varying myofiber direction throughout the tissue sample result in shear and torsion during testing, producing heterogeneous deformation. Analysis and interpretation of the biaxial data would be possible only in conjunction with FE methods.

Moulton and colleagues (22) have suggested, as an alternative or complement to biaxial mechanical testing, MRI tissue tagging, FE analysis, and nonlinear optimization to determine the nonlinear material properties of passive, diastolic myocardium. Material parameters for a proposed exponential strain energy function were determined by minimizing the least-squares difference between FE model-predicted and MRI-measured strains. FE models were constructed from early diastolic images and were loaded with the mean early to late LV and right ventricular diastolic change in pressure measured at the time of imaging. A nonlinear optimization algorithm solved the least-squares objective function for the material parameters. Although they modeled myocardium inappropriately as an isotropic material, they suggested that their parameter estimation algorithm provides the necessary framework for estimating the nonlinear, anisotropic, and heterogeneous material properties of passive myocardium in health and disease in the in vivo beating heart.

Bovendeerd et al. (3) previously described a FE model of the LV with ischemic anterior wall. The initial unloaded LV geometry was a thick-walled, truncated ellipsoid. Similar to our study, the diastolic stress-strain relationship was nonlinear, active fiber stress was the sum of passive and contractile stresses, and material properties were aligned with myocyte fiber angles. However, Bovendeerd et al. considered myocardial contractility to be an on-off effect. Specifically, ischemic myocardium was assumed to have no contractility, whereas nonischemic myocardium had normal contractility. Also, although model predictions of epicardial fiber shortening in and around the ischemic region were in qualitative agreement with experimental measurements obtained in four dogs, Bovendeerd et al. (3) made no attempt to vary material parameters so that model-derived and experimentally measured strains were in the best possible agreement.

**Relationship Between Diastolic and End-Systolic Material Properties**

As stiffness increases, the number of contracting myocytes required for akinesis also increases. Increased numbers of contractile myocytes in a region with strong stiffness are likely explained by the effect of infarct stiffness on sarcomere length. If the infarct has high stiffness, there will be less sarcomere extension at end diastole and infarct sarcomeres will generate less force per unit area. (11). However, the sarcomere length in myocytes surviving within an infarct and the effect of infarct expansion have not been measured.

**Model Limitations**

We varied the strength of active contraction in the infarcted region by varying the corresponding active stress parameter, $T_{max}$. In a previous study (11), we used the same approach to determine contractility in the BZ region of LV aneurysm that would allow a FE model to simulate myocardial deformation as observed experimentally. Alternatively, we could have varied contractility regionally by using the active stress parameter $C_a$ (as we did in our FE models of ventricular volume reduction surgery and cellular transplantation; Refs. 12, 29). This approach, however, can have marked changes in the shape of the relationship between active stress and sarcomere length (i.e., concave down, linear, or concave up). Owing to our lack of knowledge concerning myocardial mechanical properties in

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**Table 1. Average radial strain as function of stiffness and percentage of contracting myocytes**

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<thead>
<tr>
<th>Diastolic Stiffness, kPa</th>
<th>Percentage of Myocytes Actively Contracting</th>
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<tbody>
<tr>
<td></td>
<td>10</td>
</tr>
<tr>
<td>Normal (0.876)</td>
<td></td>
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<tr>
<td>Increased (5.0)</td>
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<tr>
<td>Largely increased (10.0)</td>
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**Diagram:**

![Plot of average radial strain as a function of diastolic stiffness in models in which the infarct contains no contracting myocytes.](http://ajpheart.physiology.org/ by 10.220.33.5 on October 2, 2017)
dilated and ischemic cardiomyopathy, we cannot be certain which approach is more appropriate. Nevertheless, the approach used in the present study is simpler and appears to be appropriate for the case in which there is partial loss of contractile myocytes in a ventricular region. Our model also did not consider the recent reports of myocardium as being slightly compressible or as having radial active stress (21, 34). In both cases, comparison of simulations with myocardial strain measured using MRI with tags will probably be beneficial.

The present model provides results only during diastole and at the end of systole. To include the isovolumetric contraction phase and to model a completely realistic pressure-volume relationship, we could add a circulatory model (e.g., a 2- or 3-element windkessel model). However, our time-varying elasticity approach to modeling systolic contraction is completely valid only at end systole. On the other hand, we do not believe that RS varies significantly during systole in akinetic regions of the LV wall. Two recent publications support this. Pislaru et al. (28) used tissue Doppler echocardiography to measure radial strain in pigs 60 min after 90 min of left anterior descending coronary artery ischemia followed by reperfusion. Figure 4B of Pislaru et al. (28) shows radial infarct strain to be virtually flat, with values ranging from 0 to −2% (estimated). In a second paper, Azevedo et al. (1) used MRI with tags to measure circumferential strain in dogs 24 h after 90 min of LAD ischemia followed by reperfusion. Again, Fig. 3 of Azevedo et al. (1) shows circumferential infarct strain to be virtually flat, with estimated values ranging from +1% (isovolumic contraction) to −2% (estimated). In summary, although there may be significant infarct stretching during isovolumic systole in either acute ischemia or in a completed transmural infarct, this effect seems less important in a reperfused akinetic infarct.

A convergence analysis using 256 elements confirmed our calculation of systolic function in the akinetic region. Specifically, in an infarcted region with normal diastolic stiffness, akinesis was obtained with 18% contractility. A convergence analysis evaluating dyskinesis in stiff regions was not feasible before the sharp boundary between the akinetic and normal elements and the significantly differing material properties, a problem previously encountered (13). It was also not feasible to increase the number of elements beyond 256 with current software.

Our model utilizes realistic LV geometry, diastolic myocardial material properties that are anisotropic with respect to the local muscle fiber orientation, and systolic contraction based on experimental measurements of active tension-sarcomere length relationships. This representation of the akinetic LV is the most realistic to date. One limitation is that the 3D FE mesh is based on ultrasound, a 2D imaging modality. Additionally, the orientation of muscle fibers in a human model of ischemic cardiomyopathy remains unknown.

**Therapeutic Implications**

Current methods of determining myocardial function and viability may have inadequate sensitivity and specificity to detect small regional changes (27). Furthermore, our data suggest that they may underestimate contractility in akinesia. The FE model is a powerful tool that permits localization and quantification of small regional changes in diastolic and systolic mechanics. The FE method may be an appropriate adjunct for areas of investigation that require precise identification of changes of regional myocardial function. FE modeling may therefore be useful in areas of research including cell transplantation, reperfusion, stress reduction, and antiapoptotic therapies.

**Future Directions**

Our results demonstrate that contracting myocytes are an important and necessary component of akinesis at physiological ranges of diastolic stiffness. Future studies (simulations) will model the effect of both reduced numbers of infarct myocytes and reduced infarct myocyte function. FE methodology may be used to evaluate the effect of reperfusion, stress reduction, antiapoptotic, and cell transplantation therapies.

**GRANTS**

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