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Freehand Three-Dimensional Echocardiography for Measurement of Left Ventricular Mass: In Vivo Anatomic Validation Using Explanted Human Hearts

AASHA S. GOPAL, MD, MATTHEW J. SCHNELLBAECHER, MD,* ZHANQING SHEN, MD,* OLAKUNLE O. AKINBOBOYE, MD,* PETER M. SAPIN, MD,† DONALD L. KING, MD*

New York, New York and Lexington, Kentucky

Objectives. **We sought to validate freehand three-dimensional echocardiography for measuring left ventricular mass and to compare its accuracy and variability with those of conventional echocardiographic methods.**

Background. **Accurate measurement of left ventricular mass is clinically important as a predictor of morbidity and mortality. Freehand three-dimensional echocardiography eliminates geometric assumptions used by conventional methods, minimizes image positioning errors using a line of intersection display and increases sampling of the ventricle. Preliminary studies have shown it to have high accuracy and low variability.**

Methods. **Twenty-eight patients awaiting heart transplantation were examined by conventional and freehand three-dimensional echocardiography. Left ventricular mass was determined by the M-mode ("Penn-cube") method, the two-dimensional truncated ellipsoid method and three-dimensional surface reconstruction. The ventricles of 20 explanted hearts were obtained, trimmed and weighed. Echocardiographic mass by each method was compared with true mass by linear regression. Accuracy, bias and interobserver variability were calculated.**

Results. **For three-dimensional echocardiography, the correlation coefficient, standard error of the estimate, root mean square percent error (accuracy), bias and interobserver variability were 0.992, 11.9 g, 4.8%, −4.9 g and 11.5%, respectively. For the two-dimensional truncated ellipsoid method they were 0.905, 38.5 g, 15.6%, 15.4 g and 23.3%. For the M-mode ("Penn-cube") method they were 0.721, 96.9 g, 53.0%, 109.2 g and 19.5%.**

Conclusions. **Freehand three-dimensional echocardiography for measurement of left ventricular mass has high accuracy and low variability and is superior to conventional methods in hearts of abnormal size and geometry.**

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Several studies, including the Framingham study, have established increased left ventricular mass as a predictor of increased cardiac morbidity and mortality independent of age or blood pressure (1–4). Accurate measurement of left ventricular mass is thus essential for diagnosis and assessing the efficacy of therapeutic interventions undertaken for mass regression. For many years image-guided one-dimensional M-mode echocardiographic measurement of the left ventricle has been the accepted method for estimating left ventricular mass (5–9). In addition, two-dimensional echocardiographic techniques have been validated for this purpose and recommended by the American Society of Echocardiography (10–18).

Recently, advanced computer technology used in conjunction with echocardiography has resulted in the development of practical methods for three-dimensional surface reconstruction of the left ventricle (19,20). Surface reconstruction permits computation of myocardial volume and, hence, mass, without relying on geometric assumptions of ventricular size or shape (21). In addition, the freehand three-dimensional scanner, with its line of intersection display, improves accuracy of image positioning and increases the quantity and quality of data sampling (22,23). In vitro and magnetic resonance imaging validation studies of three-dimensional echocardiography have been performed with high accuracy and low variability, suggesting that it represents a significant improvement over earlier methods (24–31). Because of these promising initial results, further validation using an in vivo human anatomic standard was thought to be warranted. The purpose of this investigation was to validate the accuracy and assess the variability of freehand three-dimensional echocardiographic surface reconstruction for determination of left ventricular mass using the explanted hearts of transplant recipients as a

From the Cardiovascular Institute, Mount Sinai Medical Center, New York, New York; *Cardiology Division, Columbia University College of Physicians and Surgeons, New York, New York; and †Cardiology Division, University of Kentucky, Lexington, Kentucky. This study was presented in part at the 10th Scientific Meeting of the American Society of Hypertension, New York, New York, May 1995; the 6th Annual Scientific Sessions of the American Society of Echocardiography, Toronto, Canada, June 1995; and the 68th Scientific Sessions of the American Heart Association, Anaheim, California, November 1995. It was supported in part by Investigatorship and Grant-in-Aid awards from the American Heart Association, New York City Affiliate. Dr. King has a financial interest in the development of the three-dimensional echocardiograph.

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Address for correspondence: Dr. Donald L. King, Cardiology Division (PH3C-342), Columbia University, 622 West 168th Street, New York, New York 10032. E-mail: Kingdon@CPMC3.CPMC.Columbia.edu.

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true anatomic standard. An additional purpose was to compare the freehand three-dimensional method to the conventional one- and two-dimensional echocardiographic methods of estimating mass in the same subjects.

Methods

Subjects. This study was approved by the Institutional Review Board, and informed consent was obtained from each subject. Twenty-eight consecutive patients waiting for heart transplantation were examined by one-, two- and three-dimensional echocardiography. The examinations were performed sequentially on the same day. Patients were unselected for ease or quality of echocardiographic imaging. Four patients died before transplantation. The remaining subjects were clinically stable and did not undergo significant changes of therapeutic regimen during their course before transplantation. After transplantation an additional four hearts were used for other purposes. Thus, the explanted hearts of 20 patients were obtained for direct measurement of ventricular mass by weight.

Three-dimensional echocardiography. Three-dimensional echocardiography (Freescan, K3 Systems, Inc.) utilized a real-time scanner (Hewlett-Packard Co.) coupled to an acoustic spatial locater and a personal computer (19,20). The three-dimensional data set comprised a series of 8 to 10 short-axis cross sections spanning the ventricle from the aortic valve plane to the epicardial apex (28). A line of intersection display was used to guide positioning of the images to ensure correct alignment of the end planes and adequate, uniform sampling of ventricular shape (20). A single data set was acquired by an experienced observer for each subject. Data acquisition typically required 6 to 8 min. End-diastolic endocardial and epicardial boundaries of each short-axis cross section were manually traced by two observers using established tracing conventions. The white endocardial echoes were traced on the white side of the black-white boundary. The epicardial-pericardial echoes were traced on the white side of the white-dark boundary with the myocardium. The right septal boundary was traced through trabeculations, leaving prominent trabeculations outside of the myocardial volume. Papillary muscles in the left ventricle were also excluded from the myocardial volume by continuing the endocardial boundary through the papillary muscle when tracing. Tracing typically required ~1 min per boundary. Each surface was reconstructed, and its contained volume computed in a few seconds using a polyhedral surface reconstruction algorithm (21). Endocardial volume was subtracted from epicardial volume, yielding myocardial volume. The latter was multiplied by myocardial density (1.05 g/ml) to obtain myocardial mass. The results of both observers were averaged. Boundary tracing and computation of results were carried out in blinded manner before explantation of the heart and weighing of the ventricle.

Two-dimensional echocardiography. Two-dimensional echocardiographic determination of left ventricular mass was performed using the same Hewlett-Packard real-time scanner and the truncated ellipsoid method recommended by the American Society of Echocardiography (17). This method employs a mid-ventricular short-axis view to obtain wall thickness and chamber radius, and apical views to obtain a maximal length of the ventricle. The truncated ellipsoid formula divides the long-axis dimension at the widest portion of the ventricle. A single data set was acquired by an experienced observer. Boundary tracing was carried out by two observers on an analysis computer (Freeland Systems) using the same tracing conventions as for three-dimensional echocardiography. The results of both observers were averaged.

One-dimensional M-mode echocardiography. Parasternal long-axis image-guided M-mode echocardiography to determine left ventricular mass was performed using the method described by Devereux and Reichek (6). This method uses a one-dimensional measurement of the chamber and septal and posterior wall thicknesses at or just below the tips of the mitral leaflets. In this method, referred to as the Penn convention, the thicknesses of the left septal and posterior endocardial echoes are included in the chamber and excluded from the wall thickness. A regression-corrected formula based on the cube function of the dimensions is used to calculate mass. Measurements from a single M-mode acquisition were made by two independent observers on three cardiac cycles and averaged. The mass determinations of both observers were averaged.

Pathologic studies. The left ventricle was trimmed according to the method of Geiser and Bove (10). The papillary muscles were removed to correspond with the echocardiographic tracing convention. The ventricle was weighed and its mass indexed to patient height (m^2).

Statistical analysis. Echocardiographic mass was compared with true mass by correlation (Pearson product moment) and simple linear regression. The sign test was performed to determine if the differences between the three methods were statistically significant. The regression lines of each echocardiographic method were compared with the line of identity using the F test. The mean of the differences between echocardiographic mass and true mass was calculated as an expression of bias. The accuracy for each method was determined by calculating the root mean square percent (rms%) error according to the formula:

$$\text{rms\%} = 100 \cdot \sqrt{\left[\sum_{1}^{n} (x_i - x_t)^2/n\right]} \Big/ \bar{x}_t,$$

where x_i = echocardiographic mass; x_t = true mass; n = number of measurements; and $\bar{x}_t$ = mean of true mass. Interobserver variability was calculated according to the formula:

$$\%\text{variability} = 100 \cdot \sqrt{\left[\sum_{1}^{n}(x_1 - x_2)^2 \Big/ n\right]} \Big/ \left[\left(\sum_{1}^{n} x_1/n\right) + \left(\sum_{1}^{n} x_2/n\right)\right] \Big/ 2,$$

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Table 1. Patient Data

Pt No.	Age (yr)/ Gender	Height (m)	Weight (kg)	BSA (m^2)	Days to Op	True Mass (g)	True Mass Index (g/m^2-height)*	3D Echo Mass (g)	2D Echo Mass (g)	M-Mode Echo Mass (g)
1	61/M	1.70	71.3	1.82	4	221	76.5	221	313	412
2	59/M	1.70	62.7	1.72	5	183	63.3	182	286	301
3	57/F	1.66	43.8	1.45	11	230	83.5	213	183	379
4	39/F	1.50	67.6	1.63	1	189	84.0	188	233	367
5	56/M	1.80	68.6	1.87	36	363	112.0	358	364	362
6	51/M	1.73	79.0	1.92	19	176	58.8	174	217	273
7	62/M	1.55	59.5	1.58	30	163	67.8	168	186	237
8	58/F	1.65	53.6	1.58	208	343	126.0	358	368	344
9	57/M	1.83	83.5	2.05	87	129	38.5	117	179	186
10	47/M	1.70	60.8	1.70	40	242	83.7	237	231	231
11	41/M	1.78	86.3	2.04	6	433	136.7	409	483	546
12	60/F	1.68	58.6	1.66	6	319	113.0	316	276	452
13	60/M	1.65	63.6	1.70	10	222	81.5	237	251	526
14	60/M	1.70	73.5	1.85	48	343	118.7	321	332	458
15	52/M	1.80	74.0	1.93	109	268	82.7	259	240	411
16	62/M	1.60	79.5	1.82	34	125	48.8	123	141	116
17	56/M	1.91	110.8	2.38	9	364	99.8	369	357	436
18	39/M	1.80	97.6	2.17	1	419	129.3	387	425	537
19	56/M	1.80	101.7	2.21	35	310	95.7	319	300	321
20	62/M	1.78	59.0	1.73	454	349	110.2	336	334	680

*Grams per meter height squared. BSA = body surface area; Echo Mass = mean mass of all ventricles by echocardiography; F = female; M = male; Op = operation; Pt = patient; True Mass = mean weight of all ventricles at autopsy; 2D = two-dimensional; 3D = three-dimensional.

where x_1 = observer 1; x_2 = observer 2; and n = number of observations.

Results

Of the 20 patients (Table 1), there were 16 men (mean age 52, range 39 to 62) and 4 women (mean age 54, range 39 to 60). Fifteen patients were in United Network of Organ Sharing (UNOS) status 1 (in hospital) and five were in UNOS status 2 (outpatient). Their diagnoses included idiopathic dilated cardiomyopathy (n = 12), ischemic cardiomyopathy (n = 6), rheumatic heart disease (n = 1) and congenital heart disease (n = 1). They were examined by M-mode, two- and three-dimensional echocardiography a mean of 58 days and a median of 25 days (range 1 to 454) before transplantation to determine left ventricular mass. Table 2 presents the statistical description of the results. The mean true mass of the ventricles was 269.5 g, median 255.0 g and SD 94.5 g (range 125 to 433). The mean true mass index of the ventricles was 90.6 g/m^2 (height), median 84 g/m^2 (height) and SD 27.4 g/m^2 (height) (range 39 to 137). The mean left ventricular mass computed by three-dimensional echocardiography was 264.6 g, median 248.0 g and SD 90.7 (range 117 to 409). The mean mass determined by two-dimensional echocardiography was 285.0 g, median 281.0 g and SD 88.4 g (range 141 to 483). The mean mass determined by M-mode echocardiography was 378.8 g, median 373 g and SD 136.3 g (range 116 to 680). A statistical analysis and comparison of the methods is summarized in Table 3. Three-dimensional echocardiographic computation of left ventricular mass had a root mean square percent error (accuracy) of 4.8%, bias of −4.9 g and interobserver variability of 11.5%. The correlation coefficient was 0.992, SEE 11.9 g and regression equation: 3D mass = 7.96 + 0.952 true mass (Fig. 1). Two-dimensional echocardiographic determination of mass had a root mean square percent error of 15.6%, bias of 15.4 g and interobserver variability of 23.3%. The correlation coefficient was 0.905, SEE 38.5 g and regression equation: 2D mass = 56.6 + 0.847 true mass (Fig. 2). One-dimensional M-mode echocardiographic determination of mass had a root mean square percent error of 53.0%, bias of 109.2 g and interobserver variability of 19.5%. The correlation coefficient was 0.721, SEE of 96.9 g and regression equation: M-mode mass = 98.2 + 1.040 true mass (Fig. 3). The sign test demonstrated that three-dimensional echocardiographic determination of ventricular mass was significantly closer to true mass than both two-dimensional and one-dimensional M-mode echocardiographic determination of mass. The F test revealed no significant difference between the regression line of three-dimensional echocardiographically determined mass and the line of identity. For two-dimensional echocardiography the F test also revealed no significant difference from the line of identity. This was due to the relatively large scatter or SD of

Table 2. Statistical Description of Results in 20 Patients

Method	Mean	Median	SD	Range
True mass (g)	269.5	255.0	94.5	125–433
True mass index (g/m^2-height)*	90.6	84.0	27.4	39–137
3D echo mass (g)	264.6	248.0	90.7	117–409
2D echo mass (g)	285.0	281.0	88.4	141–483
M-mode echo mass (g)	378.8	373.0	136.3	116–680

*Grams per meter height squared. Abbreviations as in Table 1.

Table 3. Statistical Analysis of Results*

Method	Accuracy (rms%)	Bias (echo mass − true mass) (g)	Interobserver Variability	r Coeff	Regression Equation	SEE (g)
3D echo mass	4.8%	−4.9	11.5%	0.992	3D Echo mass = 7.96 + 0.952 True mass	11.9
2D echo mass (TE)	15.6%	15.4	23.3%	0.905	2D Echo mass = 56.6 + 0.847 True mass	38.5
M-mode echo mass (Penn)	53.0%	109.2	19.5%	0.721	1D Echo mass = 98.2 +1.040 True mass	96.9

*$p < 0.001$ for all comparisons. Coeff = coefficient; Penn = "Penn-cube" formula; rms% = root mean square percent error; TE = truncated ellipsoid; other abbreviations as in Table 1.

the two-dimensional data. The regression line of M-mode echocardiographically determined mass was significantly different from the line of identity.

Discussion

The results of this study demonstrate that freehand three-dimensional echocardiographic surface reconstruction is a highly accurate method for measurement of left ventricular mass and that it has low variability and excellent reproducibility. The results also demonstrate that freehand three-dimensional echocardiography is superior to conventional M-mode and two-dimensional echocardiography for measurement of left ventricular mass. In this study, it was approximately three times more accurate than the two-dimensional truncated ellipsoid method recommended by the American Society of Echocardiography and nine times more accurate than the one-dimensional M-mode echocardiographic method (Table 3). In addition, interobserver variability for three-dimensional echocardiography was approximately one-half that of the conventional methods. The improvement achieved by three-dimensional echocardiography is attributed to its elimination of geometric assumptions and image positioning errors and to increased sampling of the ventricle. Thus, freehand three-dimensional echocardiography is regarded as a significant methodologic advance and, we believe, is now the echocardiographic method of choice for quantitative measurement of left ventricular volume, mass and ejection fraction (30).

Limitations of conventional echocardiographic methods. The M-mode and two-dimensional echocardiographic methods of estimating left ventricular mass have two major limitations—image position errors and use of geometric assumptions. Image-guided M-mode recordings are made using a single parasternal long-axis image that may not pass through the middle of the left ventricle. In a previous three-dimensional echocardiographic study using the line of intersection display to assess the position of standard views, we demonstrated that one-third of the time the parasternal long-axis view was not optimally positioned (i.e., was not within ±5 mm of the center of the ventricle) (22). Thus, one-third of the time, lateral or medial displacement of the parasternal view will result in underestimation of cavity dimension made with

Figure 1. Linear regression plot of three-dimensional (3D) echocardiographic mass versus true ventricular mass: 3D mass = 7.96 + 0.952 True mass. **Circles** = individual patient data; **solid line** = regression line; **dashed lines** = 95% confidence intervals.

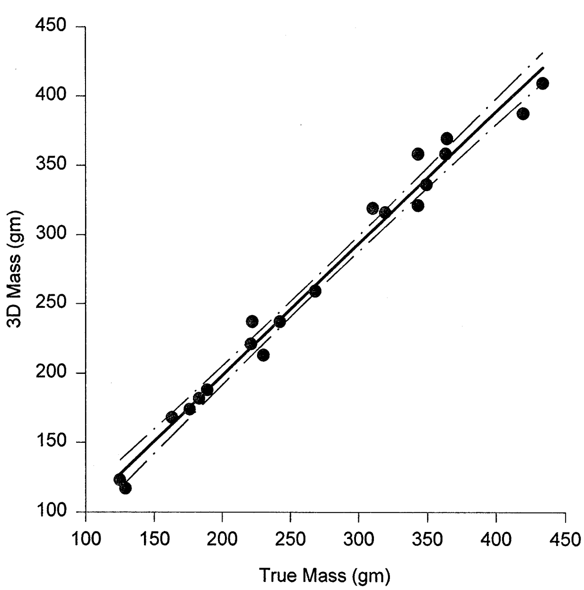
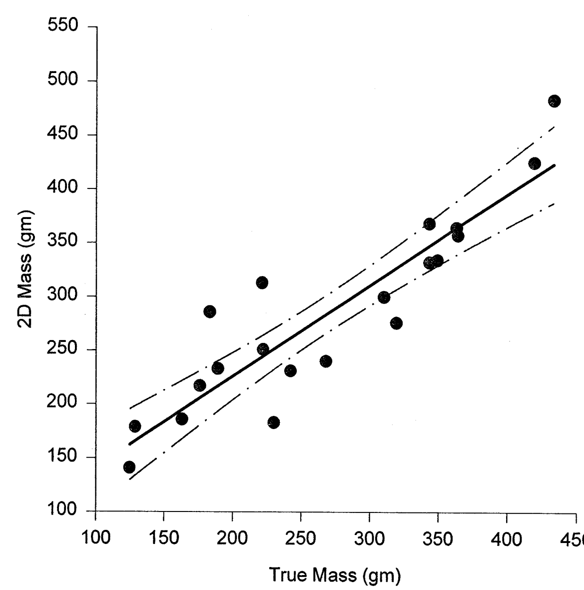


Figure 2. Linear regression plot of two-dimensional (2D) echocardiographic mass versus true ventricular mass: 2D mass = 56.6 + 0.847 True mass. Symbols as in Figure 1.



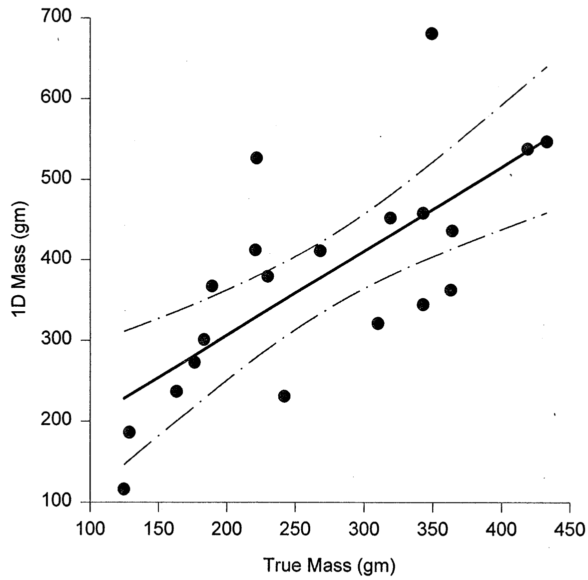


Figure 3. Linear regression plot of M-mode (1D) echocardiographic mass versus true ventricular mass: 1D mass = 98.2 + 1.040 True mass. Symbols as in Figure 1.

the M-mode cursor in that plane. In addition, the M-mode cursor is not freely steerable. It is often difficult or impossible to maneuver the transducer so that the image-guided M-mode cursor is normal to both the septal and posterior wall endocardial surfaces. Thus, oblique positioning of the M-mode cursor may result in overestimation of dimensions. These measurement errors are then cubed by the regression-corrected cube formula used to calculate mass. Finally, the one-dimensional M-mode method assumes the shape of the ventricle to be a prolate ellipsoid. As the ventricle becomes distorted by disease, its size and shape deviate significantly from this geometric model, resulting in additional errors. Despite these limitations, the one-dimensional M-mode method has been used successfully for many years in a number of important studies. These studies employed a relatively large number of subjects to overcome the inherent limitations and variability of the M-mode method.

In 1989 the American Society of Echocardiography recommended two methods for determination of left ventricular mass by two-dimensional echocardiography—the truncated-ellipsoid and the area-length methods (17). These recommendations were based on studies by Geiser and Bove (10) and subsequent investigators who reported that two-dimensional methods improved mass determination over one-dimensional M-mode techniques (11–16). Nevertheless, both methods rely on assumptions of image position and ventricular geometry. They both use unguided two-dimensional apical four-chamber and parasternal short-axis views. In both methods ventricular shape is assumed to be an ellipsoid defined by a radius obtained from either endocardial or epicardial areas on the short-axis view and by an estimate of the length of the long axis of the ventricle obtained from the apical view. These assumptions, however, are often difficult to fulfill. Erbel et al. (32) has shown in a large percentage of patients that in the apical view the ventricle is foreshortened due to anterior displacement of the imaging transducer by rib interference, thus reducing the estimate of ventricular length. We have also shown that in most patients the apical view does not pass through the center of the ventricle, further minimizing estimates of its size (22). The short-axis image is also assumed to be correctly positioned at the papillary muscles orthogonal to the long axis of the ventricle. However, it may be displaced, angled or rotated from the ideal orthogonal position distorting the calculated radii and wall thickness (22). Despite use of additional data and improved geometric assumptions, the two-dimensional techniques have not been widely used, probably because of their complexity compared with the M-mode method and because of their variability due to difficulty reproducing image position.

Advantages of freehand three-dimensional echocardiography. Freehand three-dimensional echocardiography has several significant advantages. These include freehand scanning, elimination of image position errors and geometric assumptions and improved sampling of the ventricle. In freehand scanning, motion of the transducer is not restricted or constrained by a mechanical registration device or supporting arm. The acoustic locater allows it to be hand-held and freely movable, the same as the conventional real-time transducer. By using this type of locater, the position and orientation of the transducer and its image are registered in a stationary external coordinate system. The transducer can be moved during acquisition of a data set and can acquire images from a wider field of view, including several acoustic windows in a variety of positions and orientations. This is not true of the alternate type of three-dimensional echocardiograph, the programmed scanner (33–38). The programmed scanner mechanically scans the transducer through a fixed, preprogrammed series of positions in either a linear, tilting or rotating motion. Motion of the programmed transducer is registered with respect to an internal coordinate system that has its reference point within the mechanical apparatus holding the transducer. The internal coordinate system is not stationary but moves when the mechanical apparatus holding the transducer is moved. Once scanning starts the mechanical apparatus cannot move without loss of correct registration of subsequent images, and therefore is restricted to a single position or window.

A second important advantage of freehand three-dimensional echocardiography is its ability to eliminate image positioning errors. Because the freehand scanner is freely movable and unprogrammed, it is possible to create an instantaneous, interactive display of the three-dimensional spatial relations of images as they are acquired. This display, referred to as the "line of intersection" display, enables the operator to guide and modify the image acquisition process as it occurs and thus eliminate image positioning errors (20). The display is made up of two images—a parasternal long-axis reference image and the roughly orthogonal real-time short-axis data image. The intersection of these two images is a line common to each that can be rapidly computed and displayed in each image. The position of the line of intersection in the reference image shows the relation of the real-time image to anatomic landmarks in the reference image that are otherwise not visualized. The operator can then assess the position and orientation of the real-time data images before they are acquired and eliminate errors caused by incorrect or suboptimal position and orientation. For example, the operator can more accurately define the end planes of the ventricle, can more adequately and evenly sample the ventricle and can select image position to optimize boundary definition. This approach constitutes preprocessing of data and helps to reduce or eliminate repetitive postacquisition data review and boundary tracing.

Another important advantage of freehand three-dimensional echocardiography is that it eliminates the need for formulas, models or geometric assumptions when computing quantitative variables such as volume and mass. Spatial registration of images provides the ability to compute distances and angles between all anatomic points of interest and not assume their position or the shapes they define. This information makes it possible to mathematically reconstruct the actual size and shape of the ventricle by reconstructing its surface, and thus take into account deviations of its size and shape from any assumed model. When the surface has been reconstructed, the volume contained within that surface can easily and quickly be computed by dividing it into a series of tetrahedrons.

Freehand three-dimensional echocardiography and surface reconstruction also enable use of more echocardiographic data to achieve greater and more representative sampling of the ventricle, rather than being restricted to a single one-dimensional measurement or to two cross-sectional views. The typical three-dimensional reconstruction of the ventricle uses eight to 10 short-axis images extending from the plane of the aortic valve to the apex, a four- to fivefold increase of data over the two-dimensional echocardiographic method. The use of more data results in a more representative and accurate reconstruction of the ventricle. It also results in more averaging of random boundary tracing errors and thus yields a more accurate computation of volume.

Limitations of three-dimensional echocardiography. Limitations of three-dimensional echocardiography include a slight underestimation of volume by the surface reconstruction algorithm, the additional cost of the locater, computer and software and the additional time and skill required for image acquisition and analysis. The surface reconstruction algorithm connects a series of traced boundary points on the endocardial or epicardial surfaces of the ventricle. These points are connected by straight lines, or chords. The chords tend to lie slightly inside the surface because the surface is generally concave inward. Thus, the reconstructed surface slightly underestimates true volume. In the case of mass determination, the inner endocardial volume is subtracted from the larger epicardial volume, in part canceling out this error. The small negative bias or underestimation of true mass by three-dimensional echocardiography may be related to the nature of the surface reconstruction algorithm or to the variability of boundary tracing, or both.

The three-dimensional freehand scanner is an add-on to existing conventional real-time echocardiographs. The additional cost is modest. It is operated by means of computer screen menus that are easily learned. Use of the line of intersection display to guide image positioning represents a new eye-hand coordination skill that is easily learned by experienced echocardiographers. The additional time needed to acquire a complete data set of images of the left ventricle is usually <10 min. Data analysis requires manually tracing the endocardial and epicardial boundaries of each of the 8 to 10 images comprising the data set. For a typical patient, ~1 min per boundary is needed for viewing and tracing. The time required for computer processing the traced boundaries to obtain volumes is negligible. Thus, a total of ~20 min is typically needed for boundary tracing and computation to determine left ventricular mass. When added to a routine two-dimensional echocardiographic examination, the total additional time required to obtain left ventricular mass is ~30 min.

At the present time, manual boundary tracing is considered the most accurate method for identifying the endocardial and epicardial surfaces of the ventricle for all imaging modalities. Automated and semiautomated methods of identifying these surfaces in echocardiograms have been under development for many years but have not yet reached a stage suitable for general adoption or for adaptation to three-dimensional echocardiography (39,40). The difficulties that lie in boundary tracing, whether manual or automatic, arise primarily from the low resolution of ultrasound and from the presence of acoustic noise, echo dropout and artifacts in typical echocardiograms, and not from the process of boundary tracing itself. Manual tracing of endocardial and epicardial boundaries is a skill that can be learned by technicians relatively easily, that can be performed quickly and that with practice can yield excellent results. In our experience a training period encompassing 40 to 50 three-dimensional echocardiographic examinations is necessary to attain reasonable skill and facility with the method. Experienced technicians can obtain intraobserver variability rates in the range of 5% to 6% and interobserver variability in the range of 11% to 12%, as we have shown earlier, while achieving a high degree of measurement accuracy.

Comparison with previous human anatomic validation studies. Five previous human anatomic studies validating measurement of left ventricular mass by echocardiography have been reported (6,8,12,13,18). Each of these studies compared in vivo estimates of left ventricular mass by M-mode or two-dimensional echocardiography with the weight of the ventricle at autopsy. The higher accuracy and lower variability of freehand three-dimensional echocardiography over conventional methods is confirmed when the current results are compared with the previous studies (Table 4). To properly interpret Table 4, it is important to keep in mind that the subjects of each study, as well as the methods, were different. The previous anatomic validation studies generally used hearts of more normal size and geometry than those in the present study, which were primarily dilated, spherical hearts. Comparison of these studies suggests that the conventional one- and

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Table 4. Comparison of Five Human Anatomic Validation Studies

Study (ref no.) and Method	No. of Pts	r Coeff	SD (g)	Bias (echo mass − true mass) (g)	Accuracy (bias/true mass)
Present study					
3D echo mass	20	0.99	11.9	−5.0	1.8%
2D echo mass (TE)	20	0.91	38.5	15.5	5.8%
M-mode echo mass (Penn)	20	0.72	96.9	109.3	40.6%
Byrd et al. (18)					
2D echo mass (TE)	30	0.91	41.0	32.4	15.0%
Devereux et al. (8)					
M-mode echo mass (Penn)	52	0.92	43.0	13.0	6.2%
Reichek et al. (13)					
M-mode echo mass (Penn)	18	0.86	59.0	N/A	N/A
2D echo mass (A-L)	21	0.93	31.0	N/A	N/A
Woythaler et al. (12)					
M-mode echo mass (ASE)	48	0.81	51.0	39.0	17.5%
Devereux and Reichek (6)					
M-mode echo mass (Penn)	34	0.96	29.0	N/A	N/A

A-L = area–length method; ASE = American Society of Echocardiography; N/A = not available; Pts = patients; ref = reference; SD = standard deviation of data about the regression line; other abbreviations as in Tables 1 and 3.

two-dimensional echocardiographic methods become less accurate and more variable as the size and geometry of the ventricle deviate from the original assumptions of the method, and that the resulting decreased accuracy results in overestimation of ventricular mass. The results also suggest that when more data is used, as in two- and three-dimensional echocardiography, accuracy improves and variability decreases.

Related validation studies using magnetic resonance imaging. Table 5 summarizes the statistical analyses available from four previous validation studies that used magnetic resonance imaging as a reference standard to evaluate the various echocardiographic methods of left ventricular mass measurement (28,41–43). These studies confirm the greater accuracy of three-dimensional echocardiography compared with M-mode methods, the greater variability of the M-mode methods and the tendency of the M-mode methods to overestimate ventricular mass.

Study limitations and sources of error. The results for M-mode and two-dimensional imaging in the present study are not directly comparable to those of the previous human validation studies because of the large difference between study groups in the size and shape of the hearts measured. The present study group included primarily dilated ventricles and did not include normal hearts or those with asymmetric or concentric hypertrophy or remodeling, as did previous studies. Because the characteristics of the present study group deviate significantly from the original geometric assumptions of the M-mode and two-dimensional methods, the inaccuracies and variability of these methods are expected to be worse. The very dilated hearts become spherical rather than cone-shaped or ellipsoid; the minor axis dimension becomes a chord of a sphere and is less representative of actual ventricular size; and, without guidance, accurate image positioning becomes more difficult. In addition, in the case of the M-mode method, the correction factor based on a regression of the original sample data becomes less applicable as the differences between the two study groups increases. The difference in study groups, however, does not diminish the significance of the validation of

Table 5. Validation Studies Using Magnetic Resonance Imaging

Study (ref no.) and Method	No. of Pts	r Coeff	SD (g)	Bias (echo mass − MRI) (g)	Accuracy (bias/MRI)
Missouris et al. (43)					
M-mode echo mass (Penn)	24	N/A	N/A	41.0	17.6%
M-mode echo mass (ASE)	24	N/A	N/A	87.0	37.5%
Bottini et al. (42)					
M-mode echo mass (ASE)	17	0.63	N/A	57.0	N/A
Gopal et al. (28)					
3D echo mass	15	0.90	11.1	3.5	3.2%
Germain et al. (41)					
M-mode echo mass (Penn)	20	0.87	23.4	14.0	8.8%

MRI = mean mass of all ventricles by magnetic resonance imaging; other abbreviations as in Tables 1, 3 and 4.

three-dimensional echocardiography, because it is unlikely to be less accurate in ventricles of more normal size and shape and because the results previously obtained in normal hearts and compared with magnetic resonance imaging scans are equivalent to the results obtained in the current study.

A number of procedural factors in the study may be sources of error. There was a significant time delay between the echocardiographic examination and explantation of the heart in most instances. Although these patients were well managed, stable and had no significant change in their therapeutic regimen, it is possible that there may have been some real change in ventricular mass during this interval. Mass may also have changed slightly at the time of explantation due to loss of blood from the myocardium. It was not possible to prevent this loss at the time of the operation. It is likely that this loss occurred only from the larger vessels and probably represents only a very small fraction of ventricular weight. There was also a few hours delay between explantation of the heart and weighing of the ventricle. Most of the transplantations occurred at night because of the logistics of obtaining donor hearts, and the preparation and weighing of the ventricle were carried out the next day. There may have been some loss of weight due to evaporation during this period, although efforts were made to prevent this by limiting exposure to air and drying. Another source of variation of ventricular weight was the degree to which nonmyocardial tissue was removed. To limit this variation, efforts were made to remove as much as possible without damaging the underlying myocardium. The projecting papillary muscles were removed, as well, to correspond with their exclusion from the myocardial volume during tracing. The latter was done to standardize methodology and improve reproducibility of mass computation. Although it slightly affects absolute values of myocardial mass, it should not significantly alter the results of the study.

Conclusions. Freehand three-dimensional echocardiography using surface reconstruction is a highly accurate method for measuring left ventricular mass and has low interobserver variability. Its accuracy and variability are superior to those of M-mode and two-dimensional echocardiography in hearts of abnormal size and geometry and are maintained over a wide range of ventricular size.

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