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OPTIMIZATION OF CARDIAC FIBER ORIENTATION FOR HOMOGENEOUS FIBER STRAIN AT BEGINNING OF EJECTION

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Abstract—Mathematical models of left ventricular (LV) wall mechanics show that fiber stress depends heavily on the choice of muscle fiber orientation in the wall. This finding brought us to the hypothesis that fiber orientation may be such that mechanical load in the wall is homogeneous. Aim of this study was to use the hypothesis to compute a distribution of fiber orientation within the wall.

In a finite element model of LV wall mechanics, fiber stresses and strains were calculated at beginning of ejection (BE). Local fiber orientation was quantified by helix (HA) and transverse (TA) fiber angles using a coordinate system with local r -, c -, and l -directions perpendicular to the wall, along the circumference and along the meridian, respectively. The angle between the c -direction and the projection of the fiber direction on the cl -plane (HA) varied linearly with transmural position in the wall. The angle between the c -direction and the projection of the fiber direction on the cr -plane (TA) was zero at the epicardial and endocardial surfaces. Midwall TA increased with distance from the equator. Fiber orientation was optimized so that fiber strains at BE were as homogeneous as possible.

By optimization with $TA = 0^\circ$, HA was found to vary from 81.0° at the endocardium to -35.8° at the epicardium. Inclusion of TA in the optimization changed these angles to respectively 90.1° and -48.2° while maximum TA was 15.3° . Then the standard deviation of fiber strain (ϵ_f) at BE decreased from $\pm 12.5\%$ of mean ϵ_f to $\pm 9.5\%$. The root mean square (RMS) difference between computed HA and experimental data reported in literature was 15.0° compared to an RMS difference of 11.6° for a linear regression line through the latter data.

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Keywords: Left ventricle; Fibers; Optimization; Finite element analysis.

INTRODUCTION

Within the cardiac wall, stress and strain are important determinants of the distributions over the cardiac wall of blood flow, oxygen consumption (Delhaas *et al.*, 1994) and tissue adaptation effects (Arts *et al.*, 1994). Experimental assessment of the stress and strain distributions over the wall is difficult. Strain can be accurately measured at only a limited number of sites in the wall (Prinzen *et al.*, 1986; Waldman *et al.*, 1988). The reliability of the measurement of wall stress is limited, because insertion of a force transducer damages the tissue at the site of measurement (Huisman *et al.*, 1980). In the assessment of cardiac function, stress and strain expressed with respect to muscle fiber orientation is most relevant. However, accurate knowledge of regional muscle fiber orientation is often not available.

Because of these experimental limitations, mathematical models have been developed to facilitate assessment of the distributions of stress and strain. Advances in computer hardware and numerical methods have enabled an increasing number of aspects of cardiac mechanics to be simulated. The more recent models generally consider the fibrous nature of cardiac tissue, increasingly accurate descriptions of wall shape, nonlinear stress-strain relationships and finite deformations (Arts and

Reneman, 1989; Bovendeerd *et al.*, 1992; Huyghe *et al.*, 1992; Guccione *et al.*, 1995). Unfortunately the predicted distributions of fiber stress and strain disagree. Guccione *et al.* (1995) used a measured wall geometry and distribution of fiber orientation and calculated an inhomogeneous distribution of fiber stress and strain. Bovendeerd *et al.* (1992) and Huyghe *et al.* (1992) adapted fiber orientation heuristically so that the distribution of fiber stress was more even. The thus determined fiber orientation appeared not to be significantly different from what has been measured in experiments (Nielsen *et al.*, 1991; Streeter, 1979). The latter models indicate that the distribution of fiber stress is sensitive to the distribution of fiber orientation, even within the limits of biological variance. Combining this finding with the fact that muscle fiber contraction is most efficient for a particular combination of fiber shortening and fiber stress, we came to the hypothesis that mechanical load may be distributed evenly over the wall by proper adjustment of local fiber orientation. Various experimental findings are in compliance with homogeneous mechanical loading of the LV wall. If the distribution of mechanical load is disturbed, adaptation effects, such as growth (Cooper IV *et al.*, 1985; Grossman *et al.*, 1975; Prinzen *et al.*, 1995) or changes in fiber orientation (Carew and Covell, 1979; Pearlman *et al.*, 1982) result in at least partial recovery to the original loading level.

In this study we predicted the orientation of muscle fibers using the hypothesis that mechanical load in the cardiac wall is homogeneous. In a finite element model of LV wall mechanics the distribution of fiber stress and

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strain over the wall was calculated at a single moment during the cardiac cycle for given fiber orientation and given stiffness of the fibers. In the reference state of deformation left ventricular cavity pressure was zero and wall stress was zero everywhere. The stress state at beginning of ejection was obtained by stiffening of the fibers while pressurizing the cavity. In an optimization procedure inhomogeneity of mechanical load, defined as the variance of fiber strain at the beginning of ejection, was minimized by proper adjustment of the fiber orientation. The thus predicted fiber orientation was compared with anatomical findings.

METHODS

Finite element model of left ventricular wall mechanics

Reference state. To calculate fiber stresses and strains with a finite element model a reference state must be defined. We used as a reference the state in which transmural pressure across the LV wall and the stresses in the wall were 0 kPa.

Geometry. In the reference state the LV wall is considered thick-walled and rotationally symmetric around the long axis. The center of the equatorial plane is a point of symmetry. Consequently, only the mechanics of the region between the apex and equator was considered. The shape of the LV wall in the reference state was defined by a prolate spheroidal midwall surface with a wall thickness perpendicular to the midwall. The wall shape was defined by five parameters (Appendix) whose values were chosen so that the LV had given values for: cavity volume, ratio of cavity-to-wall volume, ratio of equatorial-to-apical-wall thickness, and ratio of midwall-long-to-short-axes. The geometry parameters were also such that wall thickness decreased smoothly from equator to apex. For the evaluation of cavity and wall volumes it was assumed that the base extended vertically above the equatorial plane by a distance equal to half the semi-major axis of the midwall surface (Streeter and Hanna, 1973). The choice of parameter values of the finite element model, including LV wall geometry, are described in a separate section below.

Fiber orientation. Fiber orientation in the reference state was quantified by the helix and transverse fiber angles (Streeter, 1979) measured with respect to the local transmural, circumferential and longitudinal directions (Fig. 1). To be able to define the local transmural, circumferential and longitudinal directions, we first define a wall-bound coordinate system (u, v) (Fig. 2); the coordinate u decreases from 0 at the equator to -1 at the apex in direct proportion with distance along the midwall surface in the equator-to-apex direction; the coordinate v increases from -1 at the endocardium to $+1$ at the epicardium in direct proportion with distance in the direction perpendicular to the midwall surface. The local transmural direction was then defined as the outward normal to a surface of constant v . The local longitudinal direction is orthogonal to both the transmural and circumferential directions. The helix fiber angle was defined as the angle between the local circumferential direction

Fig. 1. Illustration of the helix (α_h) and transverse (α_t) fiber angles in the rotationally symmetric LV. The fiber angles at a point P are defined with respect to the local transmural, longitudinal and circumferential directions.

Fig. 2. Diagram showing rotationally symmetric LV geometry and coordinate systems: (a) cartesian coordinate system (x, y, z) and (b) wall-bound coordinate system (u, v); point P has coordinates (u_p, v_p). Both u and v vary linearly with distance.

and the projection of the fiber direction on the plane perpendicular to the local transmural direction. The transverse fiber angle determines the degree to which fibers cross over between inner and outer wall surfaces. It was defined as the angle between the local circumferential direction and the projection of the fiber direction on the plane perpendicular to the local longitudinal direction. The spatial distributions of the helix and transverse fiber angles are specified with respect to the wall-bound coordinate system (u, v). The helix fiber angle, α_h , varies with v according to (Fig. 3):

$$\alpha_h(v) = p_1 + p_2 v, \quad (1)$$

where p_1 and p_2 are parameters whose optimal values are to be determined. The transverse fiber angle, α_t , is zero at the wall boundaries, i.e. fibers are assumed not to end here. Because the equatorial plane is a plane of symmetry, α_t is an odd function in coordinate u (Streeter *et al.*, 1978). To satisfy the latter conditions, we used the following equation (Fig. 3):

$$\alpha_t(u, v) = p_3 (1 - v^2) \sin(\pi u/2), \quad (2)$$

where parameter p_3 has to be optimized.

Fig. 3. Variation of the fiber angles over the LV wall: (a) the helix fiber angle, α_h , changes linearly between inner and outer walls with intercept p_1 and slope p_2 ; (b) the transverse fiber angle, α_t , changes quadratically in transmural direction and sinusoidally in equator-to-apex direction. Parameter p_3 , the depth of the valley, is used to optimize α_t .

Constitutive behavior. The aim of this section is the development of a mathematical relation between the second Piola–Kirchhoff stress and the Green–Lagrange strain for cardiac tissue. Myocardial tissue is a mixture of several components. Interlacing networks of branching muscle fibers and blood vessels are tethered by collagen fibers and surrounded by intercellular fluids. The muscle fibers contain sarcomeres, protein units capable of generating contractile force under the influence of calcium ions. In the model, myocardial tissue is assumed to consist of stiff elastic muscle fibers embedded in a soft elastic tissue matrix.

The deformation of the tissue is described by the deformation gradient tensor, $\mathbf{F}$, which maps an infinitesimal material vector in the reference state, $d\mathbf{x}_0$, to a material vector, $d\mathbf{x}$, in the deformed state (Malvern, 1969):

$$d\mathbf{x} = \mathbf{F} \cdot d\mathbf{x}_0. \quad (3)$$

The Green–Lagrange strain, $\mathbf{E}$, is related to $\mathbf{F}$ by

$$\mathbf{E} = \frac{1}{2}(\mathbf{F}^T \cdot \mathbf{F} - \mathbf{I}), \quad (4)$$

where $\mathbf{I}$ is the identity tensor and superscript T stands for transpose. Strains are expressed with respect to a local coordinate system: one of the coordinate axes points in the fiber direction, $\mathbf{e}_f$, and the other two are perpendicular to it. With respect to this fiber-bound coordinate system the Green–Lagrange strain tensor, $\mathbf{E}$, has components E_{ij} . E_{11} is the strain in the fiber direction. The sarcomeres are aligned with the fiber direction (McLean and Prothero, 1992). Sarcomere length, l_s (μm), is related to strain in the fiber direction, E_{11} , by

$$l_s = l_{s,0}(2E_{11} + 1)^{1/2}, \quad (5)$$

where $l_{s,0}$ (μm) is sarcomere length in the reference state.

The total second Piola–Kirchhoff stress, $\mathbf{S}$, in the tissue is the sum of a passive component, $\mathbf{S}_p$, that arises from deformation of passive myocardial tissue and a uniaxial first Piola–Kirchhoff stress, T_a^0 , along the fiber direction, $\mathbf{e}_f$, arising from muscle fiber contraction:

$$\mathbf{S} = \mathbf{S}_p + T_a^0 \mathbf{e}_f \mathbf{e}_f \cdot (\mathbf{F}^{-1})^T. \quad (6)$$

The passive myocardial tissue was assumed to be elastic and transversely isotropic. The strain energy density, $W(\mathbf{E})$, of the passive tissue is related to the strain

components E_{ij} (adapted from Bovendeerd *et al.* (1992)):

$$W(\mathbf{E}) = a_0(\exp(a_1(I_E^2 + a_2 II_E + a_3 \mathbf{e}_f \cdot \mathbf{e}_f) - 1) + a_4(\det(2\mathbf{E} + \mathbf{I}) - 1)^2) \quad (7)$$

where

$$I_E = \text{trace}(\mathbf{E}),$$

$$II_E = \frac{1}{2}(\text{trace}(\mathbf{E} \cdot \mathbf{E}^T) - I_E^2),$$

and a_0 , a_1 , a_2 , a_3 , and a_4 are material parameters. The second Piola–Kirchhoff stress in the passive tissue, $\mathbf{S}_p$, is obtained by differentiation of equation (7) with respect to $\mathbf{E}$:

$$\mathbf{S}_p = \partial W(\mathbf{E}) / \partial \mathbf{E}. \quad (8)$$

The passive second Piola–Kirchhoff stress, $\mathbf{S}_p$, is zero in the unstrained state and increases exponentially with strain.

Muscle fiber contraction in the real LV depends on sarcomere length, sarcomere velocity of shortening, time and extracellular calcium concentration (de Tombe and ter Keurs, 1991). In the finite element simulations the first Piola–Kirchhoff fiber stress, T_a^0 (kPa) depended linearly on sarcomere length, l_s (μm), and active stiffness, K ($\text{kPa } \mu\text{m}^{-1}$):

$$T_a^0 = K(l_s - l_{s,0}). \quad (9)$$

For physiological circumstances such a linear relationship is quite an accurate description throughout the cardiac cycle (Sagawa, 1978). In the reference state sarcomeres have a uniform length, $l_{s,0}$ (μm), while cavity pressure is zero and cavity-to-wall-volume ratio corresponds to mid-diastole. In this state the left ventricular wall is stress-free, regardless of active stiffness, K . To obtain the stress state at beginning of ejection, the stiffness, K , was estimated such that at the cavity pressure of beginning of ejection a physiologically realistic cavity-to-wall-volume ratio resulted.

Equations solved. Calculations of fiber stresses and strains in the LV wall were based on the law of conservation of momentum (Malvern, 1969). Neglecting inertial (Moskowitz, 1981; Peskin, 1989) and gravitational effects, conservation of momentum expresses the static equilibrium of forces in the wall due to blood pressure in the cavity and internal stresses in the wall:

$$\nabla \cdot (\mathbf{S} \cdot \mathbf{F}^T) = \mathbf{0}. \quad (10)$$

Solution method. In principle the solution to the equations can be expressed in terms of the displacements of all points in the wall. A Galerkin-based finite element method, implemented in the package DIANA-5.1 (Diana Analysis B.V., Delft, The Netherlands), was used to calculate the displacements of a finite number of points, so-called nodes. Quadratic interpolation was used to determine the displacements of points in between the nodes. Nodes are grouped into elements which constitute the building blocks of the LV wall. To reduce the computational effort, we used the rotational symmetry of the LV wall in the model. The LV wall mesh comprised only the 1/8th-section of the LV in the region ($x \geq 0$, $y \geq 0$, $z \leq 0$) (Fig. 2). The mesh consisted of 27 twenty-node brick elements with 3 element layers in the transmural

direction and 5 in the equator-to-apex direction. Kinematic boundary conditions on the through-wall faces of the mesh allowed cavity volume changes and torsion to occur. The LV inner wall surface was loaded perpendicularly by cavity pressure while the outer wall surface experienced no external forces.

Design of finite element simulations. Finite element simulations started in the reference state of deformation, corresponding to approximately mid-diastole. The state of deformation and stress at the beginning of ejection was obtained by applying a cavity pressure of 10.64 kPa (80 mm Hg). The stiffness, K , was chosen such that after application of the cavity pressure loading, the cavity-to-wall-volume ratio was about 0.6. This volume ratio and pressure were considered representative for the beginning of ejection (Douglas *et al.*, 1991).

Quantification of mechanical load. Regional mechanical load was quantified as fiber strain at the beginning of ejection. The LV wall mesh was divided into 729 regions with similar volumes. Sarcomere length at the central point of a region was considered representative for that region. For region i , fiber strain, $\varepsilon_{f,i}$ is given by

$$\varepsilon_{f,i} = \frac{l_{s,i} - l_{s,0}}{l_{s,0}}, \quad (11)$$

where $l_{s,i}$ is the instantaneous sarcomere length in the region and $l_{s,0}$ is the sarcomere length in the reference state.

Optimization procedure

Fiber orientation was optimized to make regional differences in mechanical load as small as possible. The optimization consists of minimizing an objective function, G , defined as the variance of fiber strain at beginning of ejection normalized to the average fiber strain at beginning of ejection:

$$G(\mathbf{p}) = \sum_i w_i \left(\frac{\varepsilon_{f,i} - \varepsilon_{f,av}}{\varepsilon_{f,av}} \right)^2. \quad (12)$$

G depends on the fiber orientation parameters p_1 , p_2 , and p_3 which are stored in the vector $\mathbf{p}$. Region i , representing a fraction w_i of the total wall volume, has a representative fiber strain at beginning of ejection, $\varepsilon_{f,i}$. The average fiber strain at beginning of ejection, $\varepsilon_{f,av}$ is the wall volume-weighted sum of the regional fiber strains.

Most optimization methods require many evaluations of the objective function. Since evaluation of G with the finite element model is computationally expensive, the concept of sequential approximate optimization was used (Barthelemy and Haftka, 1993). For a given set of fiber orientation parameters, $\mathbf{p}_k$, a finite element analysis was performed to evaluate regional fiber strains, $\varepsilon_{f,i}$ at beginning of ejection. By perturbing the fiber orientation parameters one at a time by 1° and using the already available state of deformation and stress as a first estimate, the regional fiber strains for the perturbed set of fiber orientation parameters were computed, with little additional computational effort. Hence, finite difference derivatives of regional fiber strains with respect to $\mathbf{p}$ at $\mathbf{p}_k$ were obtained. Regional fiber strains, $\hat{\varepsilon}_{f,i}$ were estimated for arbitrary $\mathbf{p}$ by performing a first order Taylor

series expansion on $\varepsilon_{f,i}$ around the value $\mathbf{p}_k$:

$$\hat{\varepsilon}_{f,i}(\mathbf{p}) = \varepsilon_{f,i}(\mathbf{p}_k) + \sum_{j=1}^n (p_j - p_{k,j}) \frac{\partial}{\partial p_j} \varepsilon_{f,i}(\mathbf{p}_k), \quad i = 1, 2, \dots, N \quad (13)$$

where $p_{k,j}$ and p_j are the j th components of $\mathbf{p}_k$ and $\mathbf{p}$ respectively. The partial derivatives $\partial/\partial p_j$ were calculated as finite difference derivatives. The numbers n and N refer to the number of fiber orientation parameters, and to the number of regions in the LV wall mesh ($N = 729$) respectively. By substitution of equation (13) in equation (12), an approximation model, $\hat{G}$ is obtained which gives an estimate of the objective function, G , for an arbitrary set of fiber orientation parameters:

$$\hat{G}(\mathbf{p}) = \sum_i w_i \left(\frac{\hat{\varepsilon}_{f,i} - \hat{\varepsilon}_{f,av}}{\hat{\varepsilon}_{f,av}} \right)^2. \quad (14)$$

Repeated evaluation of $\hat{G}$ is very efficient due to the explicit dependence on $\mathbf{p}$. The function, $\hat{G}$, is minimized by a sequential quadratic programming algorithm (Schittkowski, 1986). This algorithm requires limits on the parameter values. The parameters p_1 , p_2 , and p_3 were allowed to vary in the range $(-90^\circ, +90^\circ)$, $(-90^\circ, 0^\circ)$ and $(-90^\circ, +90^\circ)$ respectively. The result of the optimization of the approximation model is a new set of fiber orientation parameters, $\mathbf{p}_{k+1}$. Two checks are performed to evaluate whether convergence has occurred. The finite element evaluations of the objective function of the current and previous iterations, $G(\mathbf{p}_k)$ and $G(\mathbf{p}_{k-1})$, should agree to within a tolerance of δ :

$$|(G(\mathbf{p}_k) - G(\mathbf{p}_{k-1}))/G(\mathbf{p}_k)| \leq \delta, \quad (15)$$

where $\delta = 0.0001$. Furthermore, the optimum of the approximation model based on parameters $\mathbf{p}_k$, $\hat{G}_{opt, \mathbf{p}_k}$ should coincide with the finite element evaluation of the objective function at $\mathbf{p}_k$, to the same tolerance of δ :

$$|(G(\mathbf{p}_k) - \hat{G}_{opt, \mathbf{p}_k})/G(\mathbf{p}_k)| \leq \delta. \quad (16)$$

If convergence has not occurred a new approximation model is set up around the parameters $\mathbf{p}_{k+1}$ and the process is repeated. Because the optimization results may depend on the starting values, it is expedient to perform optimizations with several starting values.

Applied parameter values in finite element model

Wall geometry in reference state. In potassium-arrested canine left ventricles cavity volume and wall mass were reported to be 40 ± 9 ml and 145 ± 19 g (McCulloch *et al.*, 1989). Assuming a tissue density of 1.05 g cm^{-3} measured wall volume is 138 ml. In the model we have used a cavity volume of 42 ml, and a cavity-to-wall volume ratio of 0.3. The ratio of midwall long-to-short axes was set to 2.08 (Streeter and Hanna, 1973). From preliminary calculations of fiber stress and strain we found that fiber stress was most homogeneous if we chose the ratio of equatorial-to-apical wall thickness to be 3.0. Parameter values are summarized in Table 1.

Sarcomere length in reference state. In rat LVs that were formalin-fixed at zero transmural pressure, sarcomere lengths have been measured as $2.04 \pm 0.02 \mu\text{m}$

Table 1. Parameter values for model of left ventricular (LV) wall mechanics

<i>LV wall geometry</i>	
V_h	40 ml
VR	0.3
WTR	3.0
MAR	2.08
<i>Passive material behavior</i>	
a_0	0.5 kPa
a_1	3
a_2	6
a_3	3
a_4	500 kPa
<i>Contractile material behavior</i>	
$l_{s,0}$	1.95 μm
K	77.0 kPa/ μm

Wall geometry in the reference state was chosen so that the following parameters had given values: cavity volume (V_h), ratio of cavity-to-wall-volume (VR), ratio of equatorial-to-apical-wall thickness (WTR), and ratio of midwall-long-to-short-axis (MAR). Passive material properties are described by parameters a_0 , a_1 , a_2 , a_3 , a_4 (equation (7)). Sarcomere length in the reference state is denoted by $l_{s,0}$. Active fiber stiffness at beginning of ejection is denoted by K [equation (9)]

(mean $\pm$ sd) (Grimm *et al.*, 1980, after correction for 4.2% shrinkage) and as $1.83 \pm 0.06 \mu\text{m}$ (Rodriguez *et al.*, 1993). In formalin-fixed dog LVs at zero transmural pressure, sarcomere lengths have been measured as 2.00 μm (Spotnitz *et al.*, 1966, corrected for shrinkage). In the model, sarcomere length in the reference state, $l_{s,0}$ was set to 1.95 μm for all sarcomeres in the LV wall.

Constitutive behavior. The values of passive material parameters a_0 , a_1 , a_2 and a_3 were taken from Bovendeerd *et al.* (1992) (Table 1). Equibiaxial stretching experiments on sheets of passive canine myocardium (Yin *et al.*, 1987) indicate that the ratio of fiber to cross-fiber stress ranges from 1.10 to 2.95. In the present model the values of parameters a_1 , a_2 and a_3 were set such that the ratio is 2.0 under equibiaxial loading. The absolute values of a_0 and a_1 were chosen so that calculated passive pressure-volume curves agreed with experiments on canine hearts (Nikolic *et al.*, 1988). The volume of the myocardium may change by a few percent as a result of changes in coronary inflow and outflow during the cardiac cycle (Judd *et al.*, 1991; Yin *et al.*, 1996). For simplicity, we have assumed that the LV wall is near-incompressible. The value of a_4 was chosen large enough so that in the simulations numerical stability was maintained and LV wall volume changed by less than 2%.

In experiments (ter Keurs *et al.*, 1980), the sarcomere length at which no contractile force can be generated has been measured as about 1.6 μm . For simplicity of calculation we have chosen a zero-force length equal to $l_{s,0}$ so that the reference state is stress free, regardless of the instantaneous active stiffness, K . Using the finite element model, the stiffness of the fibers was chosen so that fiber stress at beginning of ejection was physiological. This resulted in a value of $77.0 \text{ kPa } \mu\text{m}^{-1}$ for K .

Finite element mesh. The size of the elements was not changed to investigate their influence on the computed

stress and strain distributions. However, for a given distribution of fiber orientation the predicted stress and strain distributions were similar to those predicted by an independently developed finite element model of LV wall mechanics by Huyghe *et al.* (1992).

Performed optimizations

Two sets of optimizations, optim1 and optim2, were carried out. In optim1 regional differences in mechanical loading were minimized by optimizing only the helix fiber angle parameters p_1 and p_2 for the case without any fiber cross-over ($p_3 = 0^\circ$). Three optimizations were performed in which the starting values in degrees for (p_1 , p_2) were (0,0), (0, -90), and (90,0). In optim2 the fiber cross-over parameter p_3 was included. Seven different sets of starting values were tried for (p_1 , p_2 , p_3): (0, 0, 0), (0, -90, 0), (90, 0, 0), (0, 0, 90), (0, -90, -90), (0, -90, 90), and (0, 0, -90). The optimizations required between 5 and 16 finite element evaluations of mechanical load. Each finite element analysis required about one CPU-hour on a Sun SPARC-ELC workstation with 24 MB RAM.

RESULTS

In optim1 a single minimum in inhomogeneity of mechanical load was found, with optimized values of p_1 and p_2 of respectively 22.57° and -58.41° . For a wide range of starting values a fiber orientation resulted in which subendocardial fiber paths resembled a right-handed and subepicardial fiber paths a left-handed helix. At the optimum, fiber strain, ϵ_f , at the beginning of ejection was 0.103 ± 0.013 (mean $\pm$ sd), if 6% of the LV wall volume near the apex was excluded (information from the three elements in the mesh adjoining the apex). The coefficient of variation of fiber strain at beginning of ejection, defined as the standard deviation divided by the mean, was 12.5%. For the whole LV wall, fiber strain at the beginning of ejection was 0.102 ± 0.020 and the coefficient of variation 20.0%.

In optim2 a single optimum was also found: $p_1 = 20.96^\circ$, $p_2 = -69.21^\circ$ and $p_3 = 15.33^\circ$. For the computed optimum, fiber strain at the beginning of ejection was 0.111 ± 0.011 and the coefficient of variation 9.5%, if 6% of the wall volume near the apex was excluded. For the whole LV the fiber strain at the beginning of ejection (Fig. 4) was 0.111 ± 0.016 and the coefficient of variation 14.4%.

DISCUSSION

A finite element model of LV wall mechanics has been developed in which regional mechanical load can be calculated for given fiber orientation, LV cavity pressure, wall geometry and material properties. Regional mechanical load was quantified as fiber strain at the beginning of ejection. Regional differences in mechanical load have been successfully minimized by proper adjustment of fiber orientation. A helical arrangement of fibers in the LV wall formed automatically for a wide range of starting values of the parameters describing the distribution

Fig. 4. Distribution of fiber strain at the beginning of ejection after optimization of fiber orientation parameters p_1 , p_2 and p_3 . Fiber strain over whole LV wall is 0.111 ± 0.016 (mean $\pm$ sd).

of fiber orientation. Inclusion of fiber cross-over between inner and outer wall surfaces in the optimization further reduced load inhomogeneity.

For simplicity, residual load has not been incorporated in the present finite element model of LV wall mechanics. Residual circumferential strain in the unloaded LV wall (zero transmural pressure) has been revealed in the rat heart by making a longitudinal-transmural cut in the LV wall, upon which the wall opens (Omens and Fung, 1989). Several studies have emphasized the importance of residual load for accurate prediction of passive mechanical behavior (Kang and Yin, 1996), as a potential mediator during cardiac morphogenesis (Taber *et al.*, 1993), and for its potential effect on systolic wall stress (Taber, 1991). Experiments in the rat heart indicate that circumferential residual strain leads to a transmural gradient in sarcomere length in the unloaded LV of the rat, with sarcomeres in the subepicardium being longer than those in the subendocardium (Rodriguez *et al.*, 1993). At positive filling pressures, sarcomere length becomes more uniformly distributed over the LV wall of the rat (Grimm *et al.*, 1980), indicating that residual strain may contribute to homogeneity of fiber strain at beginning of ejection.

Solving optimization problems requiring stress analyses by the finite element method easily leads to unacceptably large computational efforts. Computational efficiency can be manipulated by the number of elements in the finite element mesh and by the number of time steps during the cardiac cycle included in the evaluation of the objective function. We have tried to limit the computational effort in three main ways. First, the number of finite element analyses was reduced by using a suitable optimization strategy, namely sequential approximate optimization (Barthelemy and Haftka, 1993). Second, we quantified mechanical load as regional fiber strain at the beginning of ejection relative to the diastolic reference state. Hence, evaluation of the objective function by the finite element method required only strain information at the beginning of ejection, not throughout the whole cardiac cycle. Other finite element simulations of LV wall mechanics (Bovendeerd *et al.*, 1992) show that the distribution of fiber stress at beginning of ejection

gives a good approximation of the stress distribution during the entire ejection phase. In our model of LV wall mechanics, cardiac tissue is elastic and the stiffness uniform so that homogeneity of fiber stress automatically implies homogeneity of fiber strain. Therefore, by making fiber strain at the beginning of ejection as homogeneous as possible, we expect, to a good approximation, to have made fiber strain homogeneous during the entire ejection phase. Third, we chose a simplified constitutive law for contracting cardiac tissue in which the zero-force sarcomere length equals the sarcomere length in the reference state. As a direct computational gain, the reference state is then stress-free regardless of the active stiffness so that the state of beginning of ejection can be reached by merely loading the endocardial surface with cavity pressure. To make fiber stresses at beginning of ejection physiological the active fiber stiffness was chosen such that cavity pressure and volume had physiological values (Arts *et al.*, 1991). Following optimization of fiber orientation, fiber stress at beginning of ejection is both physiological and homogeneous (with a coefficient of variation less than 10%). In conclusion, the measures we have taken to restrict computational effort have made the optimization problem more manageable.

Fiber strains near the apex remain inhomogeneous (Fig. 4), despite optimization of fiber orientation. Others (Peskin, 1989) who have calculated left ventricular fiber orientation in a mathematical model have ignored the apex on the basis that apical fibers are an integral part of the right ventricle (Thomas, 1957). We have included the apex in our model, but recognize that the description of its mechanics is probably erroneous due to an inadequate description of fiber orientation, wall geometry and possibly also material properties. After all, the apex itself is a singular point in the mathematical description of the distribution of fiber orientation. As a consequence we have presented the results of optimizing fiber orientation in the whole LV wall both with and without information from the three elements (6% of wall volume) adjoining the apex.

The choice of the number and nature of the fiber orientation parameters in the model is somewhat arbitrary. Our aim was to use as few parameters as possible that still allowed a reasonable description of measured fiber angles. Within limits, more parameters would result in more homogeneous loading of the wall as indicated in this study by the improvement in load homogeneity when adding transverse fiber angle parameter, p_3 , to the two helix angle parameters. Additional helix fiber angle parameters can be chosen on the basis of anatomical measurements which reflect that (1) helix fiber angle is a nonlinear function of transmural position, especially close to the wall boundaries (Nielsen *et al.*, 1991; Streeter, 1979; Streeter *et al.*, 1969) and (2) helix fiber angle increases towards the apex (Streeter and Hannah, 1973). Inclusion of fiber angle parameters in the optimization that allow such behavior are likely to further improve load homogeneity.

To assess the physiological relevance of the computed transmural course of helix fiber angle, comparisons were made with reported measurements (Nielsen *et al.*, 1991; Streeter, 1979) and model predictions (Arts *et al.*, 1994; Bovendeerd *et al.*, 1992; Peskin, 1989). The anatomical measurements were performed in the equatorial and

adjacent more apical regions of human and canine left ventricles (Nielsen *et al.*, 1991; Streeter, 1979) (Fig. 5). For a quantitative comparison, the root mean square (RMS) difference between the computed transmural course of helix fiber angle and a measured data set was determined (Table 2). Since the ability to describe the measured data with a straight line is limited by inherent scatter, the RMS differences of linear regression lines to the measurements were also determined. Table 2 shows that the RMS differences of the computed transmural course of helix angle are only slightly larger (range: 11.9° – 18.4°) than those of the linear regression lines (11.4° – 12.1°). Notably, the optimized helix fiber angle distribution of optim2 agrees better with the measurements than that of optim1. Also shown in Table 2 are RMS differences for predictions of helix fiber angle distributions of several mathematical models. In a finite element model of LV wall mechanics by Bovendeerd *et al.* (1992) equatorial fiber stress, averaged over the ejection period, was made as homogeneous as possible by making trial and error changes in the transmural course of helix fiber angle. The transmural course of helix fiber angle was described by four parameters in three piecewise continuous polynomials up to second order. Arts *et al.* (1994) computed a transmural distribution of helix fiber angle in a cylin-

drical model of LV wall mechanics. The helix fiber angle distribution was the result of a simulated process of cardiac remodeling in which muscle fibers could adapt their orientations to achieve a required amount of shortening during ejection. A helical fiber orientation formed automatically. Finally, Peskin (1989) computed a transmural course of fiber angle (angle between fiber and circumferential directions) that followed an inverse sine relation with extreme values of 90° and -90° at the inner and outer wall surfaces. This result was derived from mechanical equilibrium of the LV wall and from the condition that the cross-sectional area of a group of muscle fibers is constant along its length. In conclusion, judging by the RMS differences, the transmural course of helix fiber angle computed in optim1 and optim2 agrees quite well with measurements and also with predictions by mathematical models.

Comparison of computed transverse fiber angle with measurements is more difficult due to the scarcity of experimental data. The transverse fiber angle is positive above the equator and negative below but more accurate latitude-dependence could not be detected (Streeter *et al.*, 1978). Mean through-wall values have been measured as $-4.6 \pm 0.8^\circ$ (mean $\pm$ SEM) near the equator and $-3.5 \pm 0.6^\circ$ near the apex (Streeter, 1979). In our model the spatial average of α_t below the equator is -6.5° which compares reasonably well with these measurements. Reported predictions of fiber orientation by mathematical models are another available source to compare the computed transverse fiber angle field with. In a mathematical model to calculate left ventricular fiber orientation (Peskin, 1989), transverse fiber angle was zero at the inner and outer wall surfaces and greatest in the middle of the wall. The midwall transverse fiber angle was 0° at the equator position and increased towards the apex to about 18° . In conclusion, there is too little experimental data available to make a quantitative evaluation of the computed transverse fiber angle. Qualitatively, our predictions do not conflict with either available measurements or other model predictions.

The finding that an anatomically realistic distribution of fiber orientation results in rather homogeneous mechanical loading of the wall at the beginning of ejection is in agreement with other (Arts and Reneman, 1989; Bovendeerd *et al.*, 1992; Huyghe *et al.*, 1992), but not all, model studies. Results of a finite element model of LV wall mechanics by Guccione *et al.* (1995) showed there was considerable regional heterogeneity of end systolic fiber stress. The latter model incorporated measured wall

Fig. 5. Comparison of measured and computed helix fiber angle, α_h , as a function of transmural position in the wall, v . Measurements: (●) Streeter (1979), from equatorial region of human LV, (△) Nielsen *et al.* (1991), from equatorial region of canine LV, (▲) Nielsen *et al.* (1991), from adjacent more apical region of canine LV. Computations: (---) optimization of parameters p_1 and p_2 , (—) optimization of parameters p_1 , p_2 and p_3 .

Table 2. Root mean square (RMS) differences of computed transmural course of helix fiber angle with respect to measurements

Measurement	Root Mean Square Difference (degrees)					
	best linear fit to measurements	optim1	optim2	Bovendeerd, 1992	Peskin, 1989	Arts, 1994
Streeter 1979	11.4	14.4	11.6	10.6	23.8	14.7
Nielsen, 1991 A	12.1	18.4	15.0	11.0	15.5	13.8
Nielsen, 1991 B	11.4	18.5	18.3	12.2	14.4	13.2

Sources of measurements: Streeter, (1979), from equatorial region of human LV; Nielsen *et al.* (1991), A and B, from equatorial and adjacent more apical regions of canine LV respectively. Other columns show RMS differences in degrees for computed transmural course of helix fiber angle: (1) best linear fit to measurements, (2) optim1: when optimizing parameters p_1 and p_2 only, (3) optim2: when additionally optimizing p_3 , (4) Bovendeerd *et al.* (1992), and (5) Peskin (1989), and (6) Arts *et al.* (1994).

geometry and fiber orientation. Unfortunately, in their study, Guccione *et al.* (1995) did not present a sensitivity analysis of the model parameters. It may well be that small changes in fiber orientation within the anatomical range lead to more homogeneous fiber stress over the wall.

CONCLUSIONS

A finite element model of LV wall mechanics has been set up. Fiber orientation in the model, quantified by the helix and transverse fiber angles, was described by up to three parameters. Fiber orientation was optimized to make regional differences in fiber strain at the beginning of ejection as small as possible. A single optimum in fiber orientation was found when helix fiber angle was optimized for a wide range of starting values of the fiber orientation parameters. The standard deviation of the fiber strain at beginning of ejection, divided by the mean fiber strain was 12.5 %. Inclusion of the transverse fiber angle in the optimization reduced this measure of inhomogeneity to less than 10 %. The computed transmural course of helix fiber angle has RMS errors with respect to measurements ranging from 11.6° to 18.5°. Linear regression lines through the same measurement data have RMS errors between 11.4° and 12.1°. The agreement between computed and measured fiber orientations suggests that the structure of the left ventricular wall is designed for maximum homogeneity of fiber strain during ejection.

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APPENDIX: WALL GEOMETRY

To specify wall geometry in the reference state a spherical coordinate system as well as the rectangular coordinate system of Fig. 2 were used. Given the coordinates of a point with respect to the spherical coordinate system, (r, θ, ϕ) , its coordinates in the rectangular system, (x, y, z) are

$$\begin{bmatrix} x \\ y \\ z \end{bmatrix} = r \begin{bmatrix} \sin(\theta) \cos(\phi) \\ \sin(\theta) \sin(\phi) \\ \cos(\theta) \end{bmatrix}. \quad [\text{A.1}]$$

The LV wall was assumed to be rotationally symmetric. The shape of the wall was defined by specifying a midwall surface and a wall thickness perpendicular to the midwall. A point on the midwall surface at a distance r_m from the origin has position vector $\mathbf{r}_m$ given by

$$\mathbf{r}_m(\theta, \phi) = r_m(\theta) \begin{bmatrix} \sin(\theta) \cos(\phi) \\ \sin(\theta) \sin(\phi) \\ \cos(\theta) \end{bmatrix} \begin{bmatrix} \mathbf{e}_x \\ \mathbf{e}_y \\ \mathbf{e}_z \end{bmatrix}, \quad (\text{A.2})$$

where $\mathbf{e}_x, \mathbf{e}_y, \mathbf{e}_z$ are unit vectors along the cartesian coordinate axes. The shape of the midwall surface is described by the function $r_m(\theta)$ which depends on two parameters, a_m and b_m :

$$r_m(\theta) = (a_m + b_m \cos(2\theta))^{-1/2}. \quad (\text{A.3})$$

The wall thickness perpendicular to the midwall is specified by the function $t(\theta)$, which depends on three parameters, a_t, b_t , and c_t :

$$t(\theta) = a_t + b_t \cos(2\theta) + c_t \cos(4\theta). \quad (\text{A.4})$$

The unit outward normal vector to the midwall surface is given by $\mathbf{n}_m$:

$$\mathbf{n}_m(\theta, \phi) = \frac{|\partial \mathbf{r}_m|^{-1}}{|\partial \theta|} \left(\left(r_m \sin(\theta) - \frac{dr_m}{d\theta} \cos(\theta) \right) (\cos(\phi) \mathbf{e}_x + \sin(\phi) \mathbf{e}_y) + \left(r_m \cos(\theta) + \frac{dr_m}{d\theta} \sin(\theta) \right) \mathbf{e}_z \right). \quad (\text{A.5})$$

Hence the position vector, $\mathbf{r}$, of a point in the LV wall is given by

$$\mathbf{r}(\theta, \phi) = \mathbf{r}_m(\theta, \phi) + vt(\theta) \mathbf{n}_m(\theta, \phi). \quad (\text{A.6})$$

The parameter v varies linearly with transmural position from -1 at the endocardium to $+1$ at the epicardium. The used values of a_m , and b_m were 0.109 and -0.0680 cm^{-2} , respectively, and those of a_t, b_t , and c_t were 0.643, -0.289 and -0.0643 cm , respectively.