Quantification and Validation of Left Ventricular Wall Thickening by a Three-Dimensional Volume Element Magnetic Resonance Imaging Approach

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We have developed a method to quantify and map regional wall thickening throughout the left ventricle (LV) with magnetic resonance imaging. In contrast to methods that measure planar wall thickness and thickening, this method uses the three-dimensional (3D) geometry of the left ventricle to calculate the perpendicular thickness of the wall. We tested this method at three levels of increasing complexity using 1) phantom studies, 2) in vivo experiments in dogs with normal cardiac function, and 3) in vivo studies in dogs during acute ischemia. Experiments were conducted in 15 open-chest dogs imaged by a 0.38 T iron core magnet. Five short-axis images at end diastole and end systole were obtained with the spin echo technique by use of the QRS as a trigger for end diastole and the second heart sound, S2, to time end systole. After acquisition of preschismic images, acute ischemia was induced by either coronary artery ligation (n=5) or intracoronary dental rubber injection (n=5), which produced severe transmural ischemia. By use of computer-aided contouring of the endocardial and epicardial borders, each image was divided into 16 segments with radial lines originating from the midwall centroid. A 3D volume element was defined as that generated by connecting two matched planar segments in two adjacent image planes. This defined 64 volume elements comprising the entire left ventricle. Thickness and thickening before and during ischemia were then calculated by using the planar segments and the 3D volume elements. In phantom studies, the 3D method was accurate, independent of the angle of inclination of the image plane to the phantom wall, whereas the planar method showed considerable overestimation of thickness when the image plane was oblique to the phantom wall. In the dogs before induction of ischemia, the 3D method demonstrated the well-established normal taper in end-diastolic wall thickness from 1.10±0.02 cm at the base to 1.05±0.11 cm at the apex (p<0.01). By contrast, the planar method did not detect the decrease in thickness toward the apex (1.13±0.07 cm at the base vs. 1.16±0.14 cm at the apex, p=NS). During acute ischemia, thickening was calculated by both methods at the center of the ischemic zone defined by Monastral blue nonstaining and compared with the preschismic values. There was no overlap between the baseline and ischemic values of percent thickening with the 3D method (38.7±14.1% [range, 17–85%] vs. -12.8±13.0% [range, -40% to +13%], p<0.001), whereas there was considerable overlap (34 of 80 regions) with the planar method (35.5±18% [range, 3–75%] vs. -6.3±15.6% [range, -35% to +40%], p<0.001). Finally, a mathematical error model was developed that confirms that the planar thickness method is biased and that this bias is corrected by the 3D method. (Circulation 1990;81:297–307)

Previous echocardiographic studies have shown that regional left ventricular (LV) dysfunction can be detected based on wall motion abnormalities1 or regional LV wall thickening.2-5 The latter method is more precise than the former in detecting infarcted regions. However, the typical echocardiographic window may be limited to views that may not be optimal for thickening evaluation. In addition, epicardial borders, which are essential for thickening measurements, are not always detectable.
A major further limitation to the measurement of thickness and thickening by echocardiography, as well as other planar imaging methods, is the oblique course of the plane of a cross-sectional image through the LV wall, especially near the apex. This obliquity results in overestimation of the wall thickness by “in plane” analysis methods. Furthermore, any change in tilt of the LV wall with regard to the image plane between end diastole (ED) and end systole (ES) will affect the accuracy of thickening measurements considerably.

The potential of magnetic resonance imaging (MRI) for detecting regions of wall thickening abnormalities in patients has been demonstrated previously. In these studies, several potential sources of error were not assessed. First, thickening calculations were confined to “in plane” analysis without correction for slice obliquity. Furthermore, these studies used axial images, which are not perpendicular to the long axis of the LV. This imaging strategy likely increases the error in estimation of thickness due to the tilt of the image plane relative to the LV wall. Finally, in prior studies the cardiac cycle was divided into relatively long (100-msec) intervals. ES was approximated by the smallest cavity area. This estimate of the timing of ES may introduce additional error.

To overcome the above limitations, we have developed a method of calculating perpendicular wall thickness rather than planar thickness, taking advantage of the three-dimensional (3D) information inherent in MRI. Two adjacent slices are used to define a ring of 3D volume elements from which perpendicular thickness is calculated. Using five planar short-axis images, optimally timed to ED and ES, we map the LV thickening pattern based on the actual thickness perpendicular to the wall. This method overcomes the problem of unavoidable obliquity of the image planes to the LV wall, particularly near the apex. To detect ES accurately, we synchronized ES images with the first high frequency component of the second heart sound.

In the current study, we sought to validate this new method by using three models of increasing complexity. First, we used phantom studies to show the effect of the obliquity of an image plane on thickness measurements and its correction by the 3D method. Second, in a canine model, we used the normal geometry of the LV of wall thinning toward the apex, as established previously by Streeter, to validate the new method and compare it with the standard planar method. Third, we compared the relative potential of the two methods to detect a region of acute ischemia by matching the in vivo results with postmortem Monastral blue staining. Finally, we constructed an error model to quantify the effect of the image plane coursing obliquely through the myocardial wall. This model shows that there is a negligible bias error in the 3D approach and that the planar thickness is biased and becomes significant for oblique angles larger than 20°.

**Methods**

**Phantom Studies**

To verify the accuracy of 3D volume element measurement of thickness for a structure oblique to the image plane, we designed a 1-cm constant thickness cylindrical/conical phantom (Figure 1), simulating the ventricular base and apex, respectively. The phantom was filled with mineral oil (T1 [longitudinal relaxation time], ~200 msec; T2 [transverse decay time], ~35 msec). For the phantom studies, the protocol was as follows: time to echo, 15 msec; TR (time to repetition), 200 msec; resolution, 0.06 cm/pixel. This is based on a field of view of 15 cm and a 256 pixel matrix; NEX (number of excitations)=2. Five parallel short-axis images were obtained; the gap between images was maintained at 0.2 cm, and the image thickness, at 1 cm. The technique of iterative descent was used to produce a slice with a nearly square profile. This technique must be used because of the nonlinear nature of the Bloch equations, which do not allow “solution” for a perfectly

![Figure 1](http://circ.ahajournals.org/DownloadedFrom)
square pulse profile. Because an image represents information from a slice of tissue with a finite thickness, we define the image plane as that traversing the imaged slice at its center (Figure 2). Therefore, for this case the distance between two image planes is 1.2 cm. The image planes relative to the phantom are shown in Figure 1.

Images were traced and analyzed by the two methods of analysis outlined below, and the results were compared with the known constant thickness. By the planar method, the thicknesses of each adjacent image plane pair were averaged to compare these with the corresponding 3D thickness measurement with the same two image planes.

Animal Preparation

Fifteen mongrel dogs weighing 20–25 kg were anesthetized by intravenous injection of 5 mg/kg phenobarbital, intubated, and ventilated by a respirator (model 710A, Harvard Apparatus, South Natick, Massachusetts). Anesthesia was maintained throughout the experiments by additional phenobarbital as needed. Aortic pressure was monitored by a 5F 110-cm fluid-filled catheter positioned in the ascending aorta through the femoral artery and connected to a Statham pressure transducer (model P23XL, Gould, Cleveland, Ohio). The transducer was located approximately 0.5 m from the opening of the magnet. Operation of the transducer in or near a low-field magnet was tested by using a standard mercury column and inflating a bulb to graded pressures between 0–300 mm Hg. The transducer caused no image deterioration, nor did the magnet affect pressure calibration accuracy.

After left thoracotomy in the fifth intercostal space, the pericardium was opened. The left anterior descending or left circumflex artery was dissected after the first diagonal or first marginal branches, respectively, and a 2-0 silk suture was looped around the artery for later occlusion. A Gould heart-sound sensor was then positioned near the aortic arch, and its wires were extended through the anterior chest wall to the recording equipment. Two small (0.5-cm) oil-filled rubber balloons were sewn to the myocardium at the mid-LV level in the anterior and posterior interventricular grooves. These markers, which show high signal intensity on magnetic resonance images, were used to establish precisely the initial anatomic level at which the heart was to be cut in its short axis after death. Electrodes were attached to the dog’s limbs, the margins of the ribs were approximated, and the dog was positioned in the MRI system, with care taken to avoid passage of electrical wires through the imaging field. The ECG signal was telemetered to the console room by a transmitter-receiver pair (models 78100A and 78101A, Hewlett-Packard, Palo Alto, California) and used to trigger the MRI system. The phonocardiogram and aortic pressure were recorded on paper using a Gould eight-channel ink recorder system. To avoid radio-frequency interference with image quality, recordings were made just before and after, and also for brief periods during, image acquisition for verification of proper timing of ED and ES.

After baseline measurements and imaging, the dissected coronary artery was occluded in seven dogs without changing the animal’s position. In five dogs, acute ischemia was generated by injection of dental rubber (insoluble polymer) into the dissected coronary artery to create severe ischemia by obstructing collateral flow. This required that the imaging couch, to which the dog was firmly secured and immobilized, be slid from the magnet and then returned to its original position. This return to original position was ensured by an electronic digital distance scale and verified by repeat scout images.

At the end of the experiment, 20 ml Monastral blue dye was injected for 1 minute into the left atrium to cause ventricular fibrillation and allow later detection of the ischemic region by absence of staining. The heart was excised, and the LV was trimmed of the right ventricle and atria and weighed and cut into five short-axis slices corresponding to the imaging planes. This correspondence was ensured by cutting perpendicular to the long axis of the LV, first at the level established by the oil-filled markers, then at subsequent levels determined by image slice thickness plus interslice gap. The border of the ischemic zone in each slice, indicated by Monastral blue nonstaining, was then traced manually.

Imaging Technique

We used a Resonex RX4000 MRI system (Sunnyvale, California) with a 0.38 T iron core magnet and a 6-in. radio-frequency belt coil. For the animal studies, a spin echo technique without flow or respiratory compensation was used with a time to echo of 15 msec; TR was equal to the RR interval, and resolution was 0.2 cm/pixel, based on a 25-cm field of view and a 128-pixel matrix; NEX = 4. ED was defined

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**Figure 2. Schematic representation of the five image slices used to determine segmental thickness and thickening.** The same image planes were used at end diastole and end systole. The slice thickness was 1 cm, and the gap varied between 10–30% of slice thickness to encompass the left ventricle as shown. \( h_s \), distance between image planes.
by the QRS signal, which was used as a trigger to the MRI system. ES was defined by the second heart sound (S₂) recorded by phonocardiography. The time between the QRS and S₂ was entered into the MRI system before each image acquisition. Because our phonocardiograph did not display a QRS, this interval was initially approximated from the time between the first heart sound (S₁) and S₂. Imaging caused typical artifacts in the recording system corresponding to the exact timing of image acquisition relative to the cardiac cycle (Figure 3). From these artifacts, corrections were made to align the timing of the end-systolic image with the first deflection of S₂. There was no significant variation in Q-S₂ throughout the experiment.

After positioning the dog in the magnet, five axial images were acquired, encompassing the LV. From the axial image that traverses the largest LV cavity area, we selected an image plane passing through the LV apex to yield a long axis view, from which five parallel short-axis planes were derived. The thickness of the tomographic image, which represents the slice of tissue from which information is acquired, was held constant (1 cm), and the interslice gap was adjusted so that the images were evenly spaced (Figure 2). An image plane is defined as that traversing the center of the cross-sectional slice of myocardium being imaged. The midventricular image included the two midventricular oil-filled balloon markers.

Because flow artifacts variably obscured the endocardial border, we used two methods to obtain ED and ES images. We chose for analysis the image set with the clearest edge definition. The first method was a multislice, multiphase mode in which TR equaled the RR interval and the time to echo was 15 msec. The images were spaced in time to assure that the final images corresponded to S₂. Recording each image at both ED and ES required five iterations, with a change of slice order each time (e.g., for the first acquisition, basal slice was acquired at time 1, second slice at time 2, and so forth, so that slice order was 12345 from base to apex; for the second acquisition the order of slice imaging was changed, so that slice 5 was acquired at time 1, slice 1 at time 2, and so forth, with a resultant slice order of 51234). This produced the typical short-axis view in which the blood pool appeared as a black flow void. Alternatively, the same slice was imaged twice within the same RR interval, with ED defined by the R wave and ES by the first high-frequency component of S₂. The TR for ES was equal to the Q-S₂ interval, while the TR for ED was equal to the interval between S₂ and the QRS. This produced short-axis views with the blood pool appearing white. In each dog the image used for analysis was that which resulted in the most clearly defined edges.

Image Analysis and Thickening Computations

Image tracing. The acquired images were stored initially on the Resonex computer disk and subsequently transferred to a local computer (model MV8000, Data General, Westboro, Massachusetts) for further analysis. The epicardial and endocardial borders were traced on a high-resolution monitor (model ONE/25, Raster Technology, Littleton, Massachusetts) using a Hewlett-Packard digitizing tablet. Between eight and 20 contour points each were placed by the observer to contour endocardium and epicardium. An Akima smoothing algorithm then interpolated between contour points, and the resulting smooth contour was superimposed on the image for comparison. The contour points were corrected until a satisfactory match with the endocardial and epicardial borders was obtained. The papillary muscles were traced through their insertions. The right ventricular wall insertions and papillary muscles were also marked for orientation as well as the oil-filled markers at the midventricular level. The tracing procedure resulted in two sets of five contours at
both ED and ES, which were used for the analysis program.

Establishment of a precise match between images and anatomic slices. At the end of the experiment, the heart was excised, the right ventricle and atria were removed, and the LV was cut into five slices corresponding to the image planes (Figure 2). The oil-filled balloon markers were used as an aid to determine the location of the midlevel image plane. The five anatomic LV slices thus obtained were traced on a transparency indicating the papillary muscles, right ventricular insertions, and the region not stained by Monastral blue. The anatomic slices were aligned with the image planes using the right ventricular insertions, the papillary muscles, and the oil markers. In 10 hearts the border between the normal and ischemic zone was clearly defined by Monastral blue staining. These hearts were used for the comparison between thickening and ischemia in the center of the ischemic zone.

Thickness and thickening computations. Thickness was calculated by two methods as described below.

PLANAR METHOD. The planar analysis method is confined to one image at a time and does not account for information that exists in the adjacent images. A diagram of a contoured image is shown in Figure 4. By use of the midwall centroid as the origin, the contour is divided into 16 equiangular segments. The numbering of the segments begins arbitrarily from the top (segment 1, 12 o’clock) in a counterclockwise direction. An example of one such segment is shown (shaded area in Figure 4). Mean wall thickness is calculated by using the trapezoidal geometry of a segment:

\[ h_p = 2 \cdot \text{segment area}/(\text{endocardial length} + \text{epicardial length}) \]

where \( h_p \) is planar thickness. To obtain \( h_p \), the area of the trapezoid is calculated as well as the endocardial and epicardial lengths. Each length is represented by straight rather than the actual curved lines and may result in an error that decreases with greater numbers of segments used. For the 16 segments used here, the error is negligible.

3D METHOD. The calculation of the thickness by the 3D method uses two adjacent parallel image planes. As discussed above (Figure 2), although a two-dimensional image represents the information from a slice of tissue with a finite thickness, we assume that the image represents the anatomy of the plane traversing the midpoint of the image slice. The endocardial and epicardial contours in adjacent image planes define a 3D ring. As in the planar method, the contours are divided into 16 equiangular segments, which are assumed to be straight lines. Thus, segment pairs in adjacent image planes provide eight vertexes, which in turn define a six-sided 3D volume element, shown schematically in Figure 5. Although the top and bottom surfaces of this volume element lie in the image planes, the remaining four surfaces (endocardium and epicardium and the lateral boundaries) cannot be assumed to be planar. To calculate the geometric properties of the volume element, each of the six surfaces is treated as two triangles by dividing it diagonally. The area of the endocardial surface \( A_{\text{endo}} \) is computed by summing the areas of the two triangles that comprise the surface. The epicardial surface area \( A_{\text{epi}} \) is computed in the same way. The volume of the element \( V \) is computed by treating the element as a group of 12 tetrahedra. The centroid of the element is computed from the vertexes. Each tetrahedron is formed by three 3D vectors connecting the centroid to the three vertexes of a surface trian-
ngle. The volume of a tetrahedron can be computed as one sixth of the scalar triple product of the forming vectors. The volumes of the 12 tetrahedra are summed to yield the volume of the 3D element. This geometric approach is described elsewhere.  

The volume thickness (th) is found by treating the volume element as a solid trapezoid in which the endocardial and epicardial surfaces are flat and parallel. Therefore,

\[ V = h \cdot (A_{endo} + A_{epi})/2, \]

and the average thickness of the volume element vh, here defined as the actual or perpendicular thickness, is given by

\[ h_v = 2V / (A_{endo} + A_{epi}) \]

Note that vh, which represents the average thickness of the volume element, will differ from the planar thickness (i.e., will be smaller) if the image plane is oblique to the ventricular wall (Figure 5).

For each of the methods outlined above, the thickness for all segments is calculated at ED and ES. Systolic thickening (%Th) is expressed as the percent difference in thickness from ED to ES relative to the ED thickness; that is,

\[ \%Th = 100 \times (h_{es} - h_{ed})/h_{ed} \]

where h_{es} and h_{ed} are the ES and ED thicknesses, respectively.

**Statistical Analysis**

Student’s paired t tests were used to compare global parameters between the different groups. Average thickness and thickening as well as the standard deviation were calculated for each slice by the analysis program. This value was then used to calculate thickness and thickening for all the image plane levels for the entire group of normal dogs. A repeated measures ANOVA was used to assess the significance of the effects of the image plane level and the method on the measurement. An index of variability (standard deviation/mean) was calculated for each short-axis plane level, and the difference between the methods was tested by the Wilcoxon signed-rank test. Average thickening of the ischemic zone was calculated for each dog and compared with baseline thickening by Student’s paired t test.

**Bias Error Model**

To compare the two methods of analysis mathematically, a bias error model was constructed and is detailed in “Appendix.” The goal of the model was to test the accuracy of the 3D method relative to the planar method in measuring thickness. The model calculates the estimator of the thickness by the 3D and the planar methods for a parallelepiped derived from the solid trapezoid described above for varying angles of tilt with respect to the image plane.

### Table 1. Thicknesses of Cross-sectional Phantom Images

<table>
<thead>
<tr>
<th>Planar (cm)</th>
<th>3D (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (cylindrical)</td>
<td>0.98</td>
</tr>
<tr>
<td>2 (cylindrical)</td>
<td>1.00</td>
</tr>
<tr>
<td>3 (conical)</td>
<td>1.10</td>
</tr>
<tr>
<td>4 (conical)</td>
<td>1.13</td>
</tr>
</tbody>
</table>

Thicknesses of the cross-sectional phantom images in Figure 1 are shown. The planar method is compared with the three-dimensional (3D) method. The results are the average of 16 segments for each ring level. The cylindrical portion simulates the left ventricular base, and the conical portion simulates the apex. The phantom is a 1-cm constant wall thickness.

**Results**

**Validation of Wall Thickness Measurements by Use of a Phantom**

The thicknesses of the different image planes as a function of the method used to calculate thickness of a phantom (Figure 1) of constant wall thickness with cylindrical (base) and conical (apex) portions are shown in Table 1. While the planar method is accurate for the cylindrical portion of the phantom (analogous to the mid and basal portions of the LV), it overestimates the thickness of the conical portion, which is analogous to the LV apex. The 3D method yields accurate measurements irrespective of the angle between the image plane and the wall of the phantom.

**Dog Studies**

**Preoclusion measurement of LV wall thickness from base to apex.** Streeter has established that the thickness of the normal LV wall is diminished in the apical region compared with the basal or midventricular level. In a group of 15 dogs before induction of ischemia, the absolute thickness at ED for four levels, from apex to base, was calculated by both the planar and 3D methods (Figure 6 and Table 2). Since two image planes are needed for the 3D analysis, only four levels along the LV are available from the five cross-sectional images. Therefore, each 3D ring thickness was compared with the planar thickness of the image at the apical-most surface of the 3D element (image plane 2 in Figure 5). The wall thickness calculated by the planar method is, as expected, greater than that calculated by the 3D method for the apex but not for the base. This is attributable to the obliquity of the short-axis image to the LV wall at the apex. By two-way ANOVA, the 3D method demonstrates a thinner wall near the apex in comparison with the basal slices at ED, whereas the planar method shows no variation in wall thickness throughout the LV.

In addition to the derivation of the mean thickness for the different levels in the LV, the standard deviation of thickness between segments in each cross-sectional ring was calculated for the normal hearts at ED by both methods of analysis (Table 2). The 3D method yields smaller standard deviations than the planar method for all slices (Wilcoxon signed rank test, p<0.01).
Wall thickening during baseline conditions. Planar measurements of percent thickening were compared with the 3D method for the preischemic images (Table 3). Percent thickening by the planar method (36.9±21%) did not differ from that determined by the 3D method (34.4±15%). However, the variability in thickening as expressed by the standard deviation is less for the 3D than for the planar method (*p<0.01 for slice 1, *p<0.05 for slice 2, p=NS for slices 3 and 4 by the Wilcoxon signed rank test). The ratio of standard deviation to the mean is also less for the 3D than for the planar method for image planes 2 and 3 (*p<0.01).

Acute ischemia. In 10 dogs surviving an ischemic insult (five dogs each in the coronary ligation and dental rubber groups), the Monastral blue technique demonstrated an ischemic region comprising 15–40% of the LV mass. Thickening of the center of the ischemic region defined by the four central segments within the midischemic image level, before and after occlusion, was calculated by the 3D and planar methods (Figure 7). The 3D method demonstrated no overlap between the preischemic and ischemic values of percent thickening (38.7±14.1% [range, 17–85%] vs. −12.8±13.0% [range, −40% to +13%], *p<0.001), whereas there was considerable overlap (34 of 80 regions) with the planar method (35.5±18% [range, 3–75%] vs. −6.3±15.6% [range, −35% to +40%], *p<0.001).

Mathematical Error Model
To compare the 3D with the planar method in estimating the thickness of a structure oblique to an image plane, the error model (see “Appendix”) was developed. This model shows that there is a negligible bias error in the measurement of the wall thickness when using the 3D method. By contrast, there is a bias error for the planar method that increases with increasing obliquity of the image plane to the LV wall. The error by the 3D and planar methods for various tilt angles is given in Table 4.

Discussion
All existing imaging methods of calculating wall thickness and thickening base their calculations on measurements made in the plane of the image. In Figure 1, a cross-sectional image traversing the conical portion of a heart-like phantom results in overestimation of actual thickness. Therefore, differing inclination angles of the image plane to the wall for the same structure would result in differing in-plane thickness values. Although this problem is amplified toward the apex and may not be apparent at the midventricular level for the normal heart, it may

<table>
<thead>
<tr>
<th>Slice</th>
<th>Planar</th>
<th>3D</th>
<th>p</th>
<th>Planar</th>
<th>3D</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (base)</td>
<td>1.13±0.07</td>
<td>1.10±0.02*</td>
<td>NS</td>
<td>0.28±0.32</td>
<td>0.128±0.026</td>
<td>NS*</td>
</tr>
<tr>
<td>2</td>
<td>1.15±0.14</td>
<td>1.14±0.11</td>
<td>NS</td>
<td>0.12±0.039</td>
<td>0.108±0.031</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>3</td>
<td>1.14±0.17</td>
<td>1.10±0.12*</td>
<td>&lt;0.01</td>
<td>0.126±0.040</td>
<td>0.099±0.024</td>
<td>NS*</td>
</tr>
<tr>
<td>4 (apex)</td>
<td>1.16±0.14</td>
<td>1.05±0.11</td>
<td>&lt;0.01</td>
<td>0.131±0.028</td>
<td>0.088±0.03</td>
<td>&lt;0.05*</td>
</tr>
</tbody>
</table>

Data are mean±SD. Comparison of end-diastolic wall thickness was obtained by the two methods in 15 dogs before coronary occlusion. The averages and standard deviations were calculated for each slice comprising 16 segments by the three-dimensional (3D) and planar methods and are given as a function of slice location. There was no statistical difference in average wall thickness among levels 1–4 for the planar method by ANOVA.

*p<0.01 compared with slice 4 for 3D average thickness by ANOVA.

*Wilcoxon signed rank test.

Figure 6. Plot of three-dimensional (3D) versus planar wall thickness for normal hearts (n=14) at end diastole. Four slice levels are shown from base to apex. The 3D method yields thinner values toward the apex, consistent with the description of left ventricular thickness distribution as established by Streeter.
TABLE 3. Wall Thickening by the Planar and Three-Dimensional Methods for the Baseline Preischemic State

<table>
<thead>
<tr>
<th>Slice</th>
<th>Planar thickening (%)</th>
<th>3D thickening (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>1 (base)</td>
<td>41.2</td>
<td>31.3</td>
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<tr>
<td>2</td>
<td>35.4</td>
<td>20.2</td>
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<td>3</td>
<td>31.4</td>
<td>15.7</td>
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<tr>
<td>4</td>
<td>39.6</td>
<td>17.3</td>
</tr>
<tr>
<td>5 (apex)</td>
<td>37.2</td>
<td>20.1</td>
</tr>
<tr>
<td>Average</td>
<td>36.9</td>
<td>20.9</td>
</tr>
</tbody>
</table>

The standard deviation (SD) was calculated for each image plane. The index SD/Mean is used to assess the within-slice variability (16 segments).

*p<0.01 vs. the planar method (Wilcoxon signed rank test).

nonetheless introduce significant error if the image plane is not strictly perpendicular to the wall or if the heart is distorted by a disease process such as a transmural infarct, ventricular aneurysm, or certain congenital malformations. Therefore, a method of measuring thickness that is independent of the angle between the image plane and the LV wall should enhance significantly the accuracy of thickness measurements. (See "Appendix" for further discussion of this issue.)

The method described herein is designed to overcome this limitation by being independent of the angle between the measured structure and the image plane. The imaging procedure is structured to evaluate regional ventricular function by acquisition (at five image planes) of precisely timed ED and ES images comprising the entire LV. The perpendicular thickness is obtained from two adjacent slices, which by angular segmentation yield a ring-like array of 3D elements, whose thickness is obtained as described above.

The 3D volume element method was validated by phantom studies and by in vivo experiments in dogs before and during acute ischemia. In addition, a mathematical error model was constructed to analyze the bias error in both methods of thickness analysis.

**Phantom Studies**

The phantom studies in Table 1 and Figure 1 show that the 3D method to measure thickness is independent of the angle of the image plane with respect to the phantom wall and results in accurate estimate of thickness throughout the phantom, whereas the planar method does not. Techniques using in-plane analysis measure acical thickness (conical portion of the phantom) obliquely and will result in an overestimation of actual thickness even when true short-axis images are obtained.

**Canine Studies of the Taper of LV Wall Thickness From Base to Apex**

In a series of detailed anatomical studies, Streeter established that the normal LV geometry demonstrates tapering from base to apex. This anatomic feature is obscured when the planar method of wall thickness analysis is used, whereas it is evident when the 3D approach is taken.

**Thickening During Acute Ischemia**

The studies during acute ischemia were designed to test the ability of the 3D volume element method to detect a region of ischemic dysfunction. Ischemia was defined by postmortem analysis of the Monastral

![Figure 7](http://circ.ahajournals.org/)

**FIGURE 7.** Plot of thickening in the center of the ischemic zone (one slice, four segments) versus baseline thickening (same zone) in 10 dogs by the three-dimensional (3D) and planar methods. The 3D method resulted in no overlap between the preischemic and ischemic values of percent thickening (38.7±14.1% [range, 17–85%] vs. –12.8±13.0% [range, –40% to +13%), p<0.001), whereas there was considerable overlap (34 of 80 regions) with the planar method (35.5±18% [range, 3–75%] vs. –6.3±15.6% [range, –35% to +40%], p<0.001).
blue dye staining. Monastral blue is known to yield a sharp border at the regions where myocardial blood flow falls below 50% of baseline.15 Such a reduction of myocardial blood flow will result in rapid deterioration of local function.16 Thus, regions not stained by Monastral blue should show dysfunction. The current study demonstrates the ability of the 3D volume element method to measure true wall thickening independent of the image plane obliquity inherent in tomographic imaging techniques, resulting in improved accuracy of wall thickening determination. This is supported by the better discrimination (without overlap) between preischemic and ischemic function by the 3D method. Although errors in wall thickness that remain constant from ED to ES will cancel out in the calculation of percent thickening, any change in obliquity from ED to ES will introduce an error into the calculation of thickening. Therefore, planar methods may be less accurate in the calculation of thickening. The reduced variability of thickening determination in the normal heart by the 3D technique demonstrated herein may be a further manifestation of increased accuracy.

**Mathematical Error Model**

This model was used to quantify the effect of the tilt of the LV wall with respect to the image plane. It shows (see “Appendix”) that while the planar method overestimates wall thickness as tilt angle increases (6% bias error for a tilt angle of 20°), the 3D method proposed herein results in an estimate of LV wall thickness that is substantially devoid of bias over a wide range of angles.

In the current study, thickening is characterized by a standard deviation that is 44% of the mean (Table 3). This variability is similar to that reported by echocardiographic techniques17,18 and is relatively large. There are several possible explanations. First, the motion of the heart in space may cause the image plane to traverse different portions of the LV at ED and ES, which are then used for the analysis as if they were the same segments. Translation of the base of the heart along the long axis of the heart throughout the cardiac cycle is well recognized,19–22 in contrast to the apex, which moves little. Therefore, this type of error is minimal for the apical portions. Second, rotation and twist of the LV along the long axis may also contribute to imprecise matching of anatomy and image.23,24 Third, errors involved in border detection exist and are probably larger for the endocardium than the epicardium due to blood flow artifacts.

**Table 4. Bias Error for Wall Thickness**

<table>
<thead>
<tr>
<th>φ</th>
<th>0°</th>
<th>10°</th>
<th>15°</th>
<th>20°</th>
<th>25°</th>
<th>30°</th>
</tr>
</thead>
<tbody>
<tr>
<td>ε (%)</td>
<td>0</td>
<td>1.5</td>
<td>3.5</td>
<td>6.4</td>
<td>10.3</td>
<td>15.5</td>
</tr>
</tbody>
</table>

The bias error (ε) for wall thickness of a myocardial element tilted with respect to the imaging plane is shown. The tilt is given by the angle of deviation φ from the perpendicular line for that segment. See Figure 8 and Equation 3 of Appendix.

**Figure 8.** Schematic diagram of a parallelepiped annotated with the symbols used in the mathematical bias error model. Linear rather than curved lines are used. The endocardial surface is shaded. \( L \), length of the tilted endocardial surface; \( h_p \), planar thickness; \( h_L \), three-dimensional thickness perpendicular to the myocardial surface; \( h_s \), image plane separation distance; \( W_m \), the mean width for the upper and lower surfaces; \( φ \), tilt angle; \( Δ \), horizontal displacement of the epicardium in image plane 2 relative to image plane 1.

Finally, inherent inhomogeneity of regional function will introduce further variability.

The 3D method did not result in differences in thickening between the apical and basal slices (Table 3) despite known differences in wall thickness between these regions. Therefore, it is possible that in the calculation of thickening, part of the bias error was canceled when calculating the average thickening values. The magnitude of the normal thickening measured herein (34.4% for the 3D and 36.9% for the planar method) is consistent with previous echocardiographic measurements in open-chest dogs.2,3,25 Measurements of thickening by ultrasonic crystal pairs results in somewhat smaller values for thickening (31.3% in conscious closed-chest dogs26 and 20% in the anesthetized open-chest dog).27 Rapid fixation techniques at ED and ES yield 28% thickening,27 whereas cineangiography results in 33%.28 Thus, although normal thickening values are dependent on the measurement technique and the specific experimental preparation, most techniques yield 30–40% for the normal dog, consonant with our results.

In summary, a method to quantify regional thickening of the LV by MRI, based on a 3D volume element approach, was developed. This method sought to quantify actual perpendicular, as opposed to planar, thickness. An error analysis (see “Appendix”) showed that the new method is less biased and more accurate compared with planar methods. The 3D method resulted in thickness that is smaller than the planar for the apical slices (reflecting the normal taper of LV wall thickness from base to apex), less variability in normal thickening, and better discrimination of an ischemic from a nonischemic zone in a model of acute ischemia.
Appendix

This appendix, a mathematical error model, presents a summary of the error in planar thickness \( h_p \) when compared with 3D volume thickness \( h_v \) using two parallel short-axis tomographic images. It is also shown that wall tilt angle with respect to the perpendicular to the image planes can be inferred for each volume element and is valid even when the images are not perpendicular to the LV long axis.

The 3D volume element is shown in Figure 8 as an equivalent parallelepiped; that is, its three sets of opposing surfaces are parallel and of equal area. Although not required, this parallelepiped is chosen to have rectangular top and bottom surfaces. This parallelepiped is “derived” from the 3D volume element discussed in “Methods” and shown in Figure 5: 1) Its top and bottom surfaces (image planes 1 and 2) lie in the image planes of Figure 5. 2) It has the same element volume \( V \). 3) Its myocardial surface area \( A \) is the average endocardial \( (A_{endo}) \) and epicardial \( (A_{epi}) \) area of the element of Figure 5:

\[
A = \frac{1}{2} (A_{epi} + A_{endo})
\]

4) It has the same planar thickness as Figure 5. In its most general conception, that given in “Methods,” \( h_p \) is given by

\[
h_p = \frac{V}{A}
\]  

(1)

In Figure 8, the myocardial surface area is \( W_m \cdot L \), where \( W_m \) is mean width for the upper and lower surfaces and \( L \) is the slant height of the parallelepiped. The volume of the parallelepiped is the image plane separation distance \( h \) times the top and bottom area, or \( h_v = W_m \cdot h_p \), so that equation becomes

\[
h_p = \frac{(h_v - W_m \cdot h_p)}{W_m \cdot L} = h_p (\frac{h_v}{\sqrt{h^2 + \Delta^2}})
\]

or:

\[
h_p = h_v \sqrt{1 + \Delta^2/h_v^2}
\]

where \( \Delta \) is the offset distance.

Finally, let the angle \( \phi \) represent the angle that the perpendicular to the image planes makes with the wall segment as depicted in Figure 8. Then, from Figure 8, this tilt angle is given by

\[
h_p = h_v \cdot \cos \phi
\]

\[
\phi = \arctan \frac{\Delta}{h_v}
\]  

(2)

Therefore, the error made in the planar thickness is a bias error and its fractional value is

\[
e = (h_v - h_p) / h_v
\]

\[
= (1 / \cos \phi - 1)
\]  

(3)

Therefore, as suggested in Figure 8, the volume definition of thickness relates by a factor, \( \cos \phi \), to the planar thickness given by Equation 2 and represents a nonnegligible bias error for the tilted epicardial surface.

The bias error in the planar wall thickness \( \varepsilon \) as a function of the tilt angle \( \phi \) of the image plane with respect to the LV wall is given in Table 4. Note that for a nontilted image plane (LV wall 90° to the image plane) the planar and 3D methods converge whereas the bias increases with increasing tilt of the image plane to the LV wall.

It should be noted that the volume thickness can be evaluated by Equation 1 without reference to the planar thickness. Also, it is important to note that to evaluate the wall tilt angle the registry between top and bottom images must be included in the calculations. In particular, the offset distance \( \Delta \) of Figure 8 is directly dependent on having this registry. With this registry, the tilt angle \( \phi \) is correctly evaluated even when the image planes are not exact cross sections, that is, when the ventricular long axis is not perpendicular to the top and bottom planes of Figure 8.

In summary, this mathematical error model shows that there is an inherent bias error in the planar method for cases in which the image plane is not perpendicular to the LV wall and that this error is eliminated with the 3D method.

References


**KEY WORDS** • magnetic resonance imaging • ventricular function • ischemia
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