Three-Dimensional Left Ventricular Deformation in Hypertrophic Cardiomyopathy

Alistair A. Young, PhD; Christopher M. Kramer, MD; Victor A. Ferrari, MD; Leon Axel, PhD, MD; Nathaniel Reichek, MD

Background In hypertrophic cardiomyopathy, ejection fraction is normal or increased, and force-length relations are reduced. However, three-dimensional (3D) motion and deformation in vivo have not been assessed in this condition. We have reconstructed the 3D motion of the left ventricle (LV) during systole in 7 patients with hypertrophic cardiomyopathy (HCM) and 12 normal volunteers by use of magnetic resonance tagging.

Methods and Results Transmural tagging stripes were automatically tracked to subpixel resolution with an active contour model. A 3D finite-element model was used to interpolate displacement information between short- and long-axis slices and register data on a regional basis. Displacement and strain data were averaged into septal, posterior, lateral, and anterior regions at basal, midventricular, and apical levels. Radial motion (toward the central long axis) decreased slightly in patients with HCM, whereas longitudinal displacement (parallel to the long axis) of the base toward the apex was markedly reduced: 7.5±2.5mm (SD) versus 12.5±2.0 mm, P<.001. Circumferential and longitudinal shortening were both reduced in the septum (P<.01 at all levels). The principal strain associated with 3D maximal contraction was slightly depressed in many regions, significantly in the basal septum (−0.18±0.05 versus −0.22±0.02, P<.05) and anterior (−0.20±0.05 versus −0.23±0.02, P<.05) walls. In contrast, LV torsion (twist of the apex about the long axis relative to the base) was greater in HCM patients (19.9±2.4° versus 14.6±2.7°, P<.01).

Conclusions HCM patients had reduced 3D myocardial shortening on a regional basis; however, LV torsion was increased. (Circulation. 1994;90:854-867.)

Key Words • hypertrophy • cardiomyopathy • magnetic resonance imaging • mechanics

Hypertrophic cardiomyopathy (HCM) is associated with a hypertrophied and nondilated left ventricle (LV), often with an asymmetrical distribution of wall thickness, which is usually greatest in the basal anterior septum. The LV cavity is usually small or normal in size, and ejection fraction is normal or increased. However, force-length relations are reduced, indicating depressed contractility in some regions. To determine whether myocardial shortening is reduced or augmented on a regional basis in this disease, the three-dimensional motions and deformations undergone during systole at specific material points must be measured. These measurements have been facilitated in the past by implanted markers or natural landmarks. However, the trauma of implantation techniques limits their use in human studies, and few anatomically distinct natural landmarks are available.

An alternative noninvasive technique is myocardial tissue tagging with magnetic resonance imaging, in which large numbers of material markers can be generated and tracked through systole. The one- and two-dimensional motions of tags in the image plane have been studied to assess the regional variation of displacement, torsion, and shortening in normal and diseased states. One-dimensional measures of segmental length changes are sensitive to the orientation of the line segment and in general are not aligned with the direction of maximum shortening or lengthening. Similarly, two-dimensional measurements neglect out-of-plane deformations, which affect the direction and magnitude of maximum shortening. Through-plane motions may also produce artifacts in strain measurements because, in a temporal sequence of images, different tissue is generally imaged in each frame.

A complete analysis of myocardial deformation therefore requires three-dimensional estimates of strain and motion corrected for out-of-plane shears and through-plane motion. This study used a three-dimensional finite-element model of the LV to reconstruct the three-dimensional motions of material points throughout systole from orthogonal image planes. Results from 12 healthy volunteers were compared with those from 7 patients with HCM. Displacement, rotation, and strain were quantified on a regional basis and registered between hearts with the aid of the model.

Methods

Population

We studied seven patients, four male, ages 16 to 79 years, with HCM documented by echocardiography. These patients showed diffuse hypertrophy, predominantly in the basal septal region of the LV. Mean septal and posterior wall thicknesses were 2.0 and 1.3 cm, respectively, by two-dimensional guided M-mode echocardiography (Table 1). One patient had Doppler echocardiographic evidence of dynamic LV outflow obstruction with a peak gradient of 16 mm Hg. None had a history of hypertension or two-dimensional echocardiographic...
TABLE 1. Summary of Two-Dimensional Guided M-Mode Echocardiographic Data for Patient Group

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age</th>
<th>ST, cm</th>
<th>PT, cm</th>
<th>EDD, cm</th>
<th>FS, %</th>
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<tr>
<td>1</td>
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<tr>
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<td>4.9</td>
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<tr>
<td>Mean</td>
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<td>1.3</td>
<td>3.7</td>
<td>48</td>
<td>3.8</td>
</tr>
</tbody>
</table>

ST indicates septal thickness; PT, posterior thickness; EDD, end-diastolic dimension; FS, fractional shortening; and LA, left atrial dimension.

*Patient with Doppler echocardiographic evidence of dynamic left ventricular outflow obstruction with peak gradient of 16 mm Hg.

evidence of LV dysfunction or significant valvular disease. These patients form part of a group previously studied for regional variation in one-dimensional shortening measures from the tagged magnetic resonance images.13

The control group consisted of 12 healthy volunteers, 6 male, ages 19 to 37 years. This group was also imaged with conventional echocardiography. None had any evidence of abnormal cardiac function on either echocardiography or magnetic resonance imaging. The in-plane deformations during systole obtained from this group were previously analyzed by two-dimensional homogeneous strain triangles in both short- and long-axis views.15

Image Acquisition

Electrocardiographically gated magnetic resonance images were acquired with a conventional 1.5-T scanner (Signa, General Electric) with the patient supine. The imaging protocol has been described elsewhere.9,11,18 An initial set of single-phase, multislice, spin-echo coronal scout images was obtained to determine the location of the LV long axis. A multiphase, single-slice, axial cine (rapid gradient-echo) series was then obtained at the level of the mitral valve to determine the timing of end systole. Compound oblique short-axis images (orthogonal to the LV long axis)19 were obtained in five locations at five phases of the cardiac cycle from end diastole to end systole by use of spatial modulation of magnetization tagging.9 Fig 1 shows a schematic of the image slice locations. An orthogonal tagging grid of 7-mm spacing was created, consisting of two sets of parallel planes of magnetic saturation, each orthogonal to the image plane (Fig 2A). The grid was generated on detection of the R wave in approximately 10 milliseconds, followed by the first image acquisition (end diastole). By end systole (the fifth image), the tags had faded somewhat as a result of T1 relaxation and respiratory blurring but were still distinct and trackable (Fig 2B). The images had an echo time (TE) of 20 milliseconds, repetition time (TR) equal to the RR interval, 5-mm slice thickness, 10 mm between slice centers, 24-cm field of view, and 128×256 image matrix, interpolated to 256×256 (0.94 mm/pixel). A similar series of compound oblique long-axis images, parallel to the LV long axis and perpendicular to the interventricular septum (analogous to the echocardiographic four-chamber view), was then obtained in five locations at the same five phases of the cardiac cycle (Figs 1, 2C, and 2D).

Image Analysis

Images were analyzed with custom-written interactive software running on graphics workstations.20 The inner and outer boundaries (endocardial and epicardial borders) of the LV were manually traced on the images so as to enclose the LV free wall and septum (Fig 2). Thus, the outer boundary included LV free wall epicardium and RV endocardium at the septum. In the end-diastolic images, the location of the inner boundary could not be determined (before the tags in the cavity were lost because of motion of the blood, see Fig 2A), so it was inferred from the subsequent image, relative to the tags in the surrounding muscle. Right ventricular endocardial boundaries were also defined at end diastole to aid registration. In addition, the locations of the LV apex and the center of the LV at the base were defined on the most central long-axis slice at end diastole.

Tag stripes within the muscle were located and tracked through the five images from end diastole to end systole with a semiautomatic tracking procedure based on an active contour model.21 In this procedure, each stripe was subdivided into closely spaced points (three points between stripe intersections). Each stripe was modeled as a thin, flexible beam with a small inherent resistance to stretch and bending. Stripes were connected at the intersection points, and the entire mesh was deformed to minimize the corresponding intensity values in the image. This minimization was performed with gradient descent, allowing the user to guide the solution in real time with the mouse and prevent the solution from jumping to the wrong stripe between frames. The explicit continuity of the structure gave the model some immunity to image noise. Bilinear interpolation between pixel locations was used in the minimization procedure. This allowed subpixel resolution in stripe localization, since the surrounding image values were used to locate an interpolated minimum along the stripe. Experiments with a deformable silicone gel phantom undergoing controlled deformations have shown that this procedure produces accurate, unbiased estimates of displacement and
Fig 2. Spatial modulation of magnetization images of a representative case of hypertrophic cardiomyopathy showing magnetic tags and the results of stripe tracking. Squares mark active (tracked) points on the active contour model; diamond points mark inactive points used to maintain continuity. A, Short-axis time 1 (end diastole); B, short-axis time 5 (end systole); C, long-axis time 1 (end diastole); D, long-axis time 5 (end systole).

strain (approximately 9% and 5% error in the maximum and minimum principal strains, respectively). Fig 2 shows the results of the stripe tracking, with stripe points within the myocardium shown as squares and those outside the LV wall boundaries shown as diamonds. Only those points within the inner and outer boundaries were influenced by the image (attracted to dark lines). The remaining points (inactive points) were subject to very small restoring forces (resistance to stretch and bending) only. This provided a weak continuity for the structure and allowed points to become active/inactive as structures moved onto/off the image plane as a result of through-plane motion. Some interactive manipulation of the solution process was required in cases in which the tags moved more than half a stripe spacing between frames. The entire process took approximately 5 minutes for each series of 25 images.

Finite-Element Model

A three-dimensional finite-element model for the LV was constructed according to previously reported methods. The model was specified in a "cardiac" coordinate system registered to the end-diastolic configuration of each heart, as follows. A long axis for the LV was defined by the line joining the centroids of the most basal and most apical short-axis image endocardial contours. The apex and base landmarks (defined on the central long-axis slice), as well as the means of the centroids of the right ventricle endocardial contours, were projected onto this long axis. The origin of the cardiac coordinate system was placed one third of the distance from base to apex projections. The x axis was oriented toward the apex, the y axis toward the center of the right ventricle (parallel to the line joining the right ventricle centroid and its projection), and the z axis toward the posterior wall (to make a right-handed system). This procedure defined a fixed reference coordinate system for comparing motions of each heart (Fig 3).

Inner and outer surfaces of the LV at each frame were found by fitting the inner and outer boundaries drawn on the images. Each surface consisted of 16 finite elements with cubic...
interpolation in the circumferential and longitudinal directions, allowing continuity in both position and slope between elements (see Fig 3). Nodes were placed at equal angular intervals in the circumferential and longitudinal directions, starting at the septal base (\(z=0\)). These surfaces were then combined with a linear transmural interpolation into a three-dimensional model. Fig 3 shows a typical end-diastolic geometry obtained from surface fits in a control heart. The papillary muscles were excluded from the fit. Boundary information was not used to reconstruct motion or deformation but only to gain an approximate description of geometry, which then provided the interpolation necessary for reconstructing three-dimensional motion.

The result of this procedure was a model whose nodes (and element boundaries) were consistently placed with respect to the gross anatomy of the heart and whose element coordinates were oriented in circumferential (\(\xi_c\)), longitudinal (\(\xi_l\)), and transmural (\(\xi_t\)) directions throughout the ventricle (Fig 3). Similar models have been used to efficiently describe the geometry, fiber angle distribution, and connective tissue organization of the canine heart.\(^{23,24}\)

**Three-dimensional Reconstruction**

Whereas the geometry of the model was defined by use of the inner and outer boundaries, the three-dimensional motion was reconstructed solely from the displacements of the tag stripes. This procedure was similar to that described previously, except in the present study, displacements of multiple points along the stripes were fitted rather than just the stripe intersections. Each material point is in general imaged only once in the time sequence because of through-plane motion. However, the initial location and orientation of the tagging planes are known. Each stripe point imaged in each deformed state therefore provides a one-dimensional constraint on the displacement field: the displacement back to the original tagging plane (see “Appendix”). The model is thus used to interpolate these constraints between tags oriented in at least three distinct directions, allowing the three-dimensional displacement field to be determined.

For each deformed state (the latter four frames), the tracked stripe points were located within a three-dimensional model fitted to the boundaries at that time; ie, the element coordinates corresponding to each stripe point were computed. The model was then deformed to fit the displacements of the stripe points back to the original tagging plane by minimization of the projected distance from the point to the plane in the direction normal to the plane (see “Appendix”). Note that the boundaries of the LV are not used in the calculation of the displacement field.

**Deformation Fits**

The above reconstruction fits determine the positions in the original undeformed state (end diastole) of all the stripe points in each deformed state. To calculate deformation between the original state and each subsequent time, the reconstructed positions in the initial state were located within a three-dimensional model fitted to the boundaries at end diastole. This geometry was then deformed to fit the reconstructed displacements to each subsequent time (“Appendix”). Typical undeformed and deformed (end systole) models are shown in Fig 4.

**Motion Measurements and Statistical Analysis**

The displacement of material points was split into three components: one in the direction of the LV long axis (the \(x\) direction in the cardiac coordinate system), another radially directed in the \(y-z\) plane toward the central axis, and the third expressed as an angle of rotation in the \(y-z\) plane about the central axis. The radial and angular displacements were corrected for the motion of the central axis, which was defined to pass through the apex of the model and the centroid of the basal nodes at all times. Thus, the radial displacement was defined as the change in distance between the central axis and
the material point. Rotation about the central axis was defined as the change in orientation of the line connecting the point with its projection on the central axis, expressed as an angle in the y-z plane (counterclockwise-positive viewed from the apex). Components of the lagrangian strain tensor $E$ (see "Appendix") were calculated with respect to the circumferential (C), longitudinal (L), and transmural (R) coordinate directions associated with the element coordinates in the undeformed state (end diastole). Negative values in the normal strains ($E_{cc}$, $E_{ll}$, $E_{rr}$) indicate shortening, and positive values indicate lengthening ("Appendix").

The stripe tracking and model fitting procedures have been previously validated by use of a deformable phantom in the shape of a cylindrical annulus.\textsuperscript{22,25,26} Nonhomogeneous strain fields resulting from axisymmetrical axial and azimuthal shears were estimated from the displacements of magnetic tags and compared with an analytic solution.\textsuperscript{25} Fits to tag intersection data showed root mean square errors of 14% and 8% in the maximum and minimum principal strains for the axial shear case. Stripe tracking (using the active contour model) and fitting (using one-dimensional displacement constraints) resulted in a reduction of these errors to 9% and 5%, respectively.\textsuperscript{22} A fully three-dimensional fit to stripes tracked in both short- and long-axis images of a combined axial and azimuthal shear resulted in root mean square errors in the nonzero strains of 16% in $E_{rr}$, 6% in $E_{cc}$, and 6% in $E_{ll}$.\textsuperscript{26}

Only those points sufficiently constrained by the surrounding data were included in the statistical analysis. Points were included if two other points from tag planes with mutually different orientations could be found within a 10-mm radius. Displacement and strain data were averaged into basal, midventricular, and apical levels and septal, posterior, lateral, and anterior regions. These regions were defined as shown in Fig 3. Comparisons between control and patient groups were performed with a Student's $t$ test for unpaired comparisons. Within each group, comparisons of kinematic parameters at multiple regions within the LV wall were made by repeated-measures ANOVA. If a significant difference was found, the Scheffé test was applied to compare individual regions.

Results

Results from typical deformation fits to a control and an HCM heart are shown in Fig 4. The error between the reconstructed material point locations from the fitted model and the corresponding stripe data points averaged 0.47 mm for the control group and 0.57 mm for the HCM group at end systole. These were both smaller than the pixel size of 0.94 mm. An average of 3127 points were fitted per control heart and 3969 per HCM heart. As an additional check for the accuracy of the fit, the predicted locations of stripe points from the model were projected back onto the original images at end diastole and end systole and displayed as an overlay (Fig 5). Tables 2 through 7 show motion and deformation parameters extracted from the model for the control and patient groups. Average values and SDs for each group are displayed for each circumferential and longitudinal region.

Displacement

It can be seen in Tables 2 and 3 that radial motion was normal in the HCM group compared with control subjects in most regions but slightly depressed in the apical lateral and anterior walls and at the basal septum. Longitudinal displacement at end systole is shown in Fig 6, averaged for each longitudinal region (error bars indicate SD). In both groups, the apex remained approximately stationary, whereas the base descended toward the apex. There was a dramatic reduction in longitudinal displacement in HCM patients versus control at the base: 7.5±2.5 versus 12.5±2.0 mm, $P<.001$. Also, Table 2 shows a normal circumferential variation in longitudinal displacement, in which the posterior wall displaced more than the anterior at all levels ($P<.001$). This trend was abolished in HCM patients.

In both groups, the angle of rotation about the central axis was greatest at the apex and negative (clockwise) at the base. The magnitude of rotation angle was higher in HCM patients than control subjects in the apex and base, although no differences between HCM and control subjects were significant. However, one HCM patient had lower apical rotation than the others (average of 7º versus an average of 18º for the others) and was responsible for most of the scatter in this group. Subdi-
TABLE 2. Displacement Parameters for Control Group, End Diastole to End Systole

<table>
<thead>
<tr>
<th></th>
<th>Apex Displacement, mm</th>
<th>Longitudinal Displacement, mm</th>
<th>Rotation</th>
<th>Torsion</th>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septal</td>
<td>4.8 (1.0)</td>
<td>1.6 (1.4)</td>
<td>12 (4)</td>
<td>13 (3)</td>
</tr>
<tr>
<td>Posterior</td>
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<td>16 (5)</td>
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</tr>
<tr>
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Rotation and torsion about the central axis in degrees, counterclockwise-positive looking from apex. Values are regional mean (SD), n=12.

vision of the regions into epicardial, midwall, and endocardial thirds revealed that rotation magnitude was higher in the endocardial third than the epicardial third ($P<.01$ for both groups). Apical rotation averaged $16\pm6^\circ$ in endocardial regions versus $14\pm4^\circ$ in epicardial regions for the apex in HCM patients ($14\pm3^\circ$ versus $10\pm4^\circ$ in control subjects), whereas basal rotation averaged $-4\pm4^\circ$ versus $-3\pm3^\circ$ in HCM patients ($-2\pm2^\circ$ versus $-1\pm1^\circ$ in control subjects).

LV torsion is often defined as the rotation of the apex about the long axis relative to the base. In the present study, this was calculated by subtracting the base rotation from the midventricle and apex rotations for each circumferential region. Fig 7 compares torsion at each level, showing significantly greater torsion at end systole in HCM patients ($20\pm2^\circ$ versus $15\pm3^\circ$ at the apex, $P<.01$).

Strain

Shortening in the circumferential direction (Ecc) is shown in Fig 8, averaged for each circumferential

TABLE 3. Displacement Parameters for Hypertrophic Cardiomyopathy Group, End Diastole to End Systole

<table>
<thead>
<tr>
<th></th>
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<td>1.8 (1.3)</td>
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<td>22§ (4)</td>
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<td>7.3* (2.6)</td>
<td>-6 (4)</td>
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</table>

Rotation and torsion about the central axis in degrees, counterclockwise-positive looking from apex. Values are regional mean (SD), n=7.

*P<.01, §P<.03, †P<.05 hypertrophic cardiomyopathy vs control.
region. HCM patients showed circumferential contraction similar to that in the control group in most regions, except the septum (average of $-0.15 \pm 0.05$ HCM versus $-0.20 \pm 0.02$ control), which was reduced at all levels (Table 5, $P<.03$). In contrast to circumferential shortening, nearly all regions showed depressed longitudinal shortening ($E_{LL}$) in HCM patients, most dramatically in the septal and anterior base ($P<.01$). Longitudinal shortening at the base is plotted in Fig 9, showing a smaller decrease in the lateral and posterior walls compared with the septal and anterior walls. The circumferential variation of $E_{LL}$ seen in the control group at the base was preserved in the patient group (greater shortening in the posterior wall than septum and anterior wall, $P<.01$). The radial normal strain ($E_{RR}$) was consistently positive in all regions, associated with wall thickening, with no significant difference between HCM and control groups.

The circumferential-longitudinal shear strain ($E_{CL}$) was positive in all regions, associated with LV torsion about the central axis (see “Appendix”). Like torsion (measured by the rotation of the apex with respect to the base), this shear was greater in HCM patients in a number of regions (Table 5), notably in the basal posterior and lateral walls ($P<.03$). In the HCM group, however, there was a longitudinal gradient in $E_{CL}$, with

### Table 4. Lagrangian Strains for Control Group, End Diastole to End Systole

<table>
<thead>
<tr>
<th></th>
<th>$E_{CC}$</th>
<th>$E_{CL}$</th>
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<th>$E_{CR}$</th>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septal</td>
<td>$-0.20$ (0.03)</td>
<td>$-0.19$ (0.02)</td>
<td>$0.07$ (0.06)</td>
<td>$0.03$ (0.01)</td>
<td>$0.05$ (0.02)</td>
</tr>
<tr>
<td>Posterior</td>
<td>$-0.22$ (0.04)</td>
<td>$-0.20$ (0.03)</td>
<td>$0.02$ (0.08)</td>
<td>$0.03$ (0.02)</td>
<td>$0.03$ (0.04)</td>
</tr>
<tr>
<td>Lateral</td>
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<td>$-0.18$ (0.03)</td>
<td>$0.10$ (0.06)</td>
<td>$0.01$ (0.02)</td>
<td>$0.05$ (0.03)</td>
</tr>
<tr>
<td>Anterior</td>
<td>$-0.23$ (0.03)</td>
<td>$-0.18$ (0.02)</td>
<td>$0.07$ (0.07)</td>
<td>$0.03$ (0.02)</td>
<td>$0.03$ (0.02)</td>
</tr>
<tr>
<td>Mid</td>
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<td></td>
</tr>
<tr>
<td>Septal</td>
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<td>$-0.15$ (0.02)</td>
<td>$0.16$ (0.10)</td>
<td>$0.04$ (0.02)</td>
<td>$0.02$ (0.03)</td>
</tr>
<tr>
<td>Posterior</td>
<td>$-0.19$ (0.02)</td>
<td>$-0.14$ (0.04)</td>
<td>$0.14$ (0.03)</td>
<td>$0.04$ (0.02)</td>
<td>$0.02$ (0.02)</td>
</tr>
<tr>
<td>Lateral</td>
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<td>$-0.16$ (0.03)</td>
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<td>$0.03$ (0.01)</td>
<td>$0.03$ (0.02)</td>
</tr>
<tr>
<td>Anterior</td>
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<td>$-0.17$ (0.02)</td>
<td>$0.20$ (0.10)</td>
<td>$0.03$ (0.01)</td>
<td>$0.03$ (0.04)</td>
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</tr>
<tr>
<td>Septal</td>
<td>$-0.19$ (0.03)</td>
<td>$-0.14$ (0.03)</td>
<td>$0.21$ (0.10)</td>
<td>$0.03$ (0.01)</td>
<td>$-0.01$ (0.02)</td>
</tr>
<tr>
<td>Posterior</td>
<td>$-0.18$ (0.03)</td>
<td>$-0.19$ (0.03)</td>
<td>$0.20$ (0.07)</td>
<td>$0.03$ (0.01)</td>
<td>$-0.03$ (0.04)</td>
</tr>
<tr>
<td>Lateral</td>
<td>$-0.21$ (0.03)</td>
<td>$-0.19$ (0.04)</td>
<td>$0.25$ (0.09)</td>
<td>$0.04$ (0.01)</td>
<td>$-0.01$ (0.02)</td>
</tr>
<tr>
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<td>$-0.20$ (0.02)</td>
<td>$-0.15$ (0.03)</td>
<td>$0.18$ (0.10)</td>
<td>$0.03$ (0.01)</td>
<td>$-0.02$ (0.03)</td>
</tr>
</tbody>
</table>

$E_{CC}$, $E_{CL}$, $E_{RR}$ indicate circumferential, longitudinal, and radial strains; $E_{CR}$, $E_{LR}$, shear strains. Values are regional mean (SD), n=12.

### Table 5. Lagrangian Strains for Hypertrophic Cardiomyopathy Group, End Diastole to End Systole

<table>
<thead>
<tr>
<th></th>
<th>$E_{CC}$</th>
<th>$E_{CL}$</th>
<th>$E_{RR}$</th>
<th>$E_{CL}$</th>
<th>$E_{CR}$</th>
<th>$E_{LR}$</th>
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<tbody>
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<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septal</td>
<td>$-0.15$§ (0.06)</td>
<td>$-0.14$† (0.08)</td>
<td>$0.07$ (0.07)</td>
<td>$0.05$§ (0.01)</td>
<td>$0.07$ (0.03)</td>
<td>$-0.01$ (0.03)</td>
</tr>
<tr>
<td>Posterior</td>
<td>$-0.19$ (0.07)</td>
<td>$-0.10$ (0.08)</td>
<td>$0.03$ (0.05)</td>
<td>$0.02$ (0.04)</td>
<td>$0.03$ (0.02)</td>
<td>$-0.01$ (0.03)</td>
</tr>
<tr>
<td>Lateral</td>
<td>$-0.19$ (0.06)</td>
<td>$-0.11$ (0.08)</td>
<td>$0.09$ (0.10)</td>
<td>$0.01$ (0.02)</td>
<td>$0.05$ (0.02)</td>
<td>$0.03$ (0.03)</td>
</tr>
<tr>
<td>Anterior</td>
<td>$-0.19$ (0.08)</td>
<td>$-0.14$ (0.07)</td>
<td>$0.06$ (0.08)</td>
<td>$0.06$ (0.05)</td>
<td>$0.04$ (0.06)</td>
<td>$-0.01$ (0.04)</td>
</tr>
<tr>
<td>Mid</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septal</td>
<td>$-0.16$§ (0.05)</td>
<td>$-0.09$* (0.07)</td>
<td>$0.18$ (0.11)</td>
<td>$0.03$ (0.02)</td>
<td>$0.02$ (0.03)</td>
<td>$0.03$ (0.03)</td>
</tr>
<tr>
<td>Posterior</td>
<td>$-0.18$ (0.04)</td>
<td>$-0.06$* (0.04)</td>
<td>$0.14$ (0.07)</td>
<td>$0.05$ (0.01)</td>
<td>$0.03$ (0.02)</td>
<td>$0.02$ (0.02)</td>
</tr>
<tr>
<td>Lateral</td>
<td>$-0.21$ (0.03)</td>
<td>$-0.12$* (0.04)</td>
<td>$0.21$ (0.12)</td>
<td>$0.05$§ (0.02)</td>
<td>$0.00$§ (0.03)</td>
<td>$0.06$* (0.03)</td>
</tr>
<tr>
<td>Anterior</td>
<td>$-0.20$ (0.04)</td>
<td>$-0.12$* (0.04)</td>
<td>$0.18$ (0.04)</td>
<td>$0.04$ (0.01)</td>
<td>$0.03$ (0.04)</td>
<td>$0.02$ (0.02)</td>
</tr>
<tr>
<td>Base</td>
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<tr>
<td>Septal</td>
<td>$-0.14$§ (0.06)</td>
<td>$-0.06$* (0.04)</td>
<td>$0.19$ (0.08)</td>
<td>$0.01$ (0.02)</td>
<td>$-0.01$ (0.03)</td>
<td>$-0.03$ (0.03)</td>
</tr>
<tr>
<td>Posterior</td>
<td>$-0.15$ (0.03)</td>
<td>$-0.15$† (0.05)</td>
<td>$0.22$ (0.10)</td>
<td>$0.06$§ (0.01)</td>
<td>$-0.01$ (0.05)</td>
<td>$0.02$ (0.06)</td>
</tr>
<tr>
<td>Lateral</td>
<td>$-0.19$ (0.03)</td>
<td>$-0.14$§ (0.03)</td>
<td>$0.26$ (0.10)</td>
<td>$0.06$§ (0.01)</td>
<td>$-0.02$ (0.02)</td>
<td>$0.06$ (0.06)</td>
</tr>
<tr>
<td>Anterior</td>
<td>$-0.17$ (0.06)</td>
<td>$-0.06$* (0.04)</td>
<td>$0.14$ (0.06)</td>
<td>$0.00$§ (0.02)</td>
<td>$-0.02$ (0.02)</td>
<td>$0.00$ (0.02)</td>
</tr>
</tbody>
</table>

$E_{CC}$, $E_{CL}$, $E_{RR}$ indicate circumferential, longitudinal, and radial strains; $E_{CR}$, $E_{LR}$, shear strains. Values are regional mean (SD), n=7.

* $P<.01$, § $P<.03$, † $P<.05$ hypertrophic cardiomyopathy vs control.
an increase in the posterior and lateral walls and a decrease in the septal and anterior walls from apex to base (ANOVA, $P<.05$). Thus, $E_{CL}$ was lower in the patient group in the septal and anterior base. The apex-to-base variations of the septal/anterior walls are compared with the posterior/lateral walls in Fig 10. The circumferential-radial shear strain ($E_{CR}$) showed a longitudinal gradient in both groups, from positive values at the apex to negative at the base (Tables 4 and 5). $E_{CR}$ is associated with the increase in magnitude of rotation about the central axis from epicardial to endocardial layers. This transmural gradient, combined with the counterclockwise rotation at the apex and clockwise rotation at the base, results in the change of sign of $E_{CR}$ from base to apex. The longitudinal-radial shear ($E_{LR}$) showed a complex circumferential variation, with the lateral wall shearing in a more positive manner than the septum. This difference was increased in HCM patients, with increased $E_{LR}$ in the lateral wall and more negative values in the septum.

The maximum principal strain ($E_1$) was given by the most positive eigenvalue of the strain tensor $E$ and is associated with the maximum elongation experienced by the tissue at each material point. This was similar to $E_{RR}$ and was oriented approximately in the radial direction (associated with wall thickening). The minimum principal strain ($E_3$) was given by the most negative eigenvalue of $E$ and is associated with the maximum contraction experienced by the tissue at each material point (Fig 11). Maximal three-dimensional contraction in the patient group was similar to that in the control group (Tables 6 and 7) but was slightly depressed in most regions, significantly in the basal septum and anterior walls ($P<.05$). The principal direction associated with $E_1 (\phi_3)$ was oriented approximately in the C-L plane in all regions. Tables 6 and 7 show $\phi_3$ projected onto the

**TABLE 6. Principal Strains for Control Group, End Diastole to End Systole**

<table>
<thead>
<tr>
<th></th>
<th>$E_1$</th>
<th>$E_3$</th>
<th>$\phi_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septal</td>
<td>0.10 (0.06)</td>
<td>-0.25 (0.02)</td>
<td>-31 (13)</td>
</tr>
<tr>
<td>Posterior</td>
<td>0.05 (0.07)</td>
<td>-0.27 (0.03)</td>
<td>-29 (19)</td>
</tr>
<tr>
<td>Lateral</td>
<td>0.12 (0.06)</td>
<td>-0.25 (0.02)</td>
<td>-9 (17)</td>
</tr>
<tr>
<td>Anterior</td>
<td>0.08 (0.07)</td>
<td>-0.26 (0.03)</td>
<td>-25 (9)</td>
</tr>
<tr>
<td>Mid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septal</td>
<td>0.18 (0.09)</td>
<td>-0.23 (0.02)</td>
<td>-26 (10)</td>
</tr>
<tr>
<td>Posterior</td>
<td>0.15 (0.04)</td>
<td>-0.23 (0.02)</td>
<td>-31 (7)</td>
</tr>
<tr>
<td>Lateral</td>
<td>0.22 (0.09)</td>
<td>-0.24 (0.01)</td>
<td>-23 (10)</td>
</tr>
<tr>
<td>Anterior</td>
<td>0.22 (0.10)</td>
<td>-0.25 (0.02)</td>
<td>-28 (7)</td>
</tr>
<tr>
<td>Base</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septal</td>
<td>0.23 (0.10)</td>
<td>-0.22 (0.02)</td>
<td>-24 (11)</td>
</tr>
<tr>
<td>Posterior</td>
<td>0.22 (0.06)</td>
<td>-0.25 (0.02)</td>
<td>-41 (7)</td>
</tr>
<tr>
<td>Lateral</td>
<td>0.26 (0.09)</td>
<td>-0.25 (0.02)</td>
<td>-37 (7)</td>
</tr>
<tr>
<td>Anterior</td>
<td>0.20 (0.10)</td>
<td>-0.23 (0.02)</td>
<td>-20 (10)</td>
</tr>
</tbody>
</table>

$E_1$ indicates maximum principal strain; $E_3$, minimum principal strain; and $\phi_3$, principal angle associated with $E_3$, projected onto the C-L plane (positive counterclockwise from C direction). Values are regional mean (SD).

**TABLE 7. Principal Strains for Hypertrophic Cardiomyopathy Group, End Diastole to End Systole**

<table>
<thead>
<tr>
<th></th>
<th>$E_1$</th>
<th>$E_3$</th>
<th>$\phi_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septal</td>
<td>0.10 (0.08)</td>
<td>-0.23 (0.07)</td>
<td>-37 (12)</td>
</tr>
<tr>
<td>Posterior</td>
<td>0.06 (0.04)</td>
<td>-0.23 (0.06)</td>
<td>-9 (21)</td>
</tr>
<tr>
<td>Lateral</td>
<td>0.13 (0.09)</td>
<td>-0.22 (0.05)</td>
<td>-5 (15)</td>
</tr>
<tr>
<td>Anterior</td>
<td>0.12 (0.06)</td>
<td>-0.26 (0.06)</td>
<td>-21 (27)</td>
</tr>
<tr>
<td>Mid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septal</td>
<td>0.20 (0.11)</td>
<td>-0.20 (0.05)</td>
<td>-28 (14)</td>
</tr>
<tr>
<td>Posterior</td>
<td>0.16 (0.06)</td>
<td>-0.22 (0.04)</td>
<td>-21* (14)</td>
</tr>
<tr>
<td>Lateral</td>
<td>0.24 (0.12)</td>
<td>-0.25 (0.02)</td>
<td>-28 (9)</td>
</tr>
<tr>
<td>Anterior</td>
<td>0.19 (0.04)</td>
<td>-0.24 (0.04)</td>
<td>-27 (6)</td>
</tr>
<tr>
<td>Base</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septal</td>
<td>0.21 (0.07)</td>
<td>-0.18 (0.05)</td>
<td>-13 (20)</td>
</tr>
<tr>
<td>Posterior</td>
<td>0.25 (0.10)</td>
<td>-0.24 (0.04)</td>
<td>-43 (10)</td>
</tr>
<tr>
<td>Lateral</td>
<td>0.28 (0.11)</td>
<td>-0.25 (0.03)</td>
<td>-36 (4)</td>
</tr>
<tr>
<td>Anterior</td>
<td>0.16 (0.05)</td>
<td>-0.20 (0.05)</td>
<td>-1* (10)</td>
</tr>
</tbody>
</table>

$E_1$ indicates maximum principal strain; $E_3$, minimum principal strain; and $\phi_3$, principal angle associated with $E_3$, projected onto the C-L plane (positive counterclockwise from C direction). Values are regional mean (SD).

* $P<.01$, $^tP<.05$ hypertrophic cardiomyopathy vs control.

**Fig 6.** Bar graph of longitudinal displacement parallel to the central axis, averaged for each longitudinal level, showing significantly reduced displacement in the midventricular and basal levels in the hypertrophic cardiomyopathy (HCM) group. All graphs show SDs as error bars. *$P<.001$ HCM vs control.

**Fig 7.** Bar graph of torsion about the left ventricular central axis averaged for apical and midventricle regions, showing increased torsion in the hypertrophic cardiomyopathy (HCM) group at these levels. *$P<.01$, $^pP<.05$ HCM vs control.
C-L plane and expressed as an angle from the circumferential direction (counterclockwise positive). This angle was approximately -20° to -30° in the control group, aligned in the general direction of the subepicardial muscle fibers (fiber angles were not measured in this study). In the HCM group, the angle was largely unchanged, with differences in the mid posterior and basal anterior walls only.

**Discussion**

HCM is characterized primarily by LV hypertrophy: a small or normal-size cavity with increased wall thickness. The thickening is often diffuse, covering the septum and anterolateral free wall. To assess the three-dimensional motions and contraction patterns that occur in this disease, we tracked material points in the form of magnetic tags through systole and reconstructed the three-dimensional motion from short- and long-axis image series. Circumferential shortening was significantly reduced in the septum at all levels, whereas longitudinal shortening was reduced in most regions. Circumferential-longitudinal shear strain was increased in the patient group except in the basal septum and anterior walls and was associated with an increased torsion about the central longitudinal axis. The principal strain associated with greatest contraction was almost normal (slightly reduced in magnitude) in most regions but significantly depressed in the basal septum and anterior walls. These and related findings are compared with those from other studies below.

**Displacement and Torsion**

Maier et al calculated radial and angular displacements of tag stripe intersections in short-axis images of patients with HCM. They used a fixed (end-diastolic) centroid as a reference point. They found lower radial displacements (expressed as a percentage of the initial radius) in many regions in patients with HCM, significant in the septal and posterior walls. This is similar to our results, in which absolute radial displacement with respect to a moving centroid was reduced in the patient group. They also reported a normal to reduced rotation about the central axis, which was significantly reduced in the apical lateral wall in the patient group, in contrast to our findings of increased rotation and significantly increased torsion. Apart from the difference in reference centroids, their tagging scheme required a longer delay between the detection of the R wave and the first image (70 milliseconds) than ours (13 milliseconds). Analysis of the rotation between the first (13 milliseconds) and second (approximately 60 to 90 milliseconds) images in our image series revealed substantial rotations during early systole (Table 8) that may account for the difference in rotation values. Note that in the control group, the base rotated counter-
TABLE 8. Rotation and Torsion for Control and Hypertrophic Cardiomyopathy Groups Calculated Between the First and Second Images (Early Systole)

<table>
<thead>
<tr>
<th></th>
<th>Rotation (Control)</th>
<th>Torsion (Control)</th>
<th>Rotation (HCM)</th>
<th>Torsion (HCM)</th>
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<td></td>
<td></td>
</tr>
<tr>
<td>Septal</td>
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<td>5.4 (2.1)</td>
<td>5.5* (1.9)</td>
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<tr>
<td>Posterior</td>
<td>6.3 (1.5)</td>
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<td>7.2 (3.3)</td>
<td>7.3* (3.1)</td>
</tr>
<tr>
<td>Lateral</td>
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<td>2.4 (1.0)</td>
<td>4.9 (3.2)</td>
<td>4.3§ (3.3)</td>
</tr>
<tr>
<td>Anterior</td>
<td>5.2 (1.7)</td>
<td>2.4 (1.1)</td>
<td>4.9 (3.3)</td>
<td>4.2 (3.1)</td>
</tr>
<tr>
<td>Mid</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Septal</td>
<td>2.8 (1.3)</td>
<td>0.8 (0.9)</td>
<td>2.3 (1.1)</td>
<td>2.4* (1.0)</td>
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<tr>
<td>Posterior</td>
<td>4.6 (1.4)</td>
<td>1.4 (0.9)</td>
<td>4.3 (2.5)</td>
<td>4.4* (1.9)</td>
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<tr>
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<td>3.7 (1.1)</td>
<td>1.8 (0.6)</td>
<td>3.2 (2.2)</td>
<td>3.7* (2.0)</td>
</tr>
<tr>
<td>Anterior</td>
<td>4.0 (1.4)</td>
<td>1.3 (0.7)</td>
<td>2.3§ (1.6)</td>
<td>1.6 (1.2)</td>
</tr>
<tr>
<td>Base</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septal</td>
<td>2.0 (1.2)</td>
<td>...</td>
<td>-0.1* (0.7)</td>
<td>...</td>
</tr>
<tr>
<td>Posterior</td>
<td>3.2 (1.3)</td>
<td>...</td>
<td>0.1* (1.6)</td>
<td>...</td>
</tr>
<tr>
<td>Lateral</td>
<td>1.9 (1.2)</td>
<td>...</td>
<td>-0.5* (1.3)</td>
<td>...</td>
</tr>
<tr>
<td>Anterior</td>
<td>2.7 (1.7)</td>
<td>...</td>
<td>0.4* (1.2)</td>
<td>...</td>
</tr>
</tbody>
</table>

Values are in degrees, mean (SD).  
§P<.05, *P<.01 hypertrophic cardiomyopathy vs control.

clockwise during early systole (Table 8), reversing its motion in later systole (Table 2). The normal counterclockwise rotation of the base during early systole was abolished in the HCM group, leading to increased torsion in most regions. It is possible that the base also rotates counterclockwise during early systole in HCM patients but reverses its motion earlier than normal (before the second image). This requires further study at higher temporal resolution.

Torsion about the central axis is a well-documented characteristic of LV contraction and has been measured in normal humans by magnetic resonance tagging and in human transplant recipients using implanted midwall markers. The mechanism is still unknown but is probably a result of the orientation and coupling of muscle fibers through the wall. Mathematical models of LV contraction show a greatly reduced transmural stress gradient in models that allow or impose torsion. Assuming that stress generation is uniform across the wall, epicardial contraction would be expected to dominate the torsion because epicardial fibers have a greater lever arm. Hansen et al showed that torsion was relatively insensitive to alterations in preload and afterload but increased with inotropic stimulation with dobutamine or atrial pacing, suggesting that torsion is a good indicator of contractile state. MacGowan et al found a dependence of torsion on afterload within the physiological range in isolated working canine hearts, although torsion persisted during very high afterloads (isovolumic contractions). In the present study, torsion and E\text{cc} in the HCM group were increased in many regions in which the principal contraction strain was normal, suggesting that factors other than inotropic state may be affecting torsional deformation. The finding of increased torsion in HCM patients was unexpected, since myocardial fiber disarray might be expected to reduce torsion. However, Maron et al found no correlation between LV wall thickness and the amount of tissue disordered, with many thickened regions containing large proportions of organized fibers and regions of normal thickness containing disordered architecture. A thickened LV may thus contribute to torsion if a substantial amount of ordered tissue exists, especially in the epicardial regions, in which the fibers have an increased lever arm.

The longitudinal motion of the base toward the apex during systole has been documented by Rogers et al with magnetic resonance tagging. They reported an average longitudinal translation of 12.8±3.5 mm at the base and 1.6±2.2 mm at the apex, with a higher displacement at the posterior base (15.2 mm) than the anterior base (12.8 mm). These results are in agreement with our control measurements (Table 2). The greater longitudinal displacement in the posterior wall versus the anterior wall at all levels may be due to a rocking motion in which the apex moves more anterior during systole. This variation was abolished in the HCM group. The dramatic reduction in longitudinal displacement seen in HCM patients at the base, together with the relatively stationary apex in both groups, agrees with Hattori et al who measured meridional and circumferential shortening in two-dimensional echocardiograms. In that study, the distance around the midwall perimeter shortened normally in the short-axis view (16.9% circumferential shortening compared with 17.1% in control subjects), but shortening was halved in the two-chamber long-axis view (8.9% meridional shortening compared with 16.3% in control subjects).

Strain

Previously, a two-dimensional analysis of the same control group as used in this study was performed with homogeneous triangles formed from the stripe intersection points. Similar results were found in displacement and strain parameters to the present three-dimensional study. In the short-axis images, the minimum two-dimensional principal strain was oriented approximately in the circumferential direction and increased in magnitude toward the apex from the base, with greater contraction in the midventricle anterior wall than the midventricular posterior wall. In Table 4, the same longitudinal trend is seen in both E\text{cc} and E\text{3} (P<.001 for each), along with a greater contraction at midventricle in the anterior wall than the posterior, P<.001 for each. This variation between the anterior and posterior midventricle agrees with studies using implanted markers in humans and ultrasonic crystals in dogs. The two-dimensional analysis of the short-axis images also showed a change in principal angle (between the direction of maximum principal strain and the radial direction) from negative values at the apex to positive at the base. This angle was a measure of the circumferential-radial shear E\text{cr}, which was found to change sign in the present study from apex to base (Table 4) in agreement with the two-dimensional results. In the long-axis images, the minimum two-dimensional principal strain was oriented approximately in the longitudinal direction and increased toward the apex in the septal wall but not in the lateral wall. The same variations were seen in E\text{ll}. Table 4 also shows a greater E\text{ll} in the posterior wall than the anterior at the base (P<.01), concordant with
the greater longitudinal displacement in the posterior base than the anterior base seen in both the two-
dimensional and three-dimensional results ($P<.001$).

Kramer et al13 studied circumferential and longitudinal shortening in HCM patients, using the change in
distance between stripes oriented orthogonal to these
directions. Circumferential shortening was reduced in
the patient group in the septal and posterior walls at
midventricular and basal levels and in the septum and
lateral walls at the apex. This one-dimensional analysis
differs from the present three-dimensional analysis in
that the components of the circumferential and longi-
tudinal contraction in the plane of the images were
measured directly from the tag stripes, whereas the
present study reconstructed the six components of the
three-dimensional strain tensor at each point using a
smoothly continuous finite-element model. The present
study defined circumferential and longitudinal direc-
tions from the model geometry, and these may not be
aligned with any image plane. However, since the short-
and long-axis images are approximately in the circum-
ferential and longitudinal planes, respectively, the one-
dimensional circumferential and longitudinal shorten-
ing is expected to be similar to the present three-
dimensional $E_{cc}$ and $E_{ll}$. In the present study, all
regions showed reduced circumferential strain ($E_{cc}$) in
the patient group, but this was significant only in the
septum. Kramer et al13 found 13% circumferential shortening, averaged over the septum, in the HCM
group compared with 24% in the control group, corre-
sponding to strains of $-0.12$ and $-0.21$, respectively.
These are similar to our average $E_{cc}$ values of $-0.15$
and $-0.20$, respectively. They also found greater short-
ening in the lateral wall than the septal wall at the base
within the HCM group and a dramatic reduction in
longitudinal shortening at the basal septum in HCM
patients, as in the present study. A similar reduction in
average $E_{ll}$ was seen by Hattori et al37 in two-chamber
echocardiograms. Recently, two-dimensional strain es-

timates using homogeneous strain triangles in short-axis
magnetic resonance tagged images have been per-
formed.39 The least principal strain averaged $-0.17$
in the septum and $-0.21$ in the lateral wall for the HCM
group (cf $-0.15$ and $-0.19$, respectively, for $E_{cc}$ in
the present study). The three-dimensional results do not
supersede previous analyses13,15 since a one-dimen-
sional (or two-dimensional) analysis is much simpler to
perform, and other investigators will find it easier to
reproduce and build on than the more complicated
three-dimensional approach. Also, the three-dimen-
sional parameters of strain and motion are more diffi-
cult to conceptualize and present. However, an under-
standing of the three-dimensional nature of the
def ormation is essential to the interpretation of the
two-dimensional results.

Concordant with the increase in LV torsion about the
central long axis was an increase in $E_{cl}$ in many regions.
However, $E_{cl}$ was lower in the patient group in the
septal and anterior base. This was associated with a
decrease in $E_{cl}$ in the septal and anterior walls from
apex to base in the HCM group. In contrast, $E_{cl}$ was
very uniform both longitudinally and circumferentially
in the control group. The circumferential-radial trans-
verse shear $E_{cr}$ was negative at the base and positive at
the apex in both groups. This is consistent with the
finding that rotation about the central axis was higher in
magnitude in the endocardial regions than the epicar-
dial regions in both the base and the apex. This trans-
mural gradient produces the $E_{cr}$ shear. The change in
sign occurs because of the change in rotation sense from
clockwise at the base to counterclockwise at the apex
(see “Appendix”). The longitudinal-radial transverse
shear $E_{el}$ was slightly larger in the lateral wall than the
anterior and posterior walls in the control group ($P<.02$
in both cases) and larger in the lateral than the septal,
anterior, and posterior walls in the HCM group ($P<.05$
for each).

The maximum principal strain, $E_{1}$, was oriented
approximately in the radial direction and had values
similar to $E_{rr}$. The SD of these values was higher than
the other components of strain. This variation may be
due in part to the decreased resolution in the radial
direction (only two or three stripes could be tracked
across the wall). However, similar scatters in radial
normal strain and greatest principal strain have been
demonstrated in studies using implanted beads,4 which
have greater transmural resolution than magnetic reso-
nance image tagging, suggesting that some of the vari-
ation may be biological. The minimum principal strain,$E_{3}$, was oriented in the direction of the subepicardial
muscle fibers in the normal heart (approximately 20°
to 30° below circumferential). Implanted bead studies in
dog hearts have also found $E_{3}$ to act in this direction on
average, moving from $-45°$ at the epicardial to more
circumferential orientations toward the endocardium
(perpendicular to the endocardial muscle fibers).4,40

Similar directions of principal shortening were found by
Villarreal et al2 using midwall ultrasonic crystal arrays
implanted parallel to the epicardial surface. Despite the
reduction in circumferential and longitudinal shorten-
ing, the maximum contraction strain ($E_{1}$) was signifi-
cantly reduced only in the basal septum and anterior
walls. In the HCM group, the magnitude of $E_{1}$ is
maintained in many regions, despite decreases in $E_{cc}$
and $E_{ll}$, because of the increase in shear strains, mainly
the torsional shear, $E_{cr}$. This suggests that, even if the
principal contraction is normal, more of the mechanical
work in the HCM group is contributing to wall shearing
and not cavity volume reduction.

Recently, three-dimensional analyses of tagged mag-
netic resonance imaging data have been performed by
tracking the intersections of stripes with the epicardial
and endocardial boundaries in short- and long-axis
views.17,41,42 Azhari et al41 measured epicardial and
endocardial surface strains in paced reclosed-chest
dogs. The direction of principal shortening averaged
$-59°$ at the epicardium and $-26°$ at the endocardium,
slightly more longitudinal than found in the present
study. The magnitude of the principal shortening in-
creased from base to apex in endocardial regions but
not in epicardial regions. Also, they found a marked
regional variation of principal shortening, with the
anterior and posterior walls contracting differently from
the septal and lateral walls. No such variation was found
in the present study, although we have not separated
endocardial strains from epicardial strains because of
the lack of transmural resolution of stripes in the
normal subjects. The stripe spacing needs to be reduced
by at least 50% to allow higher-order variations across
the wall in the model (at present this variation is linear).
We also did not use the boundaries for deformation estimation because of the difficulty in defining the endocardial boundary in the images. This may introduce significant errors in studies that use boundary points as material markers. Some regional variation in the dog study\(^4\) may also be due to the preparation: the heart rate was maintained at a high level by pacing, and the heart was supported with a pericardial cradle. The wall thickening results are lower for the normal volunteers than those reported in Dong et al.,\(^2\) who also used the endocardial and epicardial boundaries to measure wall thickening. The limited through-wall resolution of the tags and lack of endocardial tag definition may bias the results of the present study toward the epicardial half of the wall. The wall thickening increases toward the endocardium,\(^4\) but higher-resolution tags (and images) are required to resolve this accurately.

The reduction in shortening found in many regions may be due to the myofibrillar disarray found in HCM. This may be more prevalent at the junction of the septum and LV free wall than the lateral wall.\(^43\) Hypertrophy may also affect regional strains regardless of the underlying mechanism: Palmon et al.,\(^12\)\(^\) found reduced circumferential and longitudinal segmental shortening in patients with hypertensive hypertrophy, with regional variations similar to those found in HCM patients.\(^13\) Also, Zimmer et al.,\(^44\)\(^\) found increased fiber diameter to be a determinant of impaired LV function regardless of the underlying disease.

Limitations

The model geometry is defined by fitting the inner and outer boundaries. Some information is therefore smoothed out because of the approximation of the model. Also, the image blood/muscle contrast is variable, causing errors in boundary placement. Both short- and long-axis views should be used to guide the location of the boundaries, since the contrast between blood and muscle may change in each view. The difficulty in defining endocardial boundaries on the magnetic resonance images may influence the strain estimation in regions in which the boundary has smoothed over irregularities in the endocardial surface. Interstices and trabeculae may close during systole, leading to an artifactually high estimation of contraction. Data from papillary muscles and unclear endocardial stripes were thus excluded from the fit. Since the displacement is likely to vary less than the boundaries, a more complex model (eg, using twice as many elements) may be used for geometry than the displacement field.

A linear transmural variation of displacement was used in this study. In the normal subjects, only two stripes were generally seen across the wall, with three or four stripes often seen in HCM patients. However, the linear variation was able to predict the measured displacements to within 0.6 mm on average. Higher-resolution tagged images (smaller stripe spacing) are required to resolve transmural variations in strain. Surface cardiac coils in conjunction with faster breath-hold imaging techniques may allow finer stripe spacing in the future. In addition, the reduced respiration blur from breath-hold images may allow the tracking of stripes into diastole. These improvements would allow the estimation of diastolic filling strain and kinematics. A comparison between the timing of events in systole and diastole requires a higher temporal resolution. It is possible, for example, that the “reverse rotation” of the base during early systole that occurs in normal subjects also occurs in HCM patients before the second image.

Most of the patients were older than most of the normal volunteers, and some of the differences between groups may therefore be due to aging. As more data become available, it will be possible to age match the patient group and determine whether any differences are attributable to age.

Conclusions

We examined the regional heterogeneity of three-dimensional systolic motion and deformation in normal subjects and patients with HCM. Many of the results were similar to one-dimensional and two-dimensional analyses of tagged myocardium magnetic resonance images; however, a fully three-dimensional analysis was required to examine the complex three-dimensional nonhomogeneous deformations undergone. The three-dimensional framework also allowed the study of the interplay between circumferential and longitudinal shortening, transverse and torsional shears, and the principal contraction. Although circumferential and longitudinal strains were reduced in the HCM group on a regional basis, the magnitude of the maximal contraction strain was reduced only in the basal septum and anterior walls. The magnitude of E\(_s\) may be maintained because of the increase in shear strains, mainly the torsional shear E\(_c\). This suggests that, even if the principal contraction is normal, a greater proportion of the mechanical work in the HCM group is contributing to wall shearing and not cavity volume reduction.

Appendix

Model Fitting and Strain Calculation

Model Definition

Within each element, the position \(x = (x, y, z)\) is given as a function of element coordinates \(\xi\) as a weighted average of positions at the nodes

\[
x(\xi) = \sum_{n=1}^{N} \psi_n(\xi) x_n
\]

where \(\psi_n\) are element basis functions and \(x_n\) are positions at the \(N\) nodes. For each “deformed state” (the latter four frames), the nodal values \(x_n\) are found by fitting inner and outer surfaces to the contour data at that time.\(^23\) These surfaces are then combined with a linear transmural interpolation to form three-dimensional elements.

Reconstruction Fits

Element coordinates \(\xi_d\) are found corresponding to stripe point locations \(\xi_i\) within each “deformed state” mesh by use of a modified quasi-Newton minimization procedure. At the “undeformed state” (end diastole), each data point must lie on the plane defined by the original tagging sheet. Thus, the mesh is deformed to fit the displacements back to these planes by minimizing the following objective function:

\[
e(x) = S(x) + \sum_{d=1}^{D} [n_d \cdot (x(\xi_d) - x_n)]^2
\]
where \( n_d \) is the normal to the original tagging plane for each stripe point \( d \), \( X_d \) are the corresponding data points at end diastole that lie on these planes, and \( x(\xi_d) \) are the corresponding model points. This effectively minimizes the distance between \( x(\xi_d) \) and the tagging plane corresponding to \( \xi_d \).

In the present case, there are four distinct orientations of the original tagging planes (two from each of the short- and long-axis images). The one-dimensional data constraints from all these planes are interpolated by the model basis functions to reconstruct the three-dimensional displacements of each material point.

**Deformation Fits**

Because of the approximation of the finite-element model, there is always a small error between the reconstructed “undeformed” data locations and the locations of the original tagging planes. The reconstructed points are then used to define material coordinates within the undeformed (end diastole) geometry for the deformation fits. It is therefore desirable to correct the known errors in reconstructed data point location by projecting them onto the original tagging planes. The corrected points are then located within the end-diastolic geometry (ie, the element coordinates \( \xi_d \) are recalculated within the mesh obtained by fitting the end-diastolic contours). This “undeformed state” geometry is then deformed to fit the three-dimensional displacements to each subsequent state by minimizing

\[
\varepsilon(x) = S(x) + \sum_{d=1}^{D} |x(\xi_d) - x_d|^2 \tag{3}
\]

**Smoothing**

In Equations 2 and 3, the term \( S(x) \) is a smoothing functional that regularizes the problem when the distribution of data is insufficient to constrain all the nodal parameters. In both the reconstruction and deformation fits, this is given by

\[
S(x) = \sum_{k,j} w_{ij} \left( \frac{\partial F_{ij}}{\partial \xi_k} \right)^2 d\xi \tag{4}
\]

where \( F \) is the deformation gradient tensor defined with respect to the (rectangular cartesian) cardiac coordinate system. The weights \( w_{ij} \) were set small enough to produce a negligible effect in regions containing sufficient data points (a value of 10 was used for all studies). In regions with few or no data points, the effect of the smoothing term was to reduce the variation of strain across the element. Thus, the variations in strain are dependent on the data themselves, not on the fitting process.\(^8\)

**Strain Calculation**

After the deformation fits, the deformation gradient tensor \( F \) can be calculated from the deformed mesh in a rectangular cartesian coordinate system that is rotated to be aligned in the circumferential (C), longitudinal (L), and radial (R) directions. The lagrangian strain tensor is then calculated, referred to the CLR system, as

\[
E = 1/2(FF^T - I) \tag{5}
\]

where \( I \) is the identity tensor. The diagonal components of \( E \) (\( E_{CC} \), \( E_{LL} \), \( E_{RR} \)) are called normal strains and measure the contraction (for negative values) or elongation (positive) in each direction. The off-diagonal components (\( E_{CL} \), \( E_{CR} \), \( E_{RL} \)) are shear strains that measure the change in angle between planes that are initially orthogonal.\(^4\) The eigenvalues of \( E \) (\( E_1 \), \( E_2 \), \( E_3 \)) are the principal strains, and the corresponding eigenvalues are the directions in which they act. In particular, the maximum and minimum principal strains \( (E_1, E_3) \), respectively are the maximum and minimum extension/contraction experienced by the tissue at that point. In the normal heart, with end systole as the deformed state and end diastole as the undeformed state, \( E_1 \) is positive (elongation) and is associated with wall thickening, whereas \( E_3 \) is negative and is the maximum contraction. Fig 12 shows the physical significance of components of \( E \) for two dimensions and illustrates the distinction between positive and negative shear strains. Similar figures can be drawn for \( E_{CR} \) and \( E_{RL} \) (note that in the three-dimensional case, the most negative principal strain is \( E_3 \)). Some studies\(^5,13\) calculate the principal stretches (\( A \)), which are eigenvalues of \( F \). These are converted to principal strains by

\[
E_i = 1/2(A_i^2 - 1) \tag{6}
\]

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