Anterior and posterior left ventricular sarcomere lengths behave similarly during ejection

**Guccione, J. M., W. G. O'Dell, A. D. McCulloch, and W. C. Hunter.** Anterior and posterior left ventricular sarcomere lengths behave similarly during ejection. Am. J. Physiol. 272 (Heart Circ. Physiol. 41): H469–H477, 1997.—Previous studies of regional differences in myocardial deformation between the anterior and posterior walls of the canine left ventricle were based on strain, which is not an absolute measure of deformation. We thus compared sarcomere lengths at anterior and posterior sites during ejection in isolated dog hearts. Cineradiographic imaging of regional deformation with radiopaque markers implanted near the midwall in five hearts and just below the epicardium in six hearts, combined with postmortem histology, allowed sarcomere length reconstruction throughout the cardiac cycle. The amount of sarcomere shortening accompanying left ventricular ejection was similar in both walls of the left ventricle for sarcomeres located at epicardial and midwall sites. The mean sarcomere length (taken at the middle of the ejecting range) was also similar between the anterior and posterior sites when averaged over all hearts. The similarity of sarcomere function held not only at end systole but throughout ejection and over wide ranges of ventricular pre- and afterloads. Hence functional measurements of relative myocardial shortening may not be indicative of regional sarcomere length heterogeneity.

Regional differences in the patterns of myocardial deformation between the anterior, lateral, and posterior walls of the canine left ventricle have been observed (3, 17). This is not surprising because the beating heart is a complex three-dimensional (3-D) and fiber-wound structure with mechanical properties that are nonlinear, anisotropic, time varying, and probably spatially inhomogeneous. These previous studies were based on a description of deformation in a limited region of the wall by means of strain tensors. A tensor description of strain provides information on relative stretches in any direction. However, strain is not an absolute measure of deformation because it is measured relative to an arbitrary reference configuration such as end diastole.

Recently, our laboratory developed a method that allows the “reconstruction” of absolute sarcomere lengths (SLs) and orientations at any transmural layer in the left ventricular wall during any phase of the cardiac cycle. Relative strain analyses in the anterior and posterior walls of the left ventricle were correlated with histological measurements by Villarreal and Lew (17) and Fann et al. (3), who measured the fiber orientations and related these fiber directions to the direction of maximum strain. These studies did not, however, attempt to measure absolute SLs or correct precisely for any artifactual deformation arising from the histological procedures.

We thus examined the canine left ventricle for potential regional differences in sarcomere function during ejection. We compared SLs reconstructed at posterior and anterior sites at different transmural depths in beating canine hearts operating under a wide range of hemodynamic loads. SL was reconstructed by combining cineradiography of local deformations with postmortem histology of the same region.

**METHODS**

Reconstruction of sarcomere deformation (as the component in the myofiber direction of 3-D deformation) in the isolated beating canine heart was accomplished by cineradiography of local wall deformation calibrated to SL by postmortem histology. The main stages of the procedures were sterile implantation of radiopaque marker beads, preparation of the isolated heart, recording of the bead motion for a series of pressure and volume excursions in the isolated beating heart, reconstruction of 3-D strains in the region of the implanted markers, histological analysis of the geometric relationship between the local sarcomere vector and the bead positions, and reconstruction of strain in the direction of the sarcomeres. These methods follow closely those described by Rodriguez et al. (11); only a brief summary is given here.

**Analysis of Regional Deformation**

**Bead implantation.** The initial stage involved implantation of arrays of stainless steel beads to mark local points within the ventricular wall for the subsequent cineradiographic imaging. Mongrel dogs (18–20 kg) were anesthetized with pentobarbital sodium (30–40 mg/kg), and a left lateral thoracotomy was performed under sterile conditions. Anterior and posterior sites in the left ventricular free wall were selected that were free of large vessels and near the equator (one-third of the distance from base to apex). The anterior site was located just lateral to the left anterior descending coronary artery. The posterior site was located just lateral to the posterior descending coronary artery. At each site, three beads each were placed into roughly equilateral triangles (~1 cm on a side) at ~6 and 0.5 mm from the epicardial surface. We will refer to data collected at these two depths as “midwall” and “epicardial,” respectively. The mean depths below the epicardium actually obtained at the anterior and posterior midwall sites were 4.8 ± 0.1 (SE) and 6.0 ± 0.9 mm, respectively. This difference in depth was not significant.
according to a one-way repeated-measures analysis of variance \((P > 0.23)\).  

**Surgical attachment of mitral ring.** After a 7- to 10-day recovery period, the implanted dog was reanesthetized as before, and its heart was isolated and metabolically supported by cross circulation from a second anesthetized dog (14). Oxygenated blood from the support dog was supplied directly to the coronary bed of the isolated heart, and coronary venous blood was collected through a vent in the right ventricle for return to the support dog. After cutting all mitral chordae tendineae, a Teflon support ring was sewn into the fibrous ring surrounding the mitral valve. The rigid support ring allowed the insertion of a water-filled latex balloon into the left ventricle and secured the heart to a servo pump apparatus (Vivitro Systems, Superpump System, Victoria, BC).  

**Heart suspension.** The heart was positioned with its apex-base axis horizontal, supported by a pericardial “cradle” consisting of a plastic sheet. The heart was oriented such that the anterior bead site was toward the most elevated aspect of the heart. This placed the posterior site generally below the central left ventricular axis in a lateral view. There was a concern that the gravitational weight of the heart could deform the left ventricle and thereby alter the anterior-posterior mechanical relationships. To test this, in two hearts, we rotated the heart-pump system around its long axis and compared the local deformations of the anterior and posterior sites at two angular orientations \(-45^\circ\) apart. During systolic ejection, strain data at each site showed negligible differences as a function of volume. During passive filling, however, an effect of heart orientation was noted. Thus, for the subsequent analysis, we focused on the systolic strain data.  

**Loading conditions.** Biplane cine-X-ray imaging (at 90 frames/s) was performed to track anterior-posterior bead positions over a wide range of cavity volumes and pressures in the beating isolated heart. Even though the heart was isolated, the cardiac cycle followed realistic pressure-volume loops. Computer feedback with simulated arterial loading and venous filling conditions governed the servo pump to provide physiological patterns of hemodynamic loading (15). End-diastolic volumes ranged from 20 to 50 ml, stroke volumes ranged from 7 to 30 ml, and ejection fractions were 20–60%.  

**Reconstructing 3-D deformations from cinefilms.** An automated image-analysis system was used to transform the bead positions recorded from the two orthogonal sets of cine-X-ray films into 3-D position coordinates for each time frame. From the 3-D trajectories of each bead, a local measure of the 3-D deformation was computed individually for each layer in both the anterior and posterior sites based on the relative motions of neighboring beads. With the use of the method of Rodriguez et al (11), a hybrid deformation gradient tensor was used to compute the deformation on the plane defined by the three beads implanted in any one layer. One or more beads from an adjacent layer were used to compute the out-of-plane deformation components.  

**Histological Analysis and Sarcomere Reconstruction**  

The next step involved sectioning the fixed heart for histological analysis of the local sarcomere pool. Thin (3-µm) sections were cut at the location of each transmural bead triangle. Within each section, average SLs and orientations were observed from multiple sites within the bead plane with light microscopy (×100 objective). Analysis of orthogonal sections provided the average orientation of myocardial fibers out of the plane of the beads. While the section at low power was viewed, the coordinates of the centers of the three bead implant locations were determined with respect to the coordinate system used to measure sarcomere orientation within the bead plane.  

A transformation matrix was computed to relate the sarcomere orientation and length, the “sarcomere vector,” at the locations of the bead planes at the epicardial surface and midwall to those in the intact fixed heart before the hearts were sectioned. This transformation involved mapping the histological bead locations to those in the intact heart before fixation. Combining this transformation with the out-of-plane angle from the orthogonal sections allowed reconstruction of the average sarcomere vector in the intact fixed heart. The description of the evolution of the sarcomere vector over time throughout the cardiac cycle was then accomplished by applying to this sarcomere vector the deformation between the intact fixed heart and that observed from the 3-D trajectories of neighboring beads during the various loading cycles.  

**Statistical Methods for Sarcomere Deformation Analysis**  

Experimental results in this study were from eight mongrel dogs. Five other dogs were excluded from the analysis: three hearts had weak contractile strength and two showed contracture handing when viewed histologically. Of the eight valid experiments, six hearts yielded epicardial deformation data that could be compared between the anterior and posterior sites, and five provided midwall deformation data at both sites. Unfortunately, in only three hearts did bead implantation yield deformation data simultaneously at both depths and both sites. Because comparison between depths was possible in only three hearts, we focused our analysis on a comparison of sarcomere dynamics between the anterior and posterior walls.  

We also focused our analysis on the behavior of SLs during the systolic ejection phase. To obtain a strictly objective criterion for determining the beginning and the end of ejection phase, we used only data from the period when the volume was decreasing over the central 90% of the volume range covered in that cardiac cycle. Data were pooled together from all ejections of the same heart, covering a wide range of preload and afterload.  

The chamber volume strongly affects SL, but the relationship between SL and volume (V) may vary at different sites (anterior vs. posterior) or between different hearts tested. We therefore performed a two-way repeated-measures analysis of covariance (5). We used the following regression equation:  

\[
\text{SL} = \text{Constant} + \text{Volume} + \text{Wall} + \text{Heart},
\]

where Volume is a continuous factor (anterior vs. posterior). The regression coefficient for the term Volume·Heart indicates the average effect of the anterior vs. posterior site on the SL-V relationship. Combining the coefficients for the terms Volume and Volume·Heart, we obtained the average amount of sarcomere shortening accompanying ejection (ΔSL/ΔV). The mean SL during ejection (SL, ) was obtained at each site by combining the regression coefficients for the terms Constant and Wall. So that this calculation represented an SL in the middle of the ejection range, the mean volume averaged over all ejections for a single heart was subtracted from the raw volume data for that heart before applying the regression. Data for ΔSL/ΔV and SL, are presented as means ± SE. \(P < 0.05\) was accepted as statistically significant. A preliminary analysis of a subset of the data was performed previously (7).
RESULTS

Changes in ventricular volume during the cardiac cycle are clearly expected to be strongly coupled with changes in the local SL. Thus we plotted SL as a function of left ventricular volume and compared the behavior of the sarcomeres at anterior and posterior sites. Figure 1 shows epicardial (A) and midwall (B) data throughout the cardiac cycle in which the stroke volume was maximal. For example, midwall sarcomeres at the anterior site (Fig. 1B) began their cardiac cycle at the maximal SL (upper right corner of loop) before shortening somewhat during the isovolumic contraction phase. During the ejection phase (thick line and arrow), the midwall anterior sarcomeres shortened steadily as volume fell so that the trajectory was nearly linear throughout ejection. During isovolumic relaxation, these sarcomeres were elongated slightly, and, subsequently, they were restretched to their end-diastolic length during filling.

The data shown in Fig. 1 are typical in that sarcomeres at all sites and depths shortened steadily during ejection (see arrows and the thick sections of each trace). At either depth, the $\Delta SL/\Delta V$, i.e., the slope of the approximately linear trajectory during ejection, was similar between the anterior and posterior sites. Moreover, the mean SL$_{e}$ (taken at the middle of the ejecting range) was also similar between the anterior and posterior sites.

On the other hand, we observed no consistent effect of site on the relationships between SL and cavity volume during the other phases of the cardiac cycle, i.e., during filling and the isovolumic phases. Note that the loops in Fig. 1 all have different shapes, with different relationships between trajectories during ejection and filling. Some of the diastolic differences may have been related to differential effects of gravitational forces between the anterior and posterior sites. In our experiments, the heart was situated with its long axis approximately horizontal and oriented such that the anterior site faced upward and the posterior site was located at approximately four o'clock. If we were to rotate the left ventricle around its long axis, we would then have altered the differential offset of the gravitational field at the two sites. As seen in Fig. 2, such rotation did indeed affect that portion of the trajectories relating SL to volume during diastolic filling, but there was no significant effect during systolic ejection. Thus, for the remainder of the data analysis, we focused exclusively on the relationship between SL and V during ejection.

The results presented so far were for cardiac cycles in which stroke volume was maximal, but we also compared regional SLs in hearts operating under a wide range of hemodynamic loads. At any myocardial site, the relationship between SL and V during ejection was consistent irrespective of the hemodynamic loading conditions that brought the left ventricle to that volume. This result is reminiscent of the strain-volume relationship that Douglas et al. (2) also found to be approximately independent of hemodynamic loads. Both at the epicardium (Fig. 3) and at midwall (Fig. 4), the relationships between SL and V during ejection for different preloads and afterloads were approximately linear, had similar slopes, and had comparable SLs at matching volumes. All ejections of the same heart were pooled together to obtain a slope ($\Delta SL/\Delta V$) and intercept (SL$_{e}$) for each site.

$\Delta SL/\Delta V$ values at the epicardial and midwall sites were not significantly different between the anterior and posterior walls ($P > 0.28$ and 0.44, respectively; Table 1, Fig. 5). When averaged over all hearts, $\Delta SL/\Delta V$ was 7.3 nm/ml at the anterior epicardium and 8.3 nm/ml at the posterior epicardium. Individually, $\Delta SL/\Delta V$ was 2.2–2.8 nm/ml greater at the posterior epicardium than at the anterior epicardium in three hearts, differed less than 0.6 nm/ml between the two walls in two hearts, and was 2.5 nm/ml greater at the anterior epicardium than at the posterior epicardium in one heart. On average, $\Delta SL/\Delta V$ was 8.9 nm/ml at the
Fig. 2. Effect of gravity on anterior epicardial (A), posterior epicardial (B), anterior midwall (C), and posterior midwall (D) sarcomere length vs. LV volume throughout cardiac cycle in which stroke volume was maximal. At all 4 sites, relationship between sarcomere length and volume before (solid lines) and after (dashed lines) rotating heart by 45° about LV long axis is not significantly affected during ejection phase (thick lines). Filling phase of cardiac cycle was affected to the greatest extent, especially at anterior epicardium.

Anterior midwall and 9.7 nm/ml at the posterior midwall. ΔSL/ΔV was 2.9–3.4 nm/ml greater at the posterior midwall than at the anterior midwall in two hearts, differed less than 0.8 nm/ml between the two walls in two hearts, and was 1.4 nm/ml greater at the anterior midwall than at the posterior midwall in one heart.

Similarly, there was no consistent anterior-posterior difference in the mean SL_{eo} (P > 0.33 at the epicardium and P > 0.96 at the midwall; Table 1, Fig. 6). When the SL_{eo} was averaged over all hearts, it was 2.00 μm at the anterior epicardium and 2.06 μm at the posterior epicardium. Individually, SL_{eo} was 0.11–0.17 μm longer at the posterior epicardium than at the anterior epicardium in three hearts, was 0.07–0.10 μm shorter at the posterior epicardium than at the anterior epicardium in two hearts, and differed less than 0.03 μm between the two walls in one heart. On average, SL_{eo} was 2.01 μm at the anterior midwall and 2.01 μm at the posterior midwall. SL_{eo} was 0.03–0.05 μm shorter at the posterior midwall than at the anterior midwall in two hearts, differed less than 0.01 μm between the two walls in two hearts, and was 0.07 μm longer at the posterior midwall than at the anterior midwall in one heart.

Hence we observed similar SL_{eo} values between the anterior and posterior walls despite potential regional differences in the myofiber strain. To maintain such comparable systolic lengths, sarcomeres in regions of high systolic fiber stretch (relative to an unloaded
A more revealing analysis would be to compare the changes in SL between SL$_{\text{unl}}$ and average SL$_{\text{ej}}$. At the epicardium, the difference (SL$_{\text{ej}}$ - SL$_{\text{unl}}$) was significantly greater in the posterior wall than in the anterior wall ($P < 0.04$; Table 1, Fig. 6). In fact, this was the case in all six hearts studied (Fig. 6A). Moreover, SL$_{\text{ej}}$ - SL$_{\text{unl}}$ was greater at the posterior epicardium than at the anterior epicardium both before and after rotation of the left ventricle around its long axis. At the midwall (Fig. 6B), however, there was no consistent anterior-posterior difference in SL$_{\text{ej}}$ - SL$_{\text{unl}}$ ($P > 0.55$).

In contrast to the “unloaded” diastolic state, we also compared anterior vs. posterior end-diastolic SLs at the maximal volume (EDSL$_{\text{max}}$) we achieved in each heart. The EDSL$_{\text{max}}$ values at both the epicardial and midwall ventricular configuration) require shorter sarcomeres when the left ventricle is unloaded than do sarcomeres in regions of low-systolic fiber stretch. For an approximately unloaded ventricular state, we chose the configuration at the middle of filling at the lowest preload of each heart. The SL in this state is called SL$_{\text{unl}}$. Note that left ventricular pressure in this state was ~4 mmHg, so that it does not represent a completely unloaded reference state. However, this state does represent the lowest load in terms of pressure available in our data.

SL$_{\text{unl}}$ values at the epicardial and midwall sites were not significantly different between the anterior and posterior walls ($P > 0.11$ and 0.39, respectively; Table 1, Fig. 6). When the SL$_{\text{unl}}$ was averaged over all hearts, it was 2.01 μm at the anterior epicardium and 1.94 μm at the posterior epicardium. Individually, the SL$_{\text{unl}}$ was 0.04–0.14 μm shorter at the posterior epicardium than at the anterior epicardium in five hearts and was 0.08 μm longer at the posterior epicardium than at the anterior epicardium in one heart. On average, the SL$_{\text{unl}}$ was 1.96 μm at the anterior midwall and 1.94 μm at the posterior midwall. The SL$_{\text{unl}}$ was 0.04–0.12 μm shorter at the posterior midwall than at the anterior midwall in two hearts, differed less than 0.02 μm between the two walls in two hearts, and was 0.04 μm longer at the posterior midwall than at the anterior midwall in one heart.

SL$_{\text{unl}}$ values at the epicardial and midwall sites were not significantly different between the anterior and posterior walls ($P > 0.11$ and 0.39, respectively; Table 1, Fig. 6). When the SL$_{\text{unl}}$ was averaged over all hearts, it was 2.01 μm at the anterior epicardium and 1.94 μm at the posterior epicardium. Individually, the SL$_{\text{unl}}$ was 0.04–0.14 μm shorter at the posterior epicardium than at the anterior epicardium in five hearts and was 0.08 μm longer at the posterior epicardium than at the anterior epicardium in one heart. On average, the SL$_{\text{unl}}$ was 1.96 μm at the anterior midwall and 1.94 μm at the posterior midwall. The SL$_{\text{unl}}$ was 0.04–0.12 μm shorter at the posterior midwall than at the anterior midwall in two hearts, differed less than 0.02 μm between the two walls in two hearts, and was 0.04 μm longer at the posterior midwall than at the anterior midwall in one heart.

A more revealing analysis would be to compare the changes in SL between SL$_{\text{unl}}$ and average SL$_{\text{ej}}$. At the epicardium, the difference (SL$_{\text{ej}}$ - SL$_{\text{unl}}$) was significantly greater in the posterior wall than in the anterior wall ($P < 0.04$; Table 1, Fig. 6). In fact, this was the case in all six hearts studied (Fig. 6A). Moreover, SL$_{\text{ej}}$ - SL$_{\text{unl}}$ was greater at the posterior epicardium than at the anterior epicardium both before and after rotation of the left ventricle around its long axis. At the midwall (Fig. 6B), however, there was no consistent anterior-posterior difference in SL$_{\text{ej}}$ - SL$_{\text{unl}}$ ($P > 0.55$).

In contrast to the “unloaded” diastolic state, we also compared anterior vs. posterior end-diastolic SLs at the maximal volume (EDSL$_{\text{max}}$) we achieved in each heart. The EDSL$_{\text{max}}$ values at both the epicardial and midwall...
Table 1. Comparison of sarcomere lengths and shortening between anterior and posterior sites

<table>
<thead>
<tr>
<th></th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ΔSL/ΔV</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Epicardial (n = 6)</strong></td>
<td></td>
</tr>
<tr>
<td>Anterior, mm/ml</td>
<td>7.3 ± 1.1</td>
</tr>
<tr>
<td>Posterior, mm/ml</td>
<td>8.9 ± 0.5</td>
</tr>
<tr>
<td><strong>Midwall (n = 5)</strong></td>
<td></td>
</tr>
<tr>
<td>Anterior, mm/ml</td>
<td>8.9 ± 1.5</td>
</tr>
<tr>
<td>Posterior, mm/ml</td>
<td>9.7 ± 1.0</td>
</tr>
</tbody>
</table>

**Posterior – anterior**

<table>
<thead>
<tr>
<th></th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLₜ₀</td>
<td></td>
</tr>
<tr>
<td>Epicardial, μm</td>
<td>0.05 ± 0.05</td>
</tr>
<tr>
<td>Midwall, μm</td>
<td>0.00 ± 0.02</td>
</tr>
<tr>
<td>SLₚ₀</td>
<td></td>
</tr>
<tr>
<td>Epicardial, μm</td>
<td>0.06 ± 0.03</td>
</tr>
<tr>
<td>Midwall, μm</td>
<td>−0.03 ± 0.03</td>
</tr>
<tr>
<td>SLₚ₀ − SLₚ₀</td>
<td></td>
</tr>
<tr>
<td>Epicardial, μm</td>
<td>0.12 ± 0.04</td>
</tr>
<tr>
<td>Midwall, μm</td>
<td>0.03 ± 0.04</td>
</tr>
<tr>
<td>EDSLₚ₀ max</td>
<td></td>
</tr>
<tr>
<td>Epicardial, μm</td>
<td>0.02 ± 0.04</td>
</tr>
<tr>
<td>Midwall, μm</td>
<td>0.02 ± 0.06</td>
</tr>
</tbody>
</table>

Values are means ± SE; n, no. of hearts. ΔSL/ΔV, sarcomere shortening per ejected volume; SLₜ₀, mean sarcomere length during ejection; SLₚ₀, mean sarcomere length during filling at lowest preload; SLₚ₀ − SLₚ₀, difference between SLₜ₀ and SLₚ₀; EDSLₚ₀ max, end-diastolic sarcomere length at greatest preload; NS, not significant. Significance was for test of anterior vs. posterior data. All tests used analysis of covariance with volume as a regressor, except when comparing difference in SLₚ₀, which used analysis of variance.

sites were not significantly different between the anterior and posterior walls (P > 0.88 and 0.79, respectively; Table 1). When the EDSLₚ₀ max was averaged over all hearts, it was 2.19 μm at the anterior epicardium vs. 2.17 μm at the posterior epicardium. At the midwall, the EDSLₚ₀ max averaged 2.18 μm anteriorly compared with 2.20 μm posteriorly.

**DISCUSSION**

This study demonstrated that sarcomeres at anterior vs. posterior sites functioned similarly during ejection in isolated canine hearts. The amount of sarcomere shortening accompanying left ventricular ejection was similar in both walls of the left ventricle for sarcomeres located just below the epicardium and also for those near the midwall. The mean SL (taken at the middle of the ejecting range) was also similar between the anterior and posterior sites when averaged over all hearts.

The similarity of sarcomere function held not only at end systole but throughout ejection and over wide ranges of ventricular pre- and afterloads.

This report presents the first observations of sarcomere behavior during active ejections of an intact heart. Moreover, this report also presents the first comparison of lengths between sarcomeres from different regions of the same heart. Surprisingly, although there have been previous observations of SLs in fixed hearts, no regional and only two transmural comparisons (6, 12) have been reported.

The regional similarity of sarcomere function during ejection that we observed was not necessarily an inevi-
rate such differences in finite-element models are just in development, although they have been used for simple cylindrical models (8). Thus, based solely on the differences in geometry between the two walls of the ventricle, the mathematical model predicted that sarcomeres would work during ejection at consistently longer lengths in the epicardium of the posterior site compared with the anterior site.

However, we hypothesize that if cells in the posterior epicardium were chronically forced to work at extended lengths, they would be stimulated by their mechanical environment to lay down more sarcomeres in series than their anterior counterparts, so that ejecting SLs could be equilibrated between the two walls. Consequently, when the passive ventricle is then unloaded, sarcomeres in the posterior epicardium would become shorter than anterior ones as the greater number in series are compressed. This was, in fact, observed in our data. In every heart, wall mechanics caused sarcomeres to shorten more posteriorly in the transition from a midejecting to an unloaded configuration ($SL_{ej} - SL_{uni}$ in Fig. 6), and, as a result, the epicardial sarcomeres in the unloaded state were shorter posteriorly in five of six hearts.

At midwall depth, the mathematical model (7) predicted that ejecting SLs would be similar at both the anterior and posterior sites (within 0.05 μm) if SLs were equal in the unloaded state. When the train of thought above is followed, it predicts that the mechanical environment surrounding midwall myocytes would supply little adaptive stimulus to alter SLs differentially between the anterior and posterior sites. Consequently, we would predict that anterior and posterior midwall SLs would remain similar in an unloaded heart even after myocyte adaptation was allowed. This was, in fact, the general trend observed (Fig. 6).

If differential growth by myocytes adapts them so that sarcomere function tends toward uniformity for the ejecting conditions, then differential compressions and tensions within the ventricular wall are likely to be present when such an adapted left ventricle is unloaded passively, even though there is no net transmural pressure gradient distending the ventricle. Such a ventricle is then said to contain residual stresses (4). These can be revealed by judiciously cutting apart an unloaded ventricle, which then deforms as the residual stresses are relieved. Such deformations are called residual strains, which were studied in rat hearts by Omens and Fung (10). One consistent result from that study (Fig. 7 in Ref. 10) was the difference in residual strains between the anterior and posterior sites on an equatorial ring from the left ventricle. For example, the circumferential component of residual strain was significantly greater anteriorly, which implies that a circumferentially oriented line segment was elongated significantly more on the anterior side of the unloaded ventricle compared with its length in the stress-free sectioned state attained after releasing residual stresses.

The anterior-posterior differences in residual strain that Omens and Fung (10) noted are quantitatively
compatible with the anterior-posterior differences in SL that we observed under our unloaded conditions. Before we could make such a comparison, we needed to estimate SLs in the stress-free configuration. After residual stresses have been removed by sectioning an unloaded ventricle, it then seems likely that all SLs would be uniform. Rodriguez et al. (12) have confirmed this by showing that after residual stress is removed from rat ventricles, the transmural distribution of SLs becomes uniform at 1.84 μm. Combining the data of Rodriguez et al. with that of Omens and Fung (10), one can thus predict SLs in unloaded passive rat hearts at both the anterior and posterior sites. In making this prediction, we assumed that epicardial and midwall fibers were oriented at the average fiber angles we observed and that the longitudinal principal residual strain could be derived by assuming tissue incompressibility. At the epicardial layer, anterior sarcomeres were predicted to be 1.86 μm compared with 1.80 μm posteriorly. This 0.08-μm elongation of anterior epicardial sarcomeres predicted from residual strains measured in rat hearts compares favorably with the elongation of 0.06 μm that we observed in our unloaded state. At the midwall, the difference in predicted SLs for unloaded rat hearts was much smaller (anterior = 1.83 μm; posterior = 1.80 μm), identical to the insignificant 0.03-μm difference that we found. However, note that all absolute SLs were somewhat longer in our unloaded state (e.g., anterior epicardium = 2.01 μm; posterior epicardium = 1.94 μm). This is presumably because we never fully achieved an unloaded state (chamber pressures in our unloaded state were still positive), and thus the sarcomeres were somewhat distended beyond their truly unloaded lengths.

All of our data on SLs during ejection were obtained after chordal transection; on the other hand, myocytes would have adapted with the chordae intact. A recent preliminary study (16) on two open-chest anesthetized dogs suggests that, at end systole, chordal transection increases the longitudinal-radial shear in the anterior papillary muscle and inner wall. Although chordal transection certainly caused some rearrangement in cardiac geometry, there are several reasons to expect that it may not have meaningfully altered our anterior-posterior comparison. 1) The regions we studied did not directly overlie papillary insertion points, we implanted beads near the ventricular equator (more basal than papillary roots), and the circumferential location was slightly more septal (i.e., just lateral to the anterior and posterior descending coronary arteries). 2) The major difference we observed occurred at the epicardium, and we did not examine strains from the inner half of the wall. 3) Only a differential effect (e.g., if one papillary muscle were stronger than the other) is likely to have influenced our anterior-posterior comparison. Note that the geometry of our finite-element model for ventricular mechanics (7) was also obtained after chordal transection.

Further limitations of our SL data should be noted. Rodriguez et al. (11) estimated that the typical peak to peak noise that is associated with reconstructing the SL was on the order of 0.04 μm. This is ~13% of the typical amount of sarcomere shortening over the ejecting range (i.e., 0.3 μm; see Figs. 3A and 4A). Hence our reconstruction approach might not have been able to detect small differences in sarcomere shortening of this order. Moreover, the bead array used here consists of approximately two layers at least 5 mm apart, which exceeds the typical separation in the previous report by Rodriguez et al. Due to potential transmural inhomogeneities in myocardial strain, the greater the separation, the more error that could be introduced during sarcomere reconstruction. Rodriguez et al. found an uncertainty of <0.02 μm when fiber orientation deviated from the plane of markers by <10°. In this study, all midwall layers satisfied this angular criterion, but the larger separation may have introduced somewhat greater uncertainty due to transmural inhomogeneity of strain.

Although we primarily examined SLs during ejection, uncertainties in the diastolic configuration of the isolated hearts and potential but unknowable differences in diastolic suspension of the heart between experiment and in vivo may have affected our ability to interpret data (such as SL\textsubscript{max} and EDSL\textsubscript{max} in Table 1) that were derived during diastole. Because passive myocardium becomes dramatically stiffer as it is stretched, we expect less influence from diastolic suspension on EDSL\textsubscript{max} than on any other diastolic SL. Moreover, although the magnitude of SL\textsubscript{max} was clearly affected when we altered diastolic suspension by rotating the isolated heart, SL\textsubscript{max} at the anterior epicardial site remained significantly longer than that at the posterior site.

In summary, sarcomeres at anterior vs posterior sites in isolated canine hearts functioned similarly throughout ejection over wide ranges of ventricular pre- and afterloads. A mathematical model for ventricular mechanics (7) predicted that epicardial SL\textsubscript{max} values would differ between the anterior and posterior sites if SLs were uniformly distributed when the left ventricle was in its unloaded passive configuration. Thus the anterior-posterior similarity of ejecting sarcomere function that we observed must develop despite inherent mechanical differences between the anterior and posterior regions of the left ventricle. This suggests that the ability of cardiac cells to alter their structure in response to mechanical loads allows sarcomere function during ejection to be nearly equilibrated between regions via myocyte adaptation. Such systolically governed adaptation, however, will lead to nonuniform SLs (residual strains) in the passive unloaded ventricle.

The authors thank Dr. James H. Anderson, Michael Samphilipo, and Carolyn Magee for assistance with the biplane cineradiographic procedures. We also appreciate the help of Dr. Willard Graves and David Mearns for assistance with the marker-tracking software. We also thank Dr. Brian K. Slinker for expert advice on the statistical analysis of our data. Sincere thanks also go to Ken Rent, who provided invaluable surgical assistance, to Eric Lee and Beth Jones, who spent many hours tracking markers on film, and to Michele K. Leppo for performing the histological procedures and sectioning.

This work was supported by National Heart, Lung, and Blood Institute Grant HL-26559 (to W.C. Hunter).
ANTERIOR-POSTERIOR LV SARCOMERE LENGTHS

H477

J. M. Guccione was the recipient of Individual National Research Service Award I F32-HL-08492 from the National Heart, Lung, and Blood Institute. This support is gratefully acknowledged.

Address for reprint requests: J. M. Guccione, Washington Univ. Campus Box 1185, One Brookings Dr., St. Louis, MO 63130-4899.

Received 14 February 1996; accepted in final form 2 July 1996.

REFERENCES


