Three-Dimensional Left Ventricular Midwall Dynamics in the Transplanted Human Heart

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To quantify the three-dimensional regional dynamics of the left ventricular (LV) midwall and the centroid and cross-sectional shape of the LV chamber in the transplanted human heart, 12 miniature radiopaque tantalum markers were implanted in the LV midwall of the donor heart at the time of cardiac transplantation in 15 patients. Stereo cineradiography in the late postoperative period (mean, 52 days after surgery) allowed computer-aided measurements of the three-dimensional coordinates of multiple sites in anterior, inferior, lateral, and septal LV regions at 16.7-msec intervals throughout the cardiac cycle. In awake, supine patients, from maximum to minimum LV volume, group mean translations of free wall markers ranged from 0.80 to 1.24 cm, directed toward the LV interior, whereas translations of septal wall markers were significantly less, 0.46 and 0.34 cm (p<0.01), directed away from the LV interior. A component of this translation along the septal-lateral axis was also significantly less (p<0.01) in the septum (0.19 and 0.20 cm) than in the free wall, where it ranged from 0.32 to 0.97 cm. The LV cross section was not circular, and anterior-inferior dimensions (7.18±0.66 and 6.13±0.79 cm, at maximum and minimum volumes, respectively) were significantly greater (p<0.01) than septal-lateral dimensions (5.78±0.65 and 5.12±0.48 cm), yielding an unchanging transverse elliptical LV eccentricity (0.58±0.13). The position of the LV center of volume did not change significantly from maximum to minimum volume in the direction of either the LV long axis or the anterior-inferior axis, but it did change significantly (0.55±0.23 cm, p<0.01) along the septal-lateral axis. We conclude 1) as viewed in a fixed external reference system, midwall sites in the interventricular septum of the transplanted human heart move paradoxically yet are relatively immobile compared with the three-dimensional dynamics of midwall sites in the LV free wall; 2) the transverse cross-sectional shape of the LV in the transplanted human heart is decidedly oval, with significantly greater anterior-posterior than septal-lateral dimensions at the time of maximum and minimum LV volumes; and 3) the center of volume in the transplanted human LV is remarkably stable in the directions of the LV long axis and anterior-posterior axis, suggesting a balance of forces along these axes, yet it moves significantly toward the interventricular septum, presumably counterbalancing the opposite translation during systole of the right ventricular (RV) center of volume. In effect, then, as viewed from an external reference frame, the transplanted heart appears to beat as a “double bellows” (possibly preserving the position of its overall center of mass) in which the free walls of both ventricles contract toward a relatively immobile interventricular septum in systole. We suggest that the altered shape and dynamics of the LV in the transplanted human heart are not due to significantly reduced septal contraction or anterior systolic cardiac translation but are more likely the result of an RV pressure overload. (Circulation 1990;81:1837–1848)

During the past two decades, cardiac transplantation for end-stage heart disease has evolved from an experimental procedure to an accepted therapeutic modality, with a 1-year survival rate that has increased to 80–90%, largely because of the advent of improved immunosuppres-

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sive therapy. With this improved survival, the number of cardiac transplant procedures has increased dramatically in recent years.

Although transplanted hearts are typically from young donors, are initially free of significant myocardial and coronary artery diseases, and demonstrate normal contractile characteristics and reserve as judged by afterload challenge, such hearts have undergone an obligatory ischemic interval and reperfusion, are denervated, do not have an intact pericardium, may encounter abnormal loading conditions, and sustain myocyte necrosis accompanying rejection episodes. These characteristics raise important questions concerning the normalcy of ventricular dynamics.

Previous qualitative studies of ventricular dynamics in the donor heart have yielded mixed results, with reports ranging from entirely normal systolic function with no segmental dysfunction to abnormal dynamics in all regions studied. To the best of our knowledge, however, there have been no systematic quantitative studies of three-dimensional ventricular dynamics in the transplanted human heart.

For some years, we have been implanting miniature radiopaque tantalum markers into the left ventricular (LV) midwall of the donor heart at the time of cardiac transplantation in humans. Subsequent stereo radiographic studies allow computer-aided analysis of the three-dimensional dynamics of these specific sites within the ventricular myocardium. The radiographic studies reported here were performed to provide data for two complementary analyses of three-dimensional LV dynamics, a previous examination of torsional deformation and anisotropic shortening, and the present study of the three-dimensional regional dynamics of the LV midwall and the centroid and cross-sectional shape of the LV chamber in the transplanted human heart.

Methods

Studies were conducted in 15 cardiac transplant recipients, an average of 52 days (range, 6–331 days) after surgery. Patients with biopsy-confirmed evidence of rejection requiring therapy at the time of study were not included. Long-term immunosuppressive therapy in all patients consisted of a combination of cyclosporine and prednisone.

At surgery, in a manner described previously, 12 tantalum radiopaque markers, each 0.85 mm in diameter and 2.2 mm in length, were inserted into the LV midwall to a depth of 5 mm from the outermost LV surface. As shown schematically in Figure 1, three of these markers (2, 3, and 4) were spaced uniformly along the interventricular sulcus, one marker (5) was placed near the LV apex, and three (6, 7, and 8) were placed along the anterior interventricular sulcus. These markers (2–8) were intended to silhouette the LV chamber as viewed in the 30° right anterior oblique projection. Three additional markers (10, 11, and 12) were then inserted into the lateral free wall at positions midway between the anterior and inferior markers, and two septal markers (13 and 14) were implanted at basal and midventricular levels through the tricuspid valve. These markers (10–14 and apical marker 5) were intended to silhouette the LV as viewed in the 60° left anterior oblique projection. Two radiopaque clips (1 and 9, not shown in Figure 1) were attached to the adventitia of the aortic root to allow estimation of the position of the aortic valve.

Informed consent was obtained from all patients for the implantation of LV markers and subsequent radiographic studies in accordance with the require-
ments of the committee on the use of human subjects in research at the Stanford University Medical Center. There were no complications due to the implantation of markers or subsequent studies.

Cineradiographic studies were conducted in awake, supine patients, and respiration was held at midexpiration. Biplane radiograms were obtained at 60 frames/sec for at least three full cardiac cycles by means of two orthogonal, isocentered, pulsed radiographic imaging systems (MLX LU-arm biplane unit, GE, Milwaukee, Wisconsin) in the 30° right anterior oblique and the 60° left anterior oblique projections.

At the conclusion of each study, a phantom with known dimensions was imaged. The right and left anterior oblique cinefilms were then projected by vidicon television camera onto a computer-linked monitor; the marker and phantom positions were digitized by light pen, and the resulting coordinates were stored in computer memory. Coordinates were corrected for distortion and magnification with data from the phantom, and data from the two views were merged to yield the three-dimensional coordinates of each marker at each sampling instant. Accuracy and reproducibility studies have demonstrated that marker positions can be measured in three-dimensional space with an error of 0.3±1.3 mm (mean±SD) with this system.

As previously validated, coordinates from the right anterior oblique view of markers 1–9 were used to estimate LV end-diastolic volume, end-systolic volume, stroke volume, ejection fraction, and cardiac output for each beat in each patient. Figure 2 shows a typical instantaneous volume curve from such a calculation in one of our patient studies. A summary of all volumetric parameters for the 15 patients is given in Table 1. The low ejection fractions observed are typical of those derived from the dynamics of specific myocardial sites, either from midwall markers (as in the present study) or by implanted sonomicrometer crystals in experimental animals.

A representative beat was selected from each patient study. A standard reference system was defined for this beat in the maximum volume frame

![Figure 2](http://circ.ahajournals.org/)

**Figure 2.** Instantaneous left ventricular volume curve from a patient study. Data are obtained at 60 frames/sec, and frames are assigned sequential reference numbers (1–37).

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**Table 1. Left Ventricular Volumetric Parameters for the 15 Patients**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>End-diastolic volume (ml)</td>
<td>196±45</td>
</tr>
<tr>
<td>End-systolic volume (ml)</td>
<td>125±35</td>
</tr>
<tr>
<td>Stroke volume (ml)</td>
<td>71±17</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>37±8</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>95±13</td>
</tr>
<tr>
<td>Cardiac output (l/min)</td>
<td>6.8±1.6</td>
</tr>
</tbody>
</table>

Data are mean±SD.
such that 1) the origin was placed at the midpoint of the chord between markers 2 and 8; 2) the X-Y plane contained markers 2, 5, and 8; 3) marker 8 had a positive X coordinate; and 4) marker 5 was located on the negative Y axis. Figure 3 shows three views of systolic marker motions, as viewed in this reference frame, from one of our patient studies. This reference system directs the positive X axis from the center of the LV toward the left arm, the positive Y axis toward the head, and the positive Z axis toward the sternum.

The systolic marker motions in Figure 3 are represented as vectors drawn between marker positions at maximum and minimum volumes. The justification for displaying systolic data in this fashion is illustrated in Figure 4, which shows three views of a typical three-dimensional marker trajectory as viewed in our standard reference system. The trajectory of midlateral wall marker 11 is shown in Figure 4 in the same patient whose instantaneous volumes are shown in Figure 2. Although detailed marker trajectories are typically quite complex, the general sense of the motion in systole is well conveyed by displaying the coordinates at maximum volume (frame 22 in Figures 2 and 4) and minimum volume (frame 37 in Figures 2 and 4) as in Figure 3.

The mean value of each coordinate for markers 2–8 and 9–14 was determined for the group of 15 patients at maximum and minimum volumes. The mean and standard error of the mean of the motion of each marker from maximum to minimum volume was also determined for the group and so were the components of this motion along the X, Y, and Z axes. These composite data were plotted for the group.

Anterior-inferior chord lengths from markers 2 to 8 and from markers 3 to 7 were averaged at maximum volume and again at minimum volume for the group of 15 patients. Septal-lateral chord lengths from markers 10 to 13 and from markers 11 to 14 were also averaged at maximum and minimum volumes for the group. Chord shortening (in cm and percent maximum volume value) and cross-sectional eccentricities \( e = \frac{(a^2 - b^2)^{1/2}}{a} \), where \( a \) and \( b \) are the above chord lengths were computed from these data.

The centroid of volume of the polyhedron defined by the LV markers (2–8 and 10–14, excluding the
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FIGURE 4. Three orthogonal views of a typical three-dimensional marker trajectory throughout a cardiac cycle as viewed in the standard reference system. Trajectory of midlateral wall marker 11 is shown in the same patient whose data are displayed in Figures 2 and 3. Coordinates are shown at 16.7-msec intervals from beginning filling (frame number 1, Figure 2) to maximum volume (frame number 22) to minimum volume (frame number 37). This figure can be folded along its central axes to observe the trajectory of this marker with better three-dimensional perspective.

The volume between markers 2, 8, 10, and 13 and the aortic and mitral valve rings) was calculated for each frame in each patient. This was accomplished by first defining an LV long axis in each frame extending from the apical marker (5) to the midpoint of a chord joining markers 2 and 8. The midpoint of this long axis was used as an arbitrary point within the LV cavity to serve as a common vertex (Xa, Ya, Za) for tetrahedra (Xb,i, Yb,i, Zb,i; Xc,i, Yc,i, Zc,i; andXd,i, Yd,i, and Zd,i) that completely filled the region within the markers and whose other three vertices (Xb,i, Yb,i, Zb,i; Xc,i, Yc,i, Zc,i; andXd,i, Yd,i, and Zd,i) were defined by groups of three adjacent myocardial markers (such as b=2, c=8, and d=10 for i=1; b=7, c=8, and d=10 for i=2; etc.).

The volume (VOLi) of each tetrahedron was calculated as one sixth the absolute value of the determinant,

\[
\begin{vmatrix}
X_a & Y_a & Z_a & 1 \\
X_{b,i} & Y_{b,i} & Z_{b,i} & 1 \\
X_{c,i} & Y_{c,i} & Z_{c,i} & 1 \\
X_{d,i} & Y_{d,i} & Z_{d,i} & 1
\end{vmatrix}
\]

and the total volume contained within the marker polyhedron was obtained as \(\text{VOL}_{\text{tot}} = \text{VOL}_1 + \text{VOL}_2 + \text{VOL}_3 + \ldots + \text{VOL}_n\).

The X coordinate of the centroid of each tetrahedron \(i\) was found as \(X_{Ci} = (X_a + X_{b,i} + X_{c,i} + X_{d,i})/4\), the Y coordinate as \(Y_{Ci} = (Y_a + Y_{b,i} + Y_{c,i} + Y_{d,i})/4\), and the Z coordinate as \(Z_{Ci} = (Z_a + Z_{b,i} + Z_{c,i} + Z_{d,i})/4\).

The X coordinate of the center of volume of the LV region within the markers was then found as \(X = (X_{C1} \cdot \text{VOL}_1 + X_{C2} \cdot \text{VOL}_2 + X_{C3} \cdot \text{VOL}_3 + \ldots + X_{Cn} \cdot \text{VOL}_n)/\text{VOL}_{\text{tot}}\), the Y coordinate as \(Y = (Y_{C1} \cdot \text{VOL}_1 + Y_{C2} \cdot \text{VOL}_2 + Y_{C3} \cdot \text{VOL}_3 + \ldots + Y_{Cn} \cdot \text{VOL}_n)/\text{VOL}_{\text{tot}}\), and the Z coordinate as \(Z = (Z_{C1} \cdot \text{VOL}_1 + Z_{C2} \cdot \text{VOL}_2 + Z_{C3} \cdot \text{VOL}_3 + \ldots + Z_{Cn} \cdot \text{VOL}_n)/\text{VOL}_{\text{tot}}\).

All statistical comparisons were made with Student’s \(t\) test with Bonferroni’s correction for multiple comparisons.

Results

Table 2 presents group mean marker coordinates at maximum and minimum volumes for LV sites 2–8 and 10–14 in the standard reference frame. Missing or misplaced markers in the septum or lateral wall in some hearts result in sites with fewer than 15 observations.

The group mean data in Table 2 are presented in graphical form in Figure 5. Three views are shown: 1) a right anterior oblique view, giving a perspective
TABLE 2. Group Mean Marker Coordinates at Maximum and Minimum Volumes

<table>
<thead>
<tr>
<th>Myocardial marker number</th>
<th>Coordinates (cm) at maximum volume</th>
<th>Coordinates (cm) at minimum volume</th>
<th>Observations (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>X = -3.56, Y = 0.38, Z = 0.00</td>
<td>X = -3.06, Y = -0.48, Z = 0.32</td>
<td>15</td>
</tr>
<tr>
<td>3</td>
<td>X = -2.98, Y = -1.64, Z = -0.43</td>
<td>X = -2.21, Y = -2.07, Z = 0.00</td>
<td>15</td>
</tr>
<tr>
<td>4</td>
<td>X = -2.05, Y = -4.58, Z = -0.43</td>
<td>X = -1.30, Y = -4.68, Z = -0.01</td>
<td>14</td>
</tr>
<tr>
<td>5</td>
<td>X = 0.00, Y = -7.35, Z = 0.00</td>
<td>X = 0.11, Y = -7.00, Z = 0.77</td>
<td>15</td>
</tr>
<tr>
<td>6</td>
<td>X = 2.32, Y = -5.82, Z = 0.64</td>
<td>X = 1.99, Y = -5.55, Z = 1.57</td>
<td>15</td>
</tr>
<tr>
<td>7</td>
<td>X = 3.55, Y = -3.48, Z = 0.26</td>
<td>X = 3.20, Y = -3.60, Z = 1.05</td>
<td>15</td>
</tr>
<tr>
<td>8</td>
<td>X = 3.56, Y = -0.38, Z = 0.00</td>
<td>X = 3.18, Y = -0.86, Z = 0.43</td>
<td>15</td>
</tr>
<tr>
<td>10</td>
<td>X = 1.20, Y = 0.80, Z = -2.04</td>
<td>X = 1.09, Y = -0.15, Z = -1.48</td>
<td>10</td>
</tr>
<tr>
<td>11</td>
<td>X = 1.06, Y = -1.94, Z = -2.53</td>
<td>X = 1.32, Y = -2.53, Z = -1.56</td>
<td>9</td>
</tr>
<tr>
<td>12</td>
<td>X = 0.41, Y = -4.80, Z = -1.94</td>
<td>X = 1.06, Y = -5.02, Z = -1.03</td>
<td>7</td>
</tr>
<tr>
<td>13</td>
<td>X = 0.11, Y = -1.56, Z = 3.36</td>
<td>X = 0.24, Y = -1.76, Z = 3.55</td>
<td>15</td>
</tr>
<tr>
<td>14</td>
<td>X = -0.13, Y = -3.55, Z = 2.73</td>
<td>X = -0.17, Y = -3.49, Z = 2.93</td>
<td>5</td>
</tr>
</tbody>
</table>

roughly from top to bottom in Figure 1 (through the RV to the LV, with the septum above and the lateral wall below the X-Y plane, i.e., above and below the page, respectively); 2) a left anterior oblique view, giving a perspective roughly from front to back in Figure 1 (with the anterior wall above and the inferior wall below the Y-Z plane); and 3) an end view, giving a perspective roughly from left to right in Figure 1 (with the apex above and the base below the X-Z plane). A noteworthy feature in Figure 5 is that

**Figure 5.** Three orthogonal views of mean systolic left ventricular (LV) marker motions in the standard reference system for the group of 15 patients. Marker positions are shown at maximum LV volume (numbered end of arrow) and minimum LV volume (arrowhead point). Upper right panel: 30° right anterior oblique projection; view is from septum to lateral wall (viewed downward from the top in Figure 1). Lower right panel: 60° left anterior oblique projection; view is from anterior to inferior wall (same orientation as in Figure 1). Lower left panel: View is from apex to base (left to right in Figure 1). Group mean coordinates of the centroid of the LV marker polyhedron are indicated by a vector (CV) from maximum to minimum volume in each view.
the septal markers (13 and 14) translate far less than the free wall markers in all views.

The group mean (and SEM) total translation (L) for each marker is given in Table 3. Also shown in Table 3 are the mean components (and SEM) of this motion (DX, DY, and DZ, respectively) along the X, Y, and Z axes. Note that the free wall markers exhibited total translations (L) ranging from 0.80 to 1.24 cm, whereas the total translation of the septal markers was less, 0.46 and 0.34 cm (p<0.01). The component of this translation along the Z axis (roughly normal to the interventricular septum) was also far less in the septum (0.19 and 0.20 cm, p<0.01) than in the free wall, where it ranged from 0.32 to 0.97 cm. Furthermore, septal translation was directed toward the sternum (positive Z axis) in all 15 patients.

Table 4 gives the anterior-inferior and septal-lateral chord lengths at maximum and minimum volumes for the group, with pooled basal and equatorial data. As can be seen, not only was the anterior-inferior dimension significantly greater than the septal-lateral dimension at the time of maximum and minimum volumes, but the reduction in anterior-inferior dimension was also significantly greater than the reduction in septal-lateral dimension during systole. When the LV cross section was treated as an ellipse, with major and minor axes being the anterior-inferior and septal-lateral chords, the elliptical shape was unchanged from maximum to minimum volume, as indicated by the nearly unchanged eccentricity values given in Table 4. Figure 6 shows these data to scale, emphasizing the noncircular LV cross sections observed in these hearts.

Table 5 gives the group mean values of the coordinates of the centroid of the LV polyhedron at maximum and minimum volumes. The centroid coordinates are also displayed graphically (CV) at maximum and minimum volumes in each of the three views in Figure 5. The smallest change in center of volume was observed in the X component, and the next largest was in the Y component, neither of which achieved statistical significance. The change in the Z component, however, was highly significant, primarily because of the motion of the LV free wall toward the relatively immobile septum during systole in these transplanted hearts.

To estimate the errors inherent in defining ventricular centroid coordinates from markers placed as in Figure 1, the LV was approximated by an elliptical cylinder capped by an elliptical cone at the apex. The data in Tables 2 and 4 were used to define, at maximum and minimum volumes, respectively, the semimajor axis (3.59 and 3.07 cm), semiminor axis (2.89 and 2.56 cm), and the average spacing between successive transverse marker planes (2.45 and 2.33 cm) in this model. The distance from the valve plane (unmarked) to the plane containing markers 2, 8, 10, and 13 was assumed as 1.23 cm at maximum volume and 1.17 cm at minimum volume, and the apical septal marker was assumed missing, as in Figure 1. In this model, the X, Y, and Z components of error associated with locating the true LV centroid by the

### Table 3. Group Mean Vector Components and Lengths

<table>
<thead>
<tr>
<th>Myocardial marker number</th>
<th>DX Mean (cm)</th>
<th>DX SEM (cm)</th>
<th>DY Mean (cm)</th>
<th>DY SEM (cm)</th>
<th>DZ Mean (cm)</th>
<th>DZ SEM (cm)</th>
<th>L Mean (cm)</th>
<th>L SEM (cm)</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>0.50</td>
<td>0.06</td>
<td>-0.86</td>
<td>0.12</td>
<td>0.32</td>
<td>0.06</td>
<td>1.14</td>
<td>0.09</td>
<td>15</td>
</tr>
<tr>
<td>3</td>
<td>0.77</td>
<td>0.07</td>
<td>-0.43</td>
<td>0.10</td>
<td>0.43</td>
<td>0.05</td>
<td>1.07</td>
<td>0.07</td>
<td>15</td>
</tr>
<tr>
<td>4</td>
<td>0.75</td>
<td>0.08</td>
<td>-0.10</td>
<td>0.07</td>
<td>0.42</td>
<td>0.07</td>
<td>0.98</td>
<td>0.06</td>
<td>14</td>
</tr>
<tr>
<td>5</td>
<td>0.11</td>
<td>0.08</td>
<td>0.35</td>
<td>0.07</td>
<td>0.77</td>
<td>0.11</td>
<td>0.96</td>
<td>0.09</td>
<td>15</td>
</tr>
<tr>
<td>6</td>
<td>-0.33</td>
<td>0.08</td>
<td>0.27</td>
<td>0.08</td>
<td>0.93</td>
<td>0.10</td>
<td>1.13</td>
<td>0.09</td>
<td>15</td>
</tr>
<tr>
<td>7</td>
<td>-0.35</td>
<td>0.07</td>
<td>-0.12</td>
<td>0.07</td>
<td>0.79</td>
<td>0.09</td>
<td>0.94</td>
<td>0.10</td>
<td>15</td>
</tr>
<tr>
<td>8</td>
<td>-0.38</td>
<td>0.05</td>
<td>-0.48</td>
<td>0.09</td>
<td>0.43</td>
<td>0.07</td>
<td>0.80</td>
<td>0.10</td>
<td>15</td>
</tr>
<tr>
<td>9</td>
<td>-0.11</td>
<td>0.05</td>
<td>-0.95</td>
<td>0.17</td>
<td>0.56</td>
<td>0.13</td>
<td>1.15</td>
<td>0.20</td>
<td>10</td>
</tr>
<tr>
<td>10</td>
<td>0.26</td>
<td>0.09</td>
<td>-0.59</td>
<td>0.12</td>
<td>0.97</td>
<td>0.16</td>
<td>1.24</td>
<td>0.16</td>
<td>9</td>
</tr>
<tr>
<td>11</td>
<td>0.65</td>
<td>0.11</td>
<td>-0.22</td>
<td>0.13</td>
<td>0.91</td>
<td>0.11</td>
<td>1.20</td>
<td>0.13</td>
<td>7</td>
</tr>
<tr>
<td>12</td>
<td>0.13</td>
<td>0.06</td>
<td>-0.20</td>
<td>0.06</td>
<td>0.19</td>
<td>0.06</td>
<td>0.46</td>
<td>0.05</td>
<td>15</td>
</tr>
<tr>
<td>13</td>
<td>-0.04</td>
<td>0.09</td>
<td>0.06</td>
<td>0.10</td>
<td>0.20</td>
<td>0.05</td>
<td>0.34</td>
<td>0.05</td>
<td>5</td>
</tr>
</tbody>
</table>

DX, DY, and DZ, vector components in the X, Y, and Z directions, respectively; SEM, standard error of the mean; L, vector length (L = \sqrt{DX^2+DY^2+DZ^2}); n, number of observations.

### Table 4. Cross-Sectional Dimensions and Eccentricity

<table>
<thead>
<tr>
<th></th>
<th>Anterior-inferior</th>
<th>Septal-lateral</th>
<th>Eccentricity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max volume</td>
<td>7.18 (0.66)</td>
<td>5.78 (0.65)*</td>
<td>0.58 (0.13)</td>
</tr>
<tr>
<td>Min volume</td>
<td>6.13 (0.79)</td>
<td>5.12 (0.48)*</td>
<td>0.54 (0.14)</td>
</tr>
<tr>
<td>Difference (max−min)</td>
<td>1.05 (0.20)†</td>
<td>0.66 (0.43)†</td>
<td>0.03 (0.10)</td>
</tr>
<tr>
<td>Difference (%)</td>
<td>14.9 (4.1)</td>
<td>11.0 (6.5)*</td>
<td></td>
</tr>
</tbody>
</table>

Values are pooled basal and equatorial data in cm; values in parentheses are SD.

Max volume, value at the time of maximum left ventricular volume; min volume, value at the time of minimum left ventricular volume; difference (max−min), change in value from max to min volume; difference (% max), difference (max−min) as percentage of max volume value.

*p<0.01 relative to Anterior-inferior; †p<0.01.
marker polyhedron were 0.0, −0.46, and −0.11 cm, respectively, at maximum volume and 0.0, −0.44, and −0.10 cm, respectively, at minimum volume, but the error associated with defining the motion of this centroid from maximum to minimum volume was 0.0, 0.02, and 0.01 cm, respectively. In contrast to these small errors, however, the volume contained within the marker polyhedron was only 49% of the true volume of the model; thus, the polyhedron was not used to estimate LV volumes in this study. Analysis of this model, then, suggests that inclusion of additional markers (e.g., to define the valve plane or to take wall curvature more fully into account) would have relatively little impact on the centroid data in Table 5, with the most prominent effect being to translate the Y component of the centroid approximately 0.45 cm toward the base at maximum and minimum volumes.

**Discussion**

The principal finding in the present study was that, as viewed in a fixed external reference system, midwall sites in the interventricular septum of the transplanted human heart are nearly immobile compared with the three-dimensional dynamics of midwall sites in the LV free wall. This can be seen clearly in Figure 5, where the motion of midwall septal markers 13 and 14 is markedly less than that of free wall markers 2–8 and 9–12 in all views. Septal motion was directed anteriorly in systole, without exception, in all 15 patients studied.

This finding of a relatively immobile septum is consistent with previous reports of abnormal septal motion (documented with a variety of one- and two-dimensional techniques) after a number of cardiac surgical procedures and by echocardiographic evidence suggesting abnormal motion of the interventricular septum in the transplanted human heart.

A number of previous studies suggested that postoperative abnormal septal dynamics are the result of possible septal ischemia or infarction. We feel, however, that septal contractile function was not significantly compromised by ischemia or infarction in the transplanted hearts of this study. We found that contraction, as assessed in these same beats by the systolic shortening of chords between adjacent regional marker pairs in these same patients, was only 13% less in the septum (12.3±1.9%) than in the free wall (14.1±2.4%) (p<0.03). Furthermore, septal chords did not exhibit dyskinesis or akinesis during systole that would be expected if significant ischemic damage had occurred. Thus, although septal contraction was somewhat smaller than free wall contraction, the slight difference suggests that if regional septal damage did occur it was likely to be minor.

Many studies have suggested that postoperative abnormal septal dynamics might be the result of anterior systolic motion of the entire heart as a result of altered external constraints after surgery. The donor heart is typically smaller than the recipient pericardial sac, and the pericardium is intact only posteriorly, both being factors that could allow

**TABLE 5. Centroid Position**

<table>
<thead>
<tr>
<th></th>
<th>X</th>
<th>Y</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max volume</td>
<td>0.34 (0.36)</td>
<td>−2.48 (0.52)</td>
<td>0.17 (0.26)</td>
</tr>
<tr>
<td>Min volume</td>
<td>0.48 (0.31)</td>
<td>−2.75 (0.64)</td>
<td>0.72 (0.35)</td>
</tr>
<tr>
<td>Difference (max−min)</td>
<td>0.14 (0.20)</td>
<td>−0.27 (0.30)</td>
<td>0.55 (0.23)*</td>
</tr>
</tbody>
</table>

All coordinates in cm relative to Figure 5 reference; values in parentheses are SD.

Max volume, coordinates at the time of maximum left ventricular volume; min volume, coordinates at the time of minimum left ventricular volume; difference (max−min), change in coordinates from max to min volume.

*p<0.01.
greater freedom of motion of the heart inside the chest during the cardiac cycle. The following analysis suggests, however, that the transplanted hearts studied here did not exhibit significantly greater than normal anterior systolic motion. At end diastole, posterolateral wall thickness in the transplanted human heart ranges from 11 to 14 mm.10 Posterolateral wall thickness normally increases from 21% to 92% (mean, 47%) during systole.44 By assuming midwall marker placement, symmetric lateral wall thickening about the marker, 12-mm diastolic wall thickness, 47% systolic wall thickness increase, and the maximum +9.7-mm Z-axis translation of marker 11 (Table 3), we then calculate a 12.5-mm septal-directed displacement of the endocardium for the lateral wall. The amplitude of normal posterolateral endocardial motion ranges from 9 to 14 mm, with a mean of 12 mm.19 Thus, we find that lateral wall displacements appear to be within the normal range in these 15 transplanted hearts. With lateral wall displacements within the normal range, it is unlikely that the whole heart is translating anteriorly during systole. Of note, however, although this finding agrees with the normal segmental function observed by Pflugfelder et al11 and the posterolateral wall translation shown in the example echocardiogram of Hosenpud et al10 obtained 1 month after surgery, it is less (by 3–4 mm) than the translations noted 3 months after operation19 and in the two echocardiograms shown in Guthaner et al9 (see their Figures 5 and 6). Thus, further quantitative studies are needed to investigate this point.

Septal motion, however, is clearly abnormal in these patients. At end diastole, interventricular septal thickness in the transplanted human heart ranges from 12 to 13 mm.10 Septal thickness increases normally from 14% to 57% (mean, 36%) during systole.44 By assuming a midseptal marker placement, symmetrical septal thickening about the marker, a 12-mm value for diastolic septal thickness, a 36% systolic septal thickness increase, and the septal marker 14 Z-axis translation of +2.0 mm (Table 3), we then calculate a 0.2-mm posterior-directed displacement of the left side of the septum. Normal septal motion is defined as systolic posterior excursion of the left side of the interventricular septum of 3–8 mm, typically averaging 5 mm.19 Thus, septal displacements would be considered abnormal in these transplanted hearts. Although this finding agrees with the translations exhibited by the echocardiograms in Guthaner et al9 and the finding of abnormal septal dynamics in Bhatia et al,12 it does not agree with the absence of LV segmental dysfunction in Pflugfelder et al11 and the echocardiograms in Hosenpud et al,10 which show normal left septal excursions. Additional studies are needed to investigate this point, as well.

Our data appear to be consistent with three aspects of LV shape and dynamics previously observed under conditions of experimental RV pressure overload. First, studies in anesthetized45 and conscious46–48 closed-chest dogs have shown that even relatively mild increases in mean pulmonary artery pressure can reduce significantly the LV septal-lateral dimension at end diastole and end systole, whereas the anterior-posterior and base-apex dimensions remain unchanged or lengthen slightly with respect to control values. Bemis et al49 also found that in isolated dog hearts anterior-posterior dimension increased and septal-lateral dimension decreased as RV end-diastolic pressure increased. All of these studies attributed this disproportionate shortening of the septal-lateral axis to a flattening and encroachment of the interventricular septum toward the cavity of the LV with increased right ventricular loading. Bemis et al49 also provided evidence that the pericardium was not a factor in this shape change. Using two-dimensional echocardiography in normal human hearts, Brinker et al50 have shown that acute RV pressure loading (early Mueller maneuver) also changes the shape of the LV from nearly circular to decidedly oval, with the septal flattening observed in diastole persisting throughout systole. The data in the present study (Table 4 and Figure 6) match these findings in that LV cross sections in these transplanted hearts were distinctly oval. The cross-sectional eccentricity (Table 4) in these hearts was 0.58 at maximum volume and did not change significantly during systole. Under normal loading conditions, eccentricities would be expected to be much closer to zero, because echocardiographic LV cross sections are nearly circular. Thus, this oval LV shape, unchanging throughout systole, is consistent with a hypothesis of RV pressure overload. It should be noted that normal LV septal-posterolateral dimensions range from 3.7 to 5.6 cm, with a mean value of 4.7 cm.19 Thus, after correcting for normal wall thickness, the septal-lateral dimensions found in the hearts in the present study (Table 4) are normal. This implies that the oval LV shape in these hearts is the result of a larger-than-normal anterior-inferior dimension.

Second, studies in experimental animals55,46,48 have shown that systolic shortening is disproportionately reduced in the septal-lateral axis compared with the other axes as pulmonary artery pressure is increased. The data in Table 4 are consistent with this concept in that systolic chord shortening in the septal-lateral (Z) direction was significantly less than chord shortening in the anterior-inferior (X) direction. Thus, this finding of disproportionately low septal-lateral shortening is also consistent with a hypothesis of RV pressure overload. Caution is required here, however, because Badke et al48 found that after an acute drop septal-lateral shortening was restored to control values with chronic RV pressure overloads. In Badke’s chronic preparations, however, septal-lateral shortening was invariably greater than anterior-posterior shortening, unlike that found in studies by Stool et al15 and Visser et al46 and opposite to that observed in the present study. This conflict will require further investigation.

Third, previous studies in humans and experimental animals showed that systolic septal motion abnor-
malities (in the absence of ischemia or infarction) are readily produced by even minor alterations in transseptal pressure gradients,24,34–36,45,49,50–55 with the pericardium having little influence on these dynamics.10,1256 As the normal transseptal pressure gradient is reduced, the septum is progressively displaced leftward and flattened.52,54,55 Depending on the extent of leftward septal displacement, systolic septal motion may be reduced, eliminated, or reversed (“paradoxical”).52,55 Thus, the relatively immobile, paradoxical systolic septal dynamics observed in the present study (Table 3 and Figure 5) are also consistent with a hypothesis of RV pressure overload.

It should be emphasized that the link between RV pressure overload and the LV shape and dynamics measured in these patients is speculative, although previous studies showed that transplanted hearts often exhibit signs of RV pressure overloading.11,12,56 For the first few months after surgery, RV systolic and diastolic pressures,12 mean pulmonary artery pressures,11,12,56 and mean pulmonary capillary wedge pressures10–12,56 are all typically elevated above normal levels. Subsequently, although RV systolic and diastolic pressures fall to the high normal range,12 mean pulmonary artery pressures remain elevated.11,12,56 Thus, there are signs of early and late postoperative RV pressure overloads, with RV geometric abnormalities (and concomitant tricuspid regurgitation) persisting throughout the first postoperative year.12 A recent echocardiographic study showed that the donor RV remains dilated but does not undergo hypertrophy during the first postoperative year.12 This study also detected a volume overload contraction pattern echographically, including RV dilatation, flattened diastolic septal geometry, and paradoxical systolic septal motion.12 Our finding of a marked distortion of the normally circular LV cavity in the present study, along with the persistent elevation of mean pulmonary artery pressures11,12,56 suggests concomitant RV pressure overload, as well, but this needs to be tested.

The problem of the effects of hemodynamic loading in the transplanted heart is manifold due to the complex and incompletely understood nature of ventricular interdependence. Brinker et al50 cite animal studies showing that RV loading restrains LV filling, alters LV configuration, and impairs LV performance. Santamore et al57 summarize that a small increase in right heart filling pressure can significantly increase RV volume that can, in turn, shift the LV diastolic pressure-volume curve upward and to the left (stiffer LV chamber). LV filling and systolic pressures are known to be elevated in transplanted hearts.10–12,56 Under these conditions, one may measure an increase in the transseptal pressure gradient rather than a decrease. Clearly, further studies are needed to determine the impact of these complex and interdependent interactions on myocardial geometry and dynamics.

Abnormal postoperative loading conditions and ventricular interdependence may also play a role in the paradoxical septal motion often observed after a number of other cardiac surgical procedures. Recent studies suggest that abnormal septal motion typically occurs within 2 hours after chest closure,31,33 too early to invoke adhesion formation.22,28 This may, however, reflect an early postoperative development of abnormal loading conditions on both ventricles after sternotomy closure. Such abnormal loading conditions may be related to sequelae of cardiopulmonary bypass.30 Subsequent resolution of paradoxical septal motion58 may indicate a return to normal loading conditions and interventricular interactions in the late postoperative period.

In the present study, septal motion was measured at two transverse levels along the LV long axis (i.e., markers 13 and 14 in Figure 1). It is important to specify carefully septal locations, because septal motions are quite different at different levels along the length of the septum.59,60 Hagan et al59 studied septal motion in 100 normal subjects with an ultrasonic phased array (long-axis view) and found that in each subject the superior septum moved anteriorly in systole with the aortic root and that the upper one third of the septum acted as a “hinge” for the lower two thirds that moved posteriorly. In all cases, the hinge was found in the upper third of the septum. They concluded that normal septal motion consists of anterior movement of the superior segment of the septum during systole and that below a pivot point motion consists of posterior movement of the inferior two thirds of the septum during systole. This is the basis for the clinical approach to assessing septal motion at a level just below the mitral valve leaflets.27,50 Both septal markers in this study were placed well into this region, and there was no significant difference in their dynamics. More studies will be needed, however, to characterize septal dynamics in additional, particularly more apical, sites.

It is important to emphasize the dissociation between wall motion and contraction observed in the interventricular septum in this study. Although septal contraction in these same patients was shown to be relatively normal,13 septal wall motion was paradoxical. This points out the hazards in drawing conclusions concerning regional contraction from studies of regional wall motion alone.

The three-dimensional center of volume data (Table 5 and Figure 5) were of interest. That the LV centroid position along the X axis did not change significantly during systole suggests an equilibration of forces leading to nearly balanced anterior and posterior wall motions. That the LV centroid position along the Y axis (LV long axis) did not change significantly suggests that, although mass (blood) is being expelled forcefully through the aortic valve throughout systole, the “rocket effect” of this expulsion (which would tend to drive the LV centroid toward more negative Y values) is being counterbalanced by a seemingly quite stiff coupling between external restraints, such as the outflow vessels and the LV myocardium. Of interest in this regard is the
tendency for LV free wall systolic vectors (Figure 5) to be directed roughly toward a common septal point (anteroapical region), a feature that we have observed in previous two-dimensional studies and that will require further analysis with three-dimensional analytical methods. The highly significant change in position of the LV centroid along the Z axis (toward the septum) during systole is presumably counteracted by a change in position of the RV centroid in the opposite direction along this axis (also toward the septum), leaving the midwall of the interventricular septum in a relatively constant position. In effect, as viewed from an external reference frame, the transplanted heart appears to beat as a "double bellows," in which the free walls of both ventricles contract toward a relatively immobile interventricular septum in systole.

Interestingly, even the normal heart apparently exhibits features of this "double bellows" behavior. Using mean echocardiographic values for normal hearts (9-mm septal thickness, 36% systolic wall thickening, 5-mm left septal systolic translation, and 12-mm posterolateral endocardial systolic translation), we calculate that the normal systolic excursion of the septal midwall is 3.4 mm, which is less than 30% of the normal excursion of the posterolateral endocardium. Thus, even in normal hearts, both ventricular free walls appear to move toward a relatively immobile septum.

To the best of our knowledge, these are the first published quantitative data relating the three-dimensional position and motion of LV midwall sites in human hearts. In addition to the implications in this study, these data may prove useful in developing models of LV dynamics, particularly because the data contain information not only on cardiac shape and wall motion, but also information on three-dimensional contraction and torsional deformations. Although presented here at only two time points (maximum and minimum LV volumes), the complete data sets, with all marker coordinates at 16.7-msec intervals throughout the cardiac cycle, are available on request.

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Key Words • myocardial dynamics • ventricular wall motion • heart transplantation • ventricular contraction • interventricular septum
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