

3D Echocardiography: A Review of the Current Status and Future Directions

Judy Hung, MD, Roberto Lang, MD, Frank Flachskampf, MD, Stanton K. Shernan, MD, Marti L. McCulloch, RDCS, David B. Adams, RDCS, James Thomas, MD, Mani Vannan, MD, and Thomas Ryan, MD, *Boston, Massachusetts; Chicago, Illinois; Erlangen, Germany; Galveston, Texas; Durham, North Carolina; Cleveland, Ohio; Orange, California*

Ultrasonography technology has improved markedly in the past 10 to 15 years, prompting echocardiographers to extend its use in studying cardiac structure and function. New ultrasound equipment and techniques offer superior image quality, greater accuracy, and expanding capabilities. As a result, more and improved imaging modalities are available for evaluating cardiac anatomy, ventricular function, blood flow velocity, and valvular diseases. Three-dimensional (3D) echocardiography offers the ability to improve and expand the diagnostic capabilities of cardiac ultrasound. However, as with any emerging technology, the enthusiasm to embrace a new technique must be tempered by a critical appraisal of the evidence supporting its use. It is essential to assess the limitations as well as the unique capabilities it provides. Cardiac imaging should be safe, accurate, versatile, comprehensive, and cost-effective, while providing important clinical information. Criteria for appropriate utilization should be based on current evidence and updated as new information becomes available.

To justify the use of a new 3D modality, its unique contribution to clinical practice must be critically analyzed. In this article we review the status of 3D echocardiography, examine the evidence for its use in various clinical situations, and propose guidelines for appropriate application of this technique based on available evidence.

From Massachusetts General Hospital, Boston, MA (J.H.); University of Chicago Medical Center, Chicago, IL (R.L.); University of Erlangen, Erlangen, Germany (F.F.); Brigham & Women's Hospital, Boston, MA (S.K.S.); University of Texas Medical Branch, Galveston, TX (M.L.M.); Duke University Medical Center, Durham, NC (D.B.A., T.R.); Cleveland Clinic, Cleveland, OH (J.T.); University of California Irvine Medical Center, Orange, CA (M.V.).

Reprint requests: Thomas Ryan, MD, Duke University Medical Center, Box 3975, Durham, NC 27710 (E-mail: ryan0013@mc.duke.edu).

J Am Soc Echocardiogr 2007;20:213-233.

0894-7317/\$32.00

Copyright 2007 by the American Society of Echocardiography.

doi:10.1016/j.echo.2007.01.010

BACKGROUND

Attempts to record and display ultrasound images in 3D format were first reported in the 1960s. One of the earliest studies described the acquisition of a series of parallel scans of a human orbit to reconstruct 3D anatomy.¹ Despite the limited technology of the day, these initial studies demonstrated that complex anatomic structures were ideally displayed using 3D techniques. Concerns about image quality and the computational power needed for storage and reconstruction greatly limited the early application of this methodology.

More than a decade later, investigators began to obtain 3D ultrasound images of the heart.² Through the careful tracking of a transducer, a sequence of 2-dimensional (2D) echocardiograms could be recorded, aligned, and reconstructed into a 3D data set. This methodology was limited by the need for offline data processing to create and display the 3D images. In the early 1990s, von Ramm and colleagues³ developed the first real-time 3D (RT3D) echocardiographic scanner, capable of acquiring volumetric data at frame rates sufficient to depict cardiac motion. More recently, further improvements in design and engineering have led to the commercialization of RT3D echocardiography. This methodology has evolved quickly, and different versions of RT3D imaging are currently available on several platforms.

METHODOLOGY

Reconstruction Techniques

Early approaches to 3D echocardiography were based on the principle that a 3D data set could be reconstructed from a series of 2D images. In this method, serial 2D images are obtained using either freehand scanning or a mechanically driven transducer that sequentially recorded images at predefined intervals.⁴⁻⁸ With freehand scanning, a series of images is obtained by manually tilting the transducer along a fixed plane, and a spatial locator

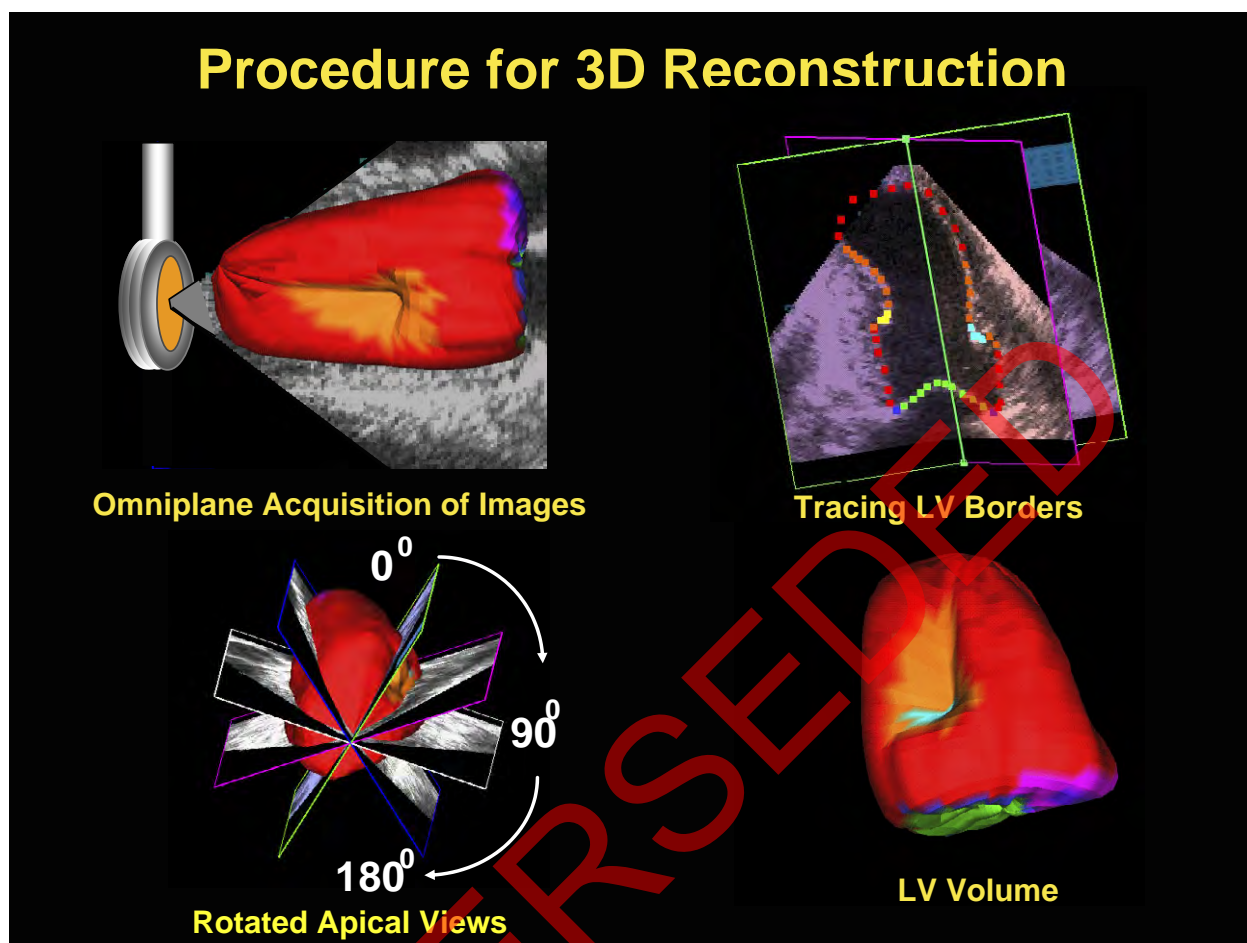


Figure 1 Left ventricular volume reconstructed from a series of rotational images obtained along a fixed apical axis.



Figure 2 Multiple transducer elements arranged in a grid-like fashion in a matrix phased-array transducer. A human hair is shown for a size comparison.

attached to the transducer translates the 3D spatial location onto a Cartesian coordinate system. This approach has several practical limitations, including the relative bulk of the acoustic spatial locators, which makes transducer manipulation difficult, and the need for a clear and direct path between the acoustic locators and the transmitter. For electromagnetic spatial locator systems, an additional problem is the potential for interference of the electromagnetic field by ferromagnetic material in close proximity to the transducer (eg, material in hospital beds and medical equipment).⁹

An alternative to freehand scanning is the use of a mechanized transducer to obtain serial images at set intervals in a parallel fashion or by pivoting around a fixed axis in a rotational, fanlike manner. Because the intervals and angles between the 2D images are defined, a 3D coordinate system can be derived from the 2D images in which the volume is more uniformly sampled than with the freehand scanning approach.

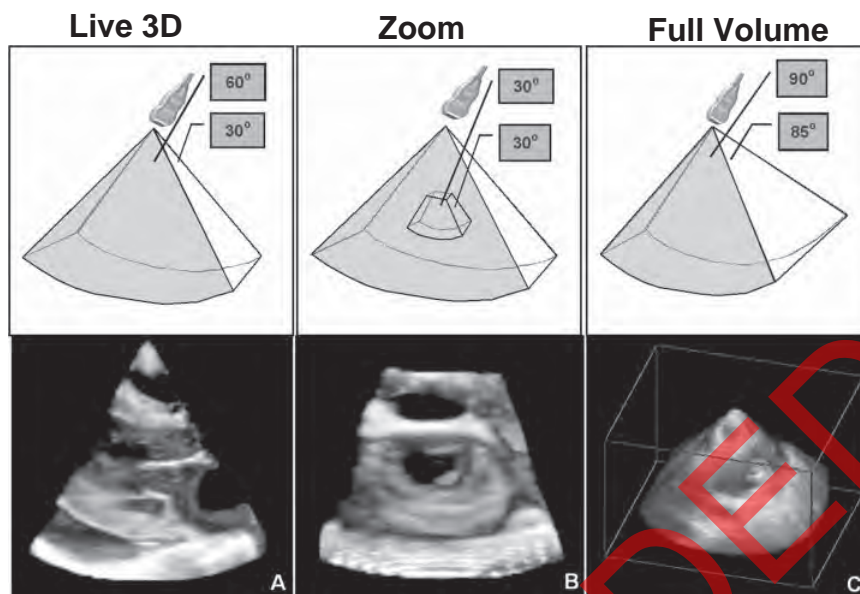


Figure 3 Three RT3D imaging modes: (A) RT3D or narrow-angle mode; (B) zoom mode; (C) wide-angle mode.

RT3D dataset

Cropped to display structures



Figure 4 An RT3D data set (A) and an RT3D data set bisected to view cardiac structures within the data set (B).

More recently, the use of a transesophageal or transthoracic multiplane probe has emerged as a readily available method to obtain rotational images at defined interval angles around a fixed axis.¹⁰⁻¹⁵ Typically, images are collected over a 180-degree

rotation at set intervals. To minimize reconstruction artifacts, sequential images are gated to both electrocardiography (ECG) and respiration. Acquisition of a complete data set typically takes 1 to 5 minutes, depending on respiratory and heart rates and the

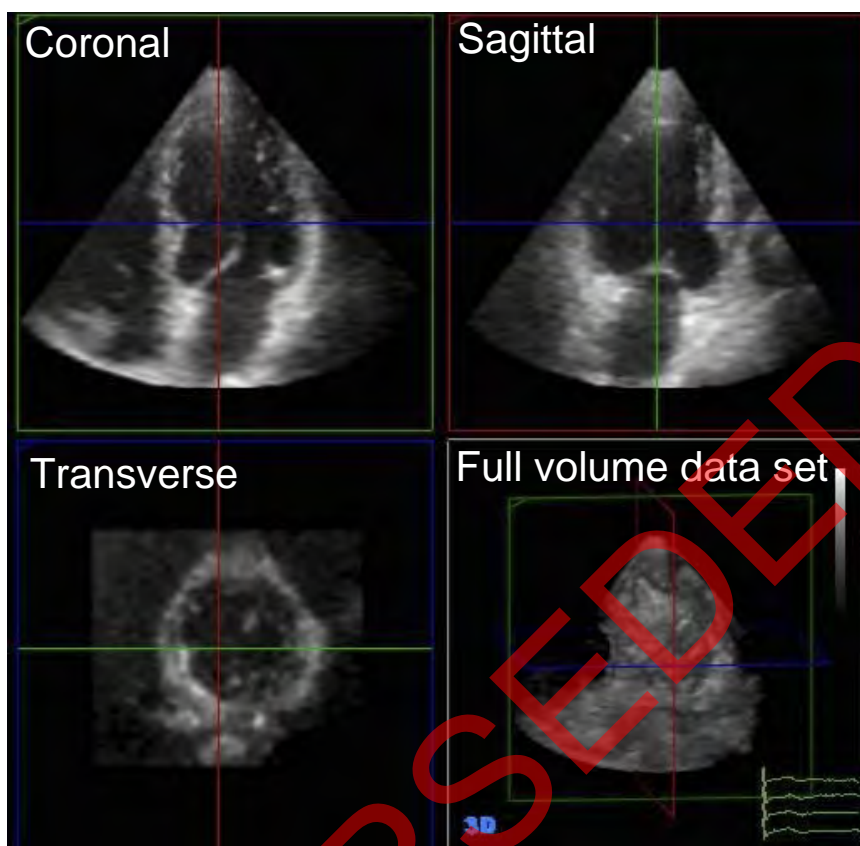


Figure 5 An RT3D data set (bottom right) cropped into coronal, sagittal, and transverse planes.

predefined spatial intervals. During cardiac surgery, respiration can be suspended during acquisition to minimize the effects of respiratory motion.

The quality of 3D reconstructions from 2D images depends on a number of factors, including the intrinsic quality of the ultrasound images, the number (or density) of the 2D images used to reconstruct the 3D image, the ability to limit motion artifact, and adequate ECG and respiratory gating. In general, the greater the number of images obtained (ie, the smaller the space intervals between images), the better the 3D reconstruction. However, increasing the number of images also lengthens the acquisition time, which can potentially introduce motion artifact. Consequently, the optimal number of images necessary for 3D reconstruction depends on the cardiac structure being examined and the resolution required. For example, 4 to 6 serial images are usually adequate for volume reconstructions of the left ventricle (LV), whereas more images are often needed to visualize more complex, rapidly moving structures, such as mitral and aortic valves.

Once the 2D images have been obtained, they are processed offline with customized or commercially available software. The cardiac structures

Table 1 A complete 3D echocardiographic protocol

- Wide-angle acquisition, parasternal long-axis window: 3D color interrogation of the aortic and mitral valves; 3D color interrogation of the tricuspid and pulmonic valves
- Wide-angle acquisition, apical 4-chamber window: 3D color interrogation of the mitral, aortic, and tricuspid valves
- Wide-angle acquisition, subcostal window: 3D color interrogation of the atrial and ventricular septa
- Wide-angle acquisition, suprasternal notch: 3D color interrogation of the descending aorta

are manually or semiautomatically traced to the 3D spatial coordinates to reconstruct a 3D image (Figure 1).

Real-Time 3D Acquisition Methods

Several studies have demonstrated that 3D reconstruction from serial 2D images provides accurate anatomic information suitable for quantitative analysis.^{4-8,10-15} However, this methodology is subject to technical limitations during image acquisition and requires significant offline data processing. The development of RT3D echocardiographic systems circumvents many of the disadvantages of reconstructive methods. RT3D echocardiography

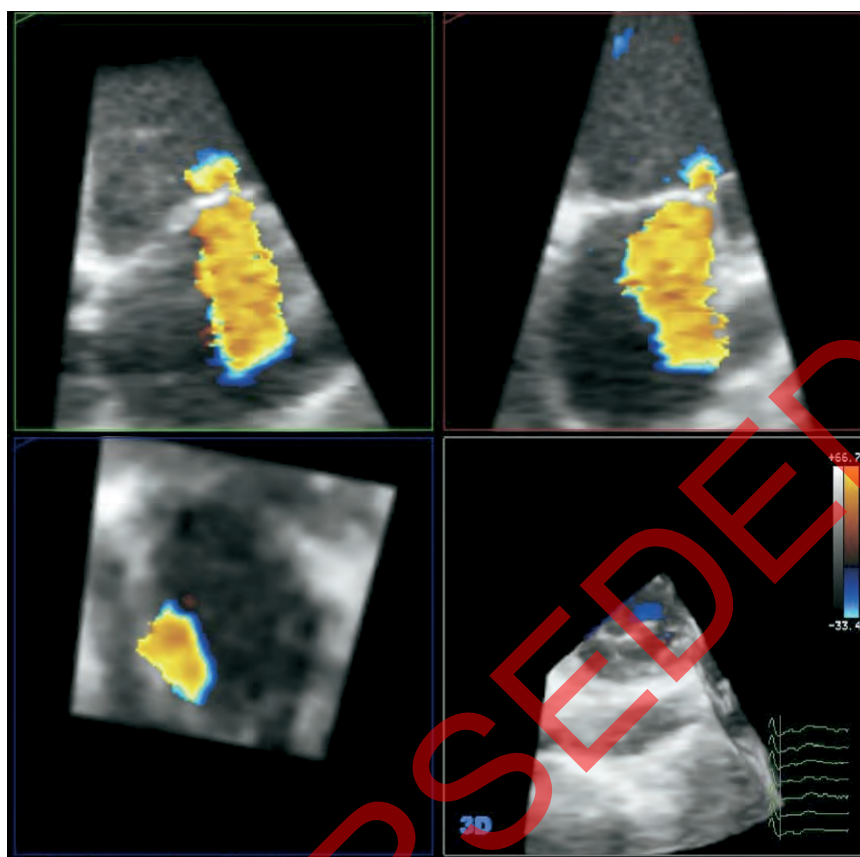


Figure 6 A 3D color Doppler display of mitral regurgitation.

uses a transducer with ultrasound elements arranged in a grid fashion (Figure 2). The earliest devices, developed by von Ramm and colleagues,^{3,16,17} used a sparse-array matrix transducer transmitting at a frequency of 2.5 or 3.5 MHz. These transducers consisted of 256 nonsimultaneous firing elements and acquired a pyramidal volume data set measuring $60^\circ \times 60^\circ$ within a single heartbeat. However, the resolution and image quality of this first-generation sparse-array transducer were relatively poor and often inferior to standard 2D images; frame rates were low; and the pyramidal volume had a narrow sector angle of 60° , resulting in an inability to accommodate larger ventricles. Moreover, the images obtained with this system were not volume-rendered online; instead, they consisted of computer-generated 2D cut planes derived from the 3D volume data set. These features limited clinical application of this pioneering technology.

Current RT3D systems use matrix-array transducer technology with a greater number of imaging elements, typically containing more than 3000 imaging elements, compared with the 256 in the sparse-array transducer. These current matrix-array transducers offer improved resolution and are rapidly becoming the primary technique for 3D

data acquisition in clinical and research practice. However, recent improvements in transducer technology have resulted in (1) a smaller transducer footprint, (2) improved side-lobe suppression, (3) greater sensitivity and penetration, and (4) harmonic capabilities that may be used for both gray-scale and contrast imaging. In addition, these matrix-array transducers display either online 3D volume-rendered images or 2 to 3 simultaneous orthogonal 2D imaging planes (ie, biplane or triplane imaging).

RT3D systems generally have 3 acquisition modes: real time (narrow), zoom (magnified), and wide angle. The real-time mode displays a pyramidal data set of approximately $50^\circ \times 30^\circ$ (Figure 3A, video clip 1).¹⁸ The zoom mode displays a smaller, magnified pyramidal data set of $30^\circ \times 30^\circ$ at a higher resolution (Figure 3B). The wide-angle mode provides a pyramidal data set of approximately $90^\circ \times 90^\circ$, which allows inclusion of a larger cardiac volume (Figure 3C, video clip 2). This wide-angle mode requires ECG gating, because the wide-angle data set is compiled by merging 4 narrower pyramidal scans obtained over 4 consecutive heartbeats. To minimize reconstruction artifacts, data should be acquired during

Table 2 Accuracy and reproducibility of LV volume determination in humans by 3D echocardiography compared with an independent standard

Publication	Technique	Study subjects	n	Method used for comparison
Gopal et al ²⁰	Reconstruction, freehand scanning with "line of intersection display," spark gap locator	Normal subjects	15	MRI
Sapin et al ²¹	Reconstruction, freehand scanning with "line of intersection display," spark gap locator	Patients evaluated for CAD	35	Cineventriculography
Buck et al ²²	Reconstruction, rotational scanning	Patients with CAD	23	MRI
Nosir et al ²³	Reconstruction, rotational scanning	Patients with CAD (31) and normal subjects (15)	46	MRI
Lange et al ²⁴	Reconstruction, rotational scanning with tissue Doppler imaging	Patients with CAD	16	Cineventriculography
Nosir et al ²⁵	Reconstruction, rotational scanning	Patients with CAD (25) and normal subjects (15)	40	MRI
Schmidt et al ²⁶	Real-time 3D acquisition	Patients with several cardiac diseases (21) and normal subjects (4)	25	MRI
Belohlavek et al ²⁷	Reconstruction, freehand scanning with electromagnetic locator	Patients with CAD (16), other cardiac diseases and normal subjects (7)	11	Electron-beam computed tomography
Lee et al ²⁸	Real-time 3D acquisition	Patients with "various cardiac disorders"	25	MRI
Mannaerts et al ²⁹	Reconstruction, freehand scanning with electromagnetic locator	Patients with CAD (16), other cardiac diseases and normal subjects (7)	29	MRI
Kawai et al ³⁰	Reconstruction, freehand scanning with electromagnetic locator	Patients with CAD (10) and other cardiac diseases	15	Gated radionuclide ventriculography
Kühl et al ³¹	Real-time 3D acquisition (sparse array)	Patients with deformed ventricles (14) and normal subjects (10)	24	MRI
Arai et al ³²	Matrix array, RT3DE	Patients with CAD and wall-motion abnormalities	25	SPECT
Jenkins et al ³³	Matrix array, RT3DE	50 patients referred for echocardiography	50	MRI
Corsi et al ³⁴	Matrix array, RT3DE	Patients referred for echocardiography	16	MRI

CAD, coronary artery disease; EDV, end-diastolic volume; ESV, end-systolic volume; MRI, magnetic resonance imaging; SD, standard deviation; SEE, standard error of the estimate; SPECT, single-photon emission computed tomography. Negative numbers in the mean difference column mean that 3D echocardiographic volumes are smaller than the volumes obtained by the technique used for comparison.

Table 2 (continued) Accuracy and reproducibility of LV volume determination in humans by 3D echocardiography compared with an independent standard

Pearson linear correlation coefficient (r)	Mean difference (bias) ±SD of the differences by Bland-Altman analysis, mL	SEE, mL	Interobserver variability, %	Comments
EDV 0.92 ESV 0.81		7 4	5-8	Better agreement of 3D than of 2D echo with MRI
EDV 0.97 EDV 0.98	13 ± 13 -1 ± 12	11 10	11 9	Better agreement of 3D than of 2D echo with MRI
EDV 0.97 ESV 0.97	-11 ± 15 -3 ± 13	15 12		2° rotational increments; better agreement of 3D than of 2D echo with MRI
EDV 0.98 ESV 0.98	-1 ± 14 -2 ± 11			2° Rotational increments
EDV+ESV (combined) 0.99	EDV: -4 ± 5 ESV: -2 ± 15	EDV+ESV combined: 5	10 7	2° rotational increments; tissue Doppler imaging (data shown here) superior to conventional imaging (data not shown)
EDV 0.98 ESV 0.99	-1 ± 14 -2 ± 11			2° rotational increments
EDV 0.98 ESV 0.82 Combined: 0.91	EDV + ESV combined: -17 ± 36	ESV+ESD combined: 28		
EDV 0.96 ESV 0.96	-5 ± 20 -7 ± 16	21 15	6 9	Variable rotational increments
EDV 0.99 ESV 0.99	+1 ± 12 +4 ± 10	11 10		Limits of agreement estimated from Bland-Altman graph
EDV 0.74 ESV 0.88	-14 ± 13 -18 ± 24			Two patients studied twice; only data for breath-holding 3D echocardiography and MRI inner contour method are shown
EDV 0.94 ESV 0.96	-7 ± 25 -4 ± 18	22 15	7 5	Limits of agreement estimated from Bland-Altman graph
EDV 0.98 ESV 0.98	-14 ± 19 -13 ± 21	18 18	2 1	Data in part obtained with a semiautomatic tracing algorithm with very high agreement with manual tracing
EDV 0.97 ESV 0.98	3 ± 14 2 ± 9		4 6	
Global LVV 0.98	-4 ± 29 EDV -3 ± 18 ESV			Semiautomated endocardial border detection

Table 3 Accuracy and reproducibility of LV mass determination by 3D echocardiography compared with an independent standard

Publication	Technique	Study setting	n	Method used for comparison
Gopal et al ³⁵	Reconstruction, freehand scanning with “line of intersection display,” spark gap locator	In vitro, autopsy hearts	11	Volume displacement
Gopal et al ³⁵	Reconstruction, freehand scanning with “line of intersection display,” spark gap locator	In vivo, patients	15	MRI
Kühl et al ³⁶	Reconstruction, rotational acquisition	In vitro, autopsy hearts	14	Volume displacement
Lee et al ²⁸	Real-time 3D acquisition	Patients with “various cardiac disorders“	25	MRI
Schmidt et al ²⁶	Real-time 3D acquisition	In vivo, open-chest sheep	21	Measurement of heart weight at necropsy
Mor-Avi et al ³⁷	Matrix array	Patients referred for echocardiography	21	MRI
Caiani et al ³⁸	Matrix array	Patients referred for echocardiography	21	MRI

CAD, coronary artery disease; *EDV*, end-diastolic volume; *ESV*, end-systolic volume; *MRI*, magnetic resonance imaging; *SD*, standard deviation; *SEE*, standard error of the estimate; *SPECT*, single-photon emission computed tomography. Negative numbers in the mean difference column mean that 3D echocardiographic volumes are smaller than the volumes obtained by the technique used for comparison.

suspended respiration if possible. Although wide-angle data sets provide a larger pyramidal scan, this is at the cost of lower resolution, which is decreased compared with the narrow-angle 3D mode.

Once a 3D data set is acquired, it must be sliced or “cropped” to visualize the cardiac structures within the pyramid (Figure 4). Multiple cropping methods are available, but a common method displays 2 or 3 imaging planes simultaneously (video clips 3a and 3b). Each of these imaging planes can be manipulated separately to appropriately align the cardiac structures. Another cropping method involves a single-slice plane that can be manually adjusted to expose and display the cardiac structures of interest (video clip 4).

Technical Factors

The technical aspects of acquiring a high-quality, diagnostic 3D echocardiogram are similar to those for 2D echocardiography. As with any new imaging technique, a learning curve exists, and recognizing and avoiding potential artifacts is critical. Many of the artifacts are related to respiratory or ECG gating and/or incorrect gain settings. The use

of optimal gain settings before acquisition is essential for accurate diagnosis. Low gain settings can artificially eliminate certain structures that then will not be viewable during postprocessing. Alternatively, using high gain settings can mask structures and lead to significant misdiagnoses. Therefore, overcompensating for the brightness of the image using the time-gain compensations is recommended, to allow the overall gain to be set at midrange values. This maneuver will allow maximum flexibility with postprocessing settings.

Most 3D echocardiographic systems use some form of gating to obtain volumetric data. Gated data sets are most challenging in patients with arrhythmias or respiratory difficulties. The confounding effects of the gating artifacts can be minimized in different ways. For example, if the gated system acquires sector slices in a sweeping motion parallel to the reference image, then every image viewed parallel to the reference image will appear normal, whereas the gated artifacts will be most noticeable when viewed from a plane orthogonal to the reference image.

Segmentation is the process by which anatomic features are extracted from the raw ultrasound

Table 3 (Continued) Accuracy and reproducibility of LV mass determination by 3D echocardiography compared with an independent standard

Pearson linear correlation coefficient (r)	Mean difference (bias) ±SD of the differences by Bland-Altman analysis, g	SEE, g	Interobserver variability, %	Comments
0.99		3		
EDV: 0.90 ESV: 0.93		11 9	13 6	Better agreement of 3D than 2D echocardiography with MRI
0.98	5 ± 10	10	4	2° rotational increments with transesophageal multiplane transducer
0.95	5 ± 26	6		Limits of agreement estimated from Bland-Altman graph
0.94	7 ± 5	9		
0.90			0-23	
0.96		11	12.5	

data. Segmentation can be accomplished using low-level techniques, such as edge detection (in 2D) and surface detection (in 3D) based on local features, such as the spatial gradient in ultrasound intensity. More sophisticated techniques attempt to extract entire boundaries or surfaces at once based on local features and the anticipated shape of the overall structure. Compression is a mathematical technique that can be applied to the original digital image file to reduce the amount of data, thereby decreasing storage requirements and improving retrieval rates. A single-volume data set from a typical RT3D echocardiographic system consists of $64 \times 64 \times 512$ bytes (approximately 2 MB), or more than 50 MB for a 1-second loop, a load that can overwhelm storage systems. Compression of the digital data files can reduce this load by about 3:1. The motion-JPEG algorithm currently used by DICOM (Digital Imaging and Communications in Medicine) and applied to individual 2D slices could be expected to achieve an approximate 20:1 compression. More advanced algorithms, such as wavelets (JPEG-2000), potentially can yield better results. The use of compression algorithms can decrease the size of data files,

optimizing storage efficiency without sacrificing image quality.¹⁹

Protocols

A complete 3D echocardiographic study includes an assessment of ventricular function, valvular morphology, and hemodynamic status. Unlike 2D echocardiography, in which standard views are described based on the plane through which they pass, 3D echocardiography is inherently volumetric. As such, it permits both an external view of the heart and multiple internal perspectives (through cropping).

Table 1 lists the components of a complete 3D echocardiographic study. A general approach is to describe cardiac structures using both the ultrasound plane and the viewing perspective. Three orthogonal planes are recommended: (1) the sagittal plane, which corresponds to a vertical, long-axis view of the heart; (2) the coronal plane, which corresponds to a 4-chamber view; and (3) the transverse plane, which corresponds to a short-axis view (Figure 5). Each plane can be viewed from 2 sides, which represent opposite perspectives; for example, the transverse plane,

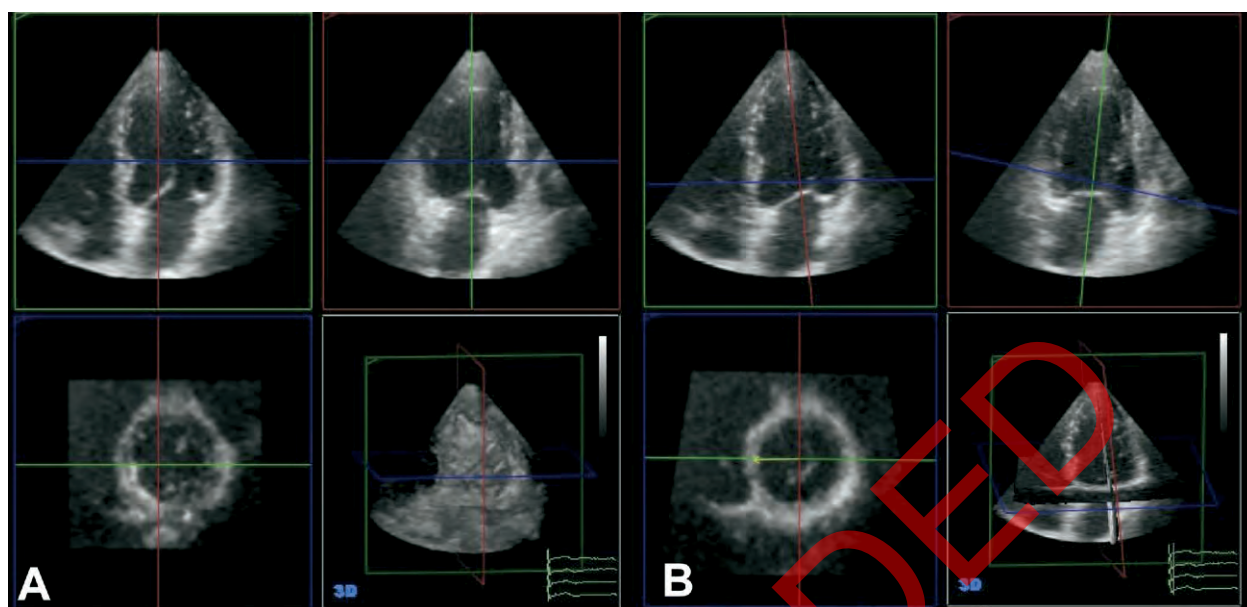
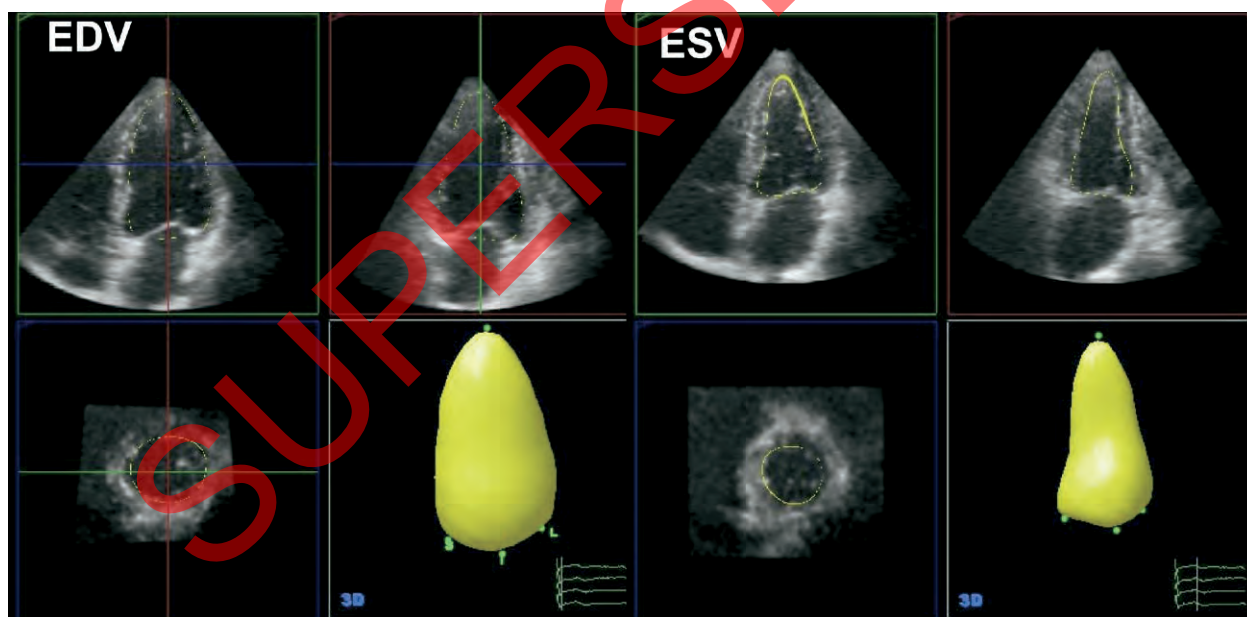


Figure 7 Simultaneous display of 3 planes (colored red, green, and blue) of an RT3D data set. Each plane is displayed in the top 2 and bottom-left panels, with the real-time 3D data set shown in the bottom-right panel. Each imaging plane can be manipulated to obtain the proper alignment for LV volume calculation (compare A and B).



EDV=end-diastolic volume; ESV=end-systolic volume

Figure 8 Left ventricular volumes calculated with a 5-point tracing algorithm obtained using 2 planes (4- and 2-chamber views).

which represents the short-axis view, can be visualized from the perspective of the apex or base; the coronal plane can be viewed from above or below; and the sagittal plane can be viewed from the left or right. The choice of narrow-angle or wide-angle imaging acquisition modes depends

on the cardiac structure to be examined. For imaging of the ventricles, it is best to use a wide-angle acquisition in the apical window (4-chamber) so as to include the entire ventricle. For smaller structures, such as the aortic valve, a narrow-angle acquisition may be adequate.



Figure 9 Regional LV volumes divided into 17 segments. The bottom graph shows change in LV volume over time for each individual LV volume segment.

As an alternative to a complete 3D study, 3D echocardiography can be performed selectively as a complement to a 2D study. Instead of a complete 3D echocardiogram, a more focused 3D imaging study may be appropriate in some cases. For example, in a patient with mitral stenosis, the 3D portion of the study may be limited to visualization and quantification of the mitral orifice. Focused 3D imaging for LV volume calculation, typically performed with an apical 4-chamber wide-angle acquisition, also can be used to complement standard 2D imaging.

The ability to extract hemodynamic information derived from 3D color Doppler ultrasonography is currently being investigated. To capture and analyze color flow imaging in 3 dimensions, the area of interest should be obtained within the 3D data set, with the angle of the ultrasound beam aligned as parallel as possible to the direction of blood flow. Depth and sector settings should be optimized for color Doppler resolution. Extraneous flows can be cropped so that only the area of interest is displayed. The color Doppler flow patterns can be analyzed in multiple views to provide a complete assessment of the color Doppler data (Figure 6).

CLINICAL APPLICATIONS

Chamber Quantification

Left Ventricle. LV chamber and mass quantification have been studied extensively using 3D echocardiography (Tables 2 and 3).²⁰⁻³⁸ Initial 3D methods to measure LV volumes used reconstruction techniques that, although more accurate and reproducible than 2D methods, required long acquisition and postprocessing times.^{20,21,30,35,39-41} Moreover, the accuracy of the volume calculations was highly dependent on image quality. The introduction of real-time imaging systems that use matrix phased-array transducers with more processing elements has significantly improved image quality. In addition, LV quantification algorithms that can interface with 3D data sets obtained with matrix phased-array transducers are now widely available and are increasingly robust.

The wide-angle acquisition mode is often used to acquire the entire LV volume, from which a detailed analysis of global and regional wall motion can be done. Images may be displayed with either orthogonal

Table 4 Accuracy and reproducibility of RV volume determination by 3D echocardiography compared with an independent standard

Publication	Technique	Study setting	n (RVs)	Method used for comparison
Jiang et al ⁵¹	Reconstruction, freehand scanning, spark gap locator	In vitro, human autopsy hearts	12	Volume of casts by water displacement
Jiang et al ⁵¹	Reconstruction, freehand scanning, spark gap locator	In vivo, animal experiments	20 "hemodynamic states"	Intracavitary balloon volume
Vogel et al ⁵⁰	Reconstruction, rotational and fanlike scanning	In vivo, patients	16	MRI
Pini et al ⁵²	Reconstruction, rotational acquisition	In vitro, sheep hearts	14	Volume of casts by water displacement
Shiota et al ⁵³	Real-time 3D acquisition	In vivo, animal experiments	14 "hemodynamic states"	Stroke volume by electromagnetic flow probe
Ota et al ⁵⁴	Real-time 3D acquisition	In vitro, canine hearts	8	Drained volumes
Ota et al ⁵⁴	Real-time 3D acquisition with saline echo contrast	In vivo, human volunteers	14	3D calculated RV stroke volume compared with 2D calculated LV stroke volume
Hubka et al ⁵⁵	Reconstruction, freehand scanning	In vitro, bovine hearts	10	Direct in vitro volume measurement

CAD, coronary artery disease; *EDV*, end-diastolic volume; *ESV*, end-systolic volume; *MRI*, magnetic resonance imaging; *SD*, standard deviation; *SEE*, standard error of the estimate; *SPECT*, single-photon emission computed tomography. Negative numbers in the mean difference column mean that 3D echocardiographic volumes are smaller than the volumes obtained by the technique used for comparison.

long-axis views or multiple short-axis views. Currently, data analysis is performed offline on a personal computer with dedicated 3D software. Data also can be analyzed online with software intrinsic to the ultrasound machine. Because a data set comprises the entire LV volume, multiple slices from different orientations can be obtained from base to apex to evaluate wall motion. If image quality is limited, then acquisition can be combined with infusion of contrast to improve the delineation of the endocardial border. An advantage of a 3D data set over 2D is the ability to manipulate the plane to align the true long axis and minor axis of the LV, hence avoiding foreshortening and oblique imaging planes (Figure 7). Once the LV axes are appropriately aligned, LV volumes can be calculated with a centroid-based algorithm that typically uses 2 or 3 planes (Figure 8), thereby shortening processing time. In addition, the LV volumes can be segmented, which allows for regional LV function assessment (Figure 9, video clip 5).

LV volume assessment by RT3D has been demonstrated to be rapid, accurate, reproducible, and superior to conventional 2D methods.⁴² The superiority of the RT3D approach has been demonstrated in various

clinical situations, but its use is limited in patients with a poor acoustic window. An alternative method of calculating ventricular volumes from an RT3D cardiac volume data set uses the disc summation method. This technique may be advantageous in patients with asymmetrical ventricles.^{22,43} LV volume and mass obtained by RT3D echocardiography compare favorably with those obtained with cardiac magnetic resonance imaging (MRI) or radionuclide volumes.^{39,42,44} In addition, RT3D echocardiography has demonstrated efficacy and accuracy in assessing LV volumes in remodeled ventricles after myocardial infarction and in assessing global LV dyssynchrony (video clips 6 and 7).^{32,45}

Preliminary clinical studies on the use of RT3D in stress echocardiography confirm the feasibility of this technique and report sensitivity and specificity comparable to 2D stress imaging.^{46,47} An advantage of RT3D stress imaging is the decreased imaging time; standard views can be obtained with only 1 or 2 image acquisitions. In preliminary clinical studies, average acquisition times decreased from 65 to 28 seconds with RT3D imaging.^{46,47}

Right Ventricle. Assessment of right ventricle (RV) function by 2D echocardiography is limited because of

Table 4 (Continued) Accuracy and reproducibility of RV volume determination by 3D echocardiography compared with an independent standard

Pearson linear correlation coefficient (r)	Mean difference (bias) \pm SD of the differences by Bland-Altman analysis, mL	SEE, mL	Interobserver variability, %	Comments
0.99	2 \pm 3	3	5	
EDV: 0.99 ESV: 0.98	-2 2	2 3	4	
EDV: 0.95 ESV: 0.87	-5 \pm 4 -6 \pm 5		4 5	
0.94-0.97	0 \pm 4	4	5	Bias (underestimation) of 2 mL by MRI in the same setup
0.8	-3 \pm 6			
0.97	0	3	4	
0.88	-4 \pm 4	2	8	
0.998	6	3		

the asymmetrical, pyramidal shape of the RV, which does not conform to simple geometric assumptions. In theory, direct visualization of the entire chamber should be possible with 3D techniques, thereby overcoming the inherent limitations of tomographic methods. To date, most studies that have applied 3D echocardiographic techniques to the RV have involved primarily rotational or freehand scanning methods (Table 4); most of these series demonstrated improved accuracy of RV function assessment.⁴⁸⁻⁵⁸ However, these 3D data sets involved reconstruction from serial 2D images with the need for offline postprocessing, thereby limiting their widespread clinical application. The recent development and availability of RT3D echocardiography has the potential to further improve the ability to assess RV chamber size, volume, and function.

Left Atrium. In a limited number of studies, left atrial volume has been accurately quantified by 3D echocardiography using both reconstructive and real-time techniques. The 3D echocardiographic methods correlate well with MRI⁵⁹⁻⁶² and appear to have accuracy comparable to 2D left atrial volume methods.⁶³

Valvular Heart Disease

The recent widespread availability of RT3D echocardiography obviates many of the practical limitations of reconstructive 3D techniques and offers the potential for greater clinical application for valvular heart disease both in standard diagnostic evaluation and in real-time guidance during surgical valve repair. This technique is ideally suited for assessing valve function given the nonplanar anatomy of the cardiac valves and the associated anatomic and spatial alterations associated with valvular heart disease.

Mitral Valve. The 3D echocardiography technique has contributed significantly to our understanding of mitral valve function and anatomy. The mitral valve is particularly suited to 3D assessment because of the complex interrelationships among the valve, chordae, papillary muscles, and myocardial walls. This technique can provide important insight into mitral valve structure, demonstrating the saddle shape of the mitral annulus, with high points located anteriorly and low points oriented in a mediolateral direction (Figure 10, video clip 8). This has helped clarify the appropriate

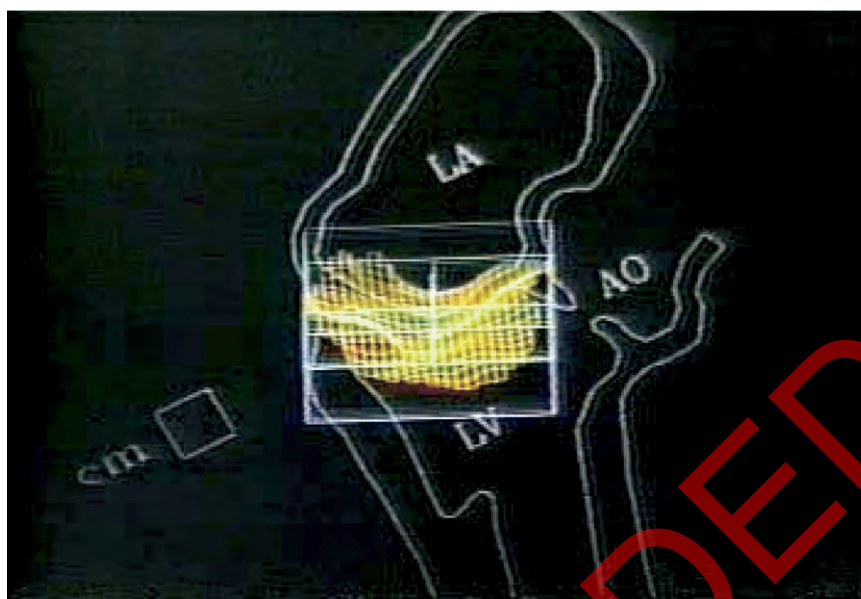


Figure 10 The bimodal shape of the mitral valve annulus demonstrated with 3D reconstruction techniques.

diagnostic imaging planes from which mitral valve prolapse should be diagnosed, thereby avoiding false-positive interpretations.^{64,65}

In addition, 3D echocardiography has provided important mechanistic insights into functional and ischemic mitral regurgitation resulting from derangements of the normal spatial relationships of the mitral valve leaflets to its chordal attachments, papillary muscles, and the LV.^{13,66} Distortion of the normal spatial relationship between the LV and mitral valve apparatus results in papillary muscle displacement and tethering of the leaflets, leading to incomplete closure of the leaflets and mitral regurgitation (video clip 9). The 3D echocardiography technique^{67,69} has identified changes in annular shape occurring with functional mitral regurgitation.^{67,69} These mechanistic and anatomic insights based on 3D analysis have provided the basis for the development of new approaches to treating ischemic mitral regurgitation.⁷⁰⁻⁷⁴

Three-dimensional echocardiography has been used to define and localize mitral leaflet lesions in mitral valve prolapse, endocarditis, and congenital mitral abnormalities.⁷⁵⁻⁸⁰ This application has been particularly important in guiding surgical repair (video clips 10 and 11).⁸¹⁻⁸³

The RT3D approach has also demonstrated efficacy in quantifying mitral regurgitation by using 3D guidance to directly measure the proximal flow convergence region.^{84,85} It has provided insight into how premitral orifice geometry affects the calculation of mitral valve area in mitral stenosis.⁸⁶ Calculation of mitral valve area by 3D echocardiography has been demonstrated to be accurate, reproducible, and less variable than conventional 2D methods (video clip

12).⁸⁷⁻⁹¹ and thus has been recommended as the first-line method.⁹² In addition, 3D echocardiography has been used for guidance during percutaneous mitral valvuloplasty.^{93,94}

Aortic Valve. Three-dimensional echocardiography has been applied for anatomic assessment of the aortic valve and root morphology and to calculate the valve area in aortic stenosis.⁹⁵⁻⁹⁹ The technique has been used to delineate aortic flow patterns^{100,101} and has demonstrated feasibility and accuracy in quantifying aortic regurgitation.^{102,103} Other applications have included the detection and localization of aortic valve vegetations, assessment of congenital outflow obstruction abnormalities, and demonstration of morphological changes in the valve after balloon dilation.¹⁰³⁻¹⁰⁷

Tricuspid and Pulmonary Valves. Compared with the aortic and mitral valves, the tricuspid and pulmonary valves have been less widely studied with 3D echocardiography. This technique has demonstrated anatomic changes with rheumatic and degenerative tricuspid valve disease.¹⁰⁸⁻¹¹⁰ and has accurately reconstructed congenital tricuspid valve abnormalities, such as atrioventricular canal defects.^{111,112} For the pulmonary valve, 3D assessment has been limited to descriptive case reports defining anatomic abnormalities associated with pulmonary valve stenosis and endocarditis.^{113,114}

Congenital Heart Disease

Clinical investigations examining the role of 3D echocardiography in patients with congenital heart disease have emphasized the unique perspective provided by 3D imaging and the versatility of the technique in

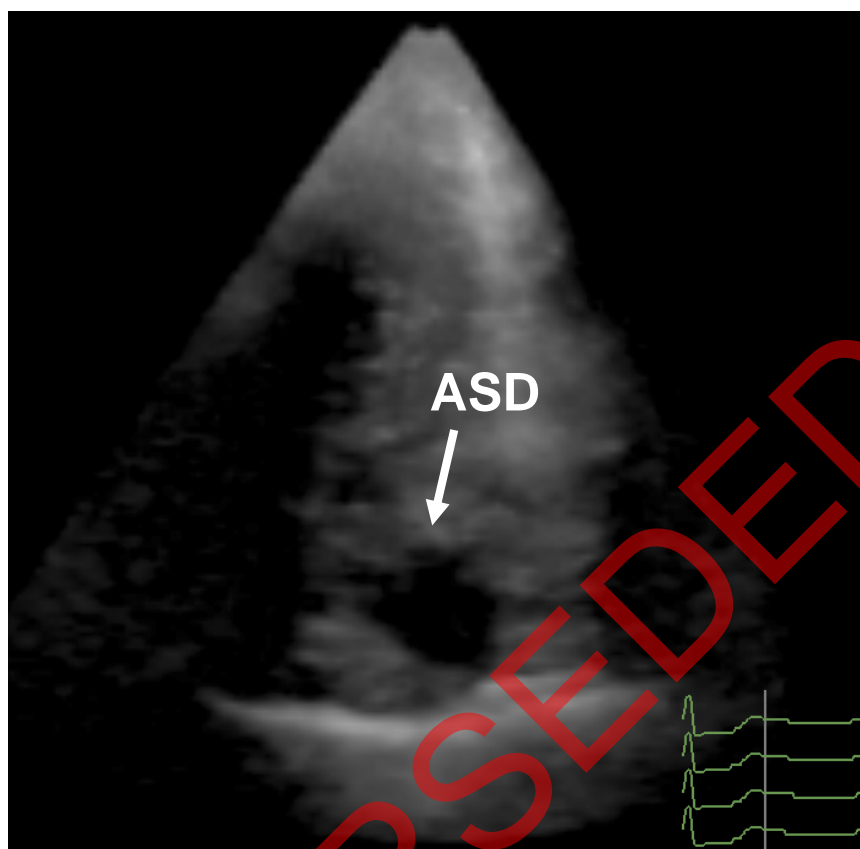


Figure 11 An atrial septal defect viewed en face from the 3D data set.

patients with simple defects or complex conditions and in the postoperative state.^{115,116} Three-dimensional echocardiography, using both reconstruction methods and RT3D, has been used to detect several forms of congenital heart disease. The ability to record and analyze the entire cardiac structure and the ability to display complex spatial relationships are potential advantages of 3D imaging over 2D echocardiography. In addition, the decreased examination time afforded by RT3D echocardiography may reduce the need for sedation in some children.¹¹⁶

In patients with atrial septal defects, 3D echocardiography can record the size and shape of the defect. It also can show the precise location of the defect and the extent of residual surrounding tissue. In patients with secundum atrial septal defects (Figure 11, video clip 13), the extent of the retroaortic rim often determines the feasibility of repair with percutaneous closure devices. Three-dimensional echocardiography also has been used after atrial septal defect closure to evaluate the success of the procedure and identify the origin of residual shunting.¹¹⁷ In patients with ventricular septal defects, the ability to interrogate the entire septum is frequently cited as an advantage of the 3D technique.^{118,119} A novel application of 3D imaging in patients with ventricular septal defects involves using

offline reconstruction to measure the shape and size of the color flow jet, which allows for accurate measurement of the magnitude of shunting in patients with isolated ventricular septal defects.¹¹⁹

Various 3D echocardiographic techniques have been used to evaluate RV and LV size and function in patients with congenital heart disease. The approach to the LV is similar to that described previously and permits quantification of dimension, volume, mass, and ejection fraction.¹²⁰ Owing to the ellipsoidal shape of the LV, the advantages of 3D over 2D echocardiographic techniques are limited, because simple geometric assumptions can be used to calculate LV volumes; however, the RV's asymmetrical shape invalidates the simple geometric assumptions used for LV volume calculations. In this case, the ability to record and analyze the entire chamber rather than relying on simplifying assumptions has proven superior.⁴⁸ In patients with congenital heart diseases that involve RV pathology, 3D echocardiography correlates well with MRI for the measurement of RV volume.^{48,121,122}

Three-dimensional echocardiography has been successfully applied to the detection and assessment of several anatomic defects. For example, the circumferential extent and severity of discrete

subaortic membranes have been successfully visualized with 3D echocardiography.^{119,120} With the apical view, a unique en face image of the membrane can be recorded, which permits analysis of the effective orifice area and the dynamic nature of the defect. Congenital malformations of the mitral valve also have been assessed with 3D echocardiography.⁸⁰ The complex nature of these defects can make a thorough anatomic evaluation difficult. In such cases, the perspective provided by 3D echocardiography can provide a complete preoperative assessment of the extent and severity of the valvular abnormality.

Intraoperative Applications

The accuracy, feasibility, and value of 3D echocardiography also have been demonstrated in the intraoperative environment. Intraoperative 3D echocardiography provides accurate and often additional anatomic information compared with 2D transesophageal (TEE) imaging.¹²³ In limited studies examining 2D and 3D TEE intraoperative evaluation of mitral valve prolapse anatomy, 3D TEE evaluation provided complementary and additional information compared with 2D TEE for localization of prolapsed scallops (video clip 14).^{77,124} Intraoperative 3D TEE also has been used to identify distortion and folding of the mitral annulus as a cause of functional mitral stenosis or worsening mitral regurgitation during beating-heart surgery.¹²⁵ Finally, intraoperative 3D TEE has proven valuable in patients undergoing surgery for congenital heart lesions. For example, the superiority of intraoperative 3D TEE compared with 2D has been demonstrated by its ability to provide en face and oblique views of left atrioventricular valve malformations in patients undergoing reoperation for persistent regurgitant lesions after previous repair of atrioventricular septal defects.^{78,126}

Intraoperative epicardial RT3D echocardiography has been used to improve spatial orientation and assess the extent of septal thickening, mitral valve systolic anterior motion, and postsurgical LV outflow tract patency in a patient with hypertrophic cardiomyopathy undergoing septal myectomy.¹²⁷ It also has been used to guide and monitor off-pump atrial septal defect closure in a beating-heart animal model.¹²⁸ Finally, intraoperative epicardial and postoperative transthoracic RT3D echocardiography has been used to evaluate changes in LV volume and function during cardiac surgery in patients undergoing infarct exclusion surgery for ischemic cardiomyopathy.⁶⁹ In contrast to 3D echocardiographic imaging, conventional 2D methods may not accurately quantify LV volumes in patients with severe ischemic cardio-

myopathy, especially in the presence of significant geometric changes due to LV aneurysm.

Contrast Echocardiography

The use of contrast with 3D echocardiography to improve quantification of LV volumes offers several advantages. The RT3D technique (single or full volume) provides the most practical approach. Triggering, although not essential, increases the signal-to-noise ratio and thus is superior to nontriggered imaging.³⁸ Preliminary clinical studies have shown promise with regard to improved LV surface identification and volume and ejection fraction measurement.^{129,130}

Another evolving application of contrast 3D echocardiography is in the evaluation of myocardial perfusion. The ability to record the entire LV and to quantify the full extent of hypoperfused myocardium is a potential advantage of this approach.¹³¹⁻¹³³ However, the problem of microbubble destruction, even with triggered imaging, remains a challenge. This is especially true when matrix array transducers are used, which results in suboptimal myocardial opacification due to high acoustic power. Further technological developments should lead to improvements in all of these areas and will contribute to more practical applications of contrast 3D echocardiography.

FUTURE DIRECTIONS

Ongoing developments in 3D echocardiography include technological innovations and expanding clinical applications. Automated surface extraction and quantification, single-heartbeat full-volume acquisition, transesophageal RT3D imaging, the ability to navigate within the 3D volume, and stereoscopic visualization of 3D images are some of the technological advances that can be expected over the next several years. These will further enhance the quality and clinical applications of 3D echocardiography. In addition, standardized and focused 3D protocols will be developed and refined to optimize clinical application of this technique.

Tagging and/or tracking the LV surface in real time may provide new approaches to quantifying myocardial mechanics, such as regional shape and strain. This approach has great potential and will complement and likely compare favorably with the quantitative ability of cardiac MRI. The superior temporal resolution of echocardiography should offer unique advantages for this purpose. In the future, combining the greater temporal resolution of 3D echocardiography with the excellent spatial resolution of MRI (or computed tomography) may yield an imaging data set with

unsurpassed anatomic and physiological information, an approach called "fusion imaging."

CONCLUSION

Three-dimensional echocardiography is a safe, noninvasive imaging modality that is complementary and supplementary to 2D imaging and can be used to assess cardiovascular function and anatomy in various clinical settings. At present, available evidence suggests that 3D echocardiography provides improved accuracy and reproducibility over 2D methods for LV volume and function calculation and the derivation of mitral valve area in patients with mitral stenosis. Further technological improvements and additional clinical studies will broaden the list of appropriate applications for this exciting new ultrasound modality.

We wish to thank Vivian McGee, Patty Phipps, and Gloria L. Healy for their editing and writing assistance.

REFERENCES

1. Baum G, Greenwood I. Orbital lesion localization by three-dimensional ultrasonography. *N Y State J Med* 1961;61:4149-57.
2. Dekker DL, Piziali RL, Dong E Jr. A system for ultrasonically imaging the human heart in three dimensions. *Comput Biomed Res* 1974;7:544-53.
3. Sheikh K, Smith SW, von Ramm O, Kisslo J. Real-time, three-dimensional echocardiography: feasibility and initial use. *Echocardiography* 1991;8:119-25.
4. King DL, Harrison MR, King DL Jr, Gopal AS, Martin RP, DeMaria AN. Improved reproducibility of left atrial and left ventricular measurements by guided three-dimensional echocardiography. *J Am Coll Cardiol* 1992;20:1238-45.
5. Siu SC, Rivera JM, Guerrero JL, Handschumacher MD, Lethor JP, Weyman AE, et al. Three-dimensional echocardiography: in vivo validation for left ventricular volume and function. *Circulation* 1993;88:1715-23.
6. Jiang L, Vazquez de Prada JA, Handschumacher MD, Guerrero JL, Vlahakes GJ, King ME, et al. Three-dimensional echocardiography: in vivo validation for right ventricular free wall mass as an index of hypertrophy. *J Am Coll Cardiol* 1994;23:1715-22.
7. Gopal AS, Schnellbaecher MJ, Shen Z, Boxt LM, Katz J, King DL. Freehand three-dimensional echocardiography for determination of left ventricular volume and mass in patients with abnormal ventricles: comparison with magnetic resonance imaging. *J Am Soc Echocardiogr* 1997;10:853-61.
8. Handschumacher MD, Lethor JP, Siu SC, Mele D, Rivera JM, Picard MH, et al. A new integrated system for three-dimensional echocardiographic reconstruction: development and validation for ventricular volume with application in human subjects. *J Am Coll Cardiol* 1993;21:743-53.
9. King DL. Errors as a result of metal in the near environment when using an electromagnetic locator with freehand three-dimensional echocardiography. *J Am Soc Echocardiogr* 2002;15:731-5.
10. Pai RG, Jintapakorn W, Tanimoto M, Cao QL, Pandian N, Shah PM. Three-dimensional echocardiographic reconstruction of the left ventricle by a transesophageal tomographic technique: in vitro and in vivo validation of its volume measurement. *Echocardiography* 1996;13:613-22.
11. Franke A, Flachskampf FA, Kuhl HP, Klues HG, Job FP, Merx M, et al. Three-dimensional reconstruction of multiplanar transesophageal echocardiography images: a methodologic report with case examples. *Z Kardiol* 1995;84:633-42 [in German].
12. Roelandt J, Salustri A, Mumm B, Vletter W. Precordial three-dimensional echocardiography with a rotational imaging probe: methods and initial clinical experience. *Echocardiography* 1995;12:243-52.
13. Otsuji Y, Handschumacher MD, Schwammenthal E, Jiang L, Song JK, Guerrero JL, et al. Insights from three-dimensional echocardiography into the mechanism of functional mitral regurgitation: direct in vivo demonstration of altered leaflet tethering geometry. *Circulation* 1997;96:1999-2008.
14. Pandian NG, Roelandt J, Nanda NC, Sugeng L, Cao QL, Azevedo J, et al. Dynamic three-dimensional echocardiography: methods and clinical potential. *Echocardiography* 1994;11:237-59.
15. Hozumi T, Yoshikawa J, Yoshida K, Akasaka T, Takagi T, Yamamuro A. Three-dimensional echocardiographic measurement of left ventricular volumes and ejection fraction using a multiplane transesophageal probe in patients. *Am J Cardiol* 1996;78:1077-80.
16. von Ramm OT, Smith SW. Real-time volumetric ultrasound imaging system. *J Dig Imaging* 1990;3:261-6.
17. Snyder JE, Kisslo J, von Ramm O. Real-time orthogonal mode scanning of the heart, I: system design. *J Am Coll Cardiol* 1986;7:1279-85.
18. Sugeng L, Weinert L, Thiele K, Lang RM. Real-time three-dimensional echocardiography using a novel matrix array transducer. *Echocardiography* 2003;20:623-35.
19. Hang X, Greenberg NL, Shiota T, Firstenberg MS, Thomas JD. Compression of real time volumetric echocardiographic data using modified SPIHT based on the three-dimensional wavelet packet transform. *Comput Cardiol* 2000;27:123-6.
20. Gopal AS, Keller AM, Rigling R, King DL Jr, King DL. Left ventricular volume and endocardial surface area by three-dimensional echocardiography: comparison with two-dimensional echocardiography and nuclear magnetic resonance imaging in normal subjects. *J Am Coll Cardiol* 1993;22:258-70.
21. Sapin PM, Schroder KM, Gopal AS, Smith MD, DeMaria AN, King DL. Comparison of two- and three-dimensional echocardiography with cineventriculography for measurement of left ventricular volume in patients. *J Am Coll Cardiol* 1994;24:1054-63.
22. Buck T, Hunold P, Wentz KU, Tkalec W, Nesser HJ, Erbel R. Tomographic three-dimensional echocardiographic determination of chamber size and systolic function in patients with left ventricular aneurysm: comparison to magnetic resonance imaging, cineventriculography, and two-dimensional echocardiography. *Circulation* 1997;96:4286-97.
23. Nosir YFM, Lequin MH, Kasprzak JD, van Domburg RT, Wletter WB, Yao J, et al. Measurements and day-to-day variabilities of left ventricular volumes and ejection fraction by three-dimensional echocardiography and comparison with magnetic resonance imaging. *Am J Cardiol* 1998;82:209-14.

24. Lange A, Palka P, Nowicki A, Olszewski R, Anderson T, Adamus J, et al. Three-dimensional echocardiographic evaluation of left ventricular volume. Comparison of Doppler myocardial imaging and standard gray-scale imaging with cineventriculography: an in vitro and in vivo study. *Am Heart J* 1998;135:970-9.
25. Nosir YFM, Stoker J, Kasprzak JD, Lequin MH, Dall'Agata A, Ten Cate FJ, et al. Paraplane analysis from precordial three-dimensional data sets for rapid and accurate quantification of left ventricular volume and function: a comparison with magnetic resonance imaging. *Am Heart J* 1999;137:134-43.
26. Schmidt MA, Ohazama CJ, Agyeman KO, Freidlin RZ, Jones M, Laurienzo JM, et al. Real-time three-dimensional echocardiography for measurement of left ventricular volumes. *Am J Cardiol* 1999;84:1434-9.
27. Belohlavek M, Tanabe K, Jakrapanichakul D, Breen JF, Seward JB. Rapid three-dimensional echocardiography: clinically feasible alternative for precise and accurate measurement of left ventricular volumes. *Circulation* 2001;103:2882-4.
28. Lee D, Fuisz AR, Fan PH, Hsu TL, Liu CP, Chiang HT. Real-time 3-dimensional echocardiographic evaluation of left ventricular volume: correlation with magnetic resonance imaging. A validation study. *J Am Soc Echocardiogr* 2001;14:1001-9.
29. Mannaerts HFJ, van der Heide JA, Kamp O, Papavassiliou T, Marcus JT, Beek A, et al. Quantification of left ventricular volumes and ejection fraction using freehand transthoracic three-dimensional echocardiography: comparison with magnetic resonance imaging. *J Am Soc Echocardiogr* 2003;16:101-9.
30. Kawai J, Tanabe K, Morioka S, Shiotani H. Rapid freehand scanning three-dimensional echocardiography: accurate measurement of left ventricular volumes and ejection fraction compared with quantitative gated scintigraphy. *J Am Soc Echocardiogr* 2003;16:110-5.
31. Kuhl HP, Schreckenberg M, Rulands D, Katoh M, Schafer W, Schummers G, et al. High-resolution transthoracic real-time echocardiography: quantitation of cardiac volumes and function using semi-automatic border detection and comparison with cardiac magnetic resonance imaging. *J Am Coll Cardiol* 2004;43:2083-90.
32. Arai K, Hozumi T, Matsumura Y, Sugioka K, Takemoto Y, Yamagishi H, et al. Accuracy of measurement of left ventricular volume and ejection fraction by new real-time three-dimensional echocardiography in patients with wall motion abnormalities secondary to myocardial infarction. *Am J Cardiol* 2004;94:552-8.
33. Jenkins C, Bricknell K, Hanekom L, Marwick TH. Reproducibility and accuracy of echocardiographic measurements of left ventricular parameters using real-time three-dimensional echocardiography. *J Am Coll Cardiol* 2004;44:878-86.
34. Corsi C, Lang RM, Veronesi F, Weinert L, Caiani EG, MacEneaney P, et al. Volumetric quantification of global and regional left ventricular function from real-time three-dimensional echocardiographic images. *Circulation* 2005;112:1161-70.
35. Gopal AS, Keller AM, Shen Z, Sapin PM, Schroeder KM, King DL Jr, et al. Three-dimensional echocardiography: in vitro and in vivo validation of left ventricular mass and comparison with conventional echocardiographic methods. *J Am Coll Cardiol* 1994;24:504-13.
36. Kühl H, Franke A, Frielingsdorf J, Flaskamp C, Krebs W, Flachskampf FA, et al. Determination of left ventricular mass and circumferential wall thickness by three-dimensional reconstruction: in vitro validation of a new method using a multiplane transesophageal transducer. *J Am Soc Echocardiogr* 1997;10:107-19.
37. Mor-Avi V, Sugeng L, Weinert L, MacEneaney P, Caiani EG, Koch R, et al. Fast measurement of left ventricular mass with real-time three-dimensional echocardiography: comparison with magnetic resonance imaging. *Circulation* 2004;110:1814-8.
38. Caiani EG, Coon P, Corsi C, Goonewardena S, Bardo D, Rafer P, et al. Dual triggering improves the accuracy of left ventricular volume measurements by contrast-enhanced real-time 3-dimensional echocardiography. *J Am Soc Echocardiogr* 2005;18:1292-8.
39. Sapin PM, Schroeder KD, Smith MD, DeMaria AN, King DL. Three-dimensional echocardiographic measurement of left ventricular volume in vitro: comparison with two-dimensional echocardiography and cineventriculography. *J Am Coll Cardiol* 1993;22:1530-7.
40. Leotta DF, Munt B, Bolson EL, Kraft C, Martin RW, Otto CM, et al. Quantitative three-dimensional echocardiography by rapid imaging from multiple transthoracic windows: in vitro validation and initial in vivo studies. *J Am Soc Echocardiogr* 1997;10:830-9.
41. Mele D, Teoli R, Cittanti C, Pisanisi G, Guardigli G, Levine RA, et al. Assessment of left ventricular volume and function by integration of simplified 3D echocardiography, tissue harmonic imaging and automated extraction of endocardial borders. *Int J Card Imaging* 2004;20:191-202.
42. Jacobs LD, Salgo IS, Goonewardena S, Weinert L, Coon P, Bardo D, et al. Rapid quantification of left ventricular volume from real-time three-dimensional echocardiographic data. *Eur Heart J* 2006;27:460-8.
43. Qin JX, Shiota T, Asher CR, Smedira NG, Shin JH, Agler DA, et al. Usefulness of real-time three-dimensional echocardiography for evaluation of myectomy in patients with hypertrophic cardiomyopathy. *Am J Cardiol* 2004;94:964-6.
44. Caiani EG, Corsi C, Sugeng L, MacEneaney P, Weinert L, Mor-Avi V, et al. Improved quantification of left ventricular mass based on endo- and epicardial surface detection using real-time three-dimensional echocardiography. *Heart* 2006;92:213-9.
45. Kapetanakis S, Kearney MT, Siva A, Gall N, Cooklin M, Monaghan MJ. Real-time three-dimensional echocardiography: a novel technique to quantify global left ventricular mechanical dyssynchrony. *Circulation* 2005;112:992-1000.
46. Matsumura Y, Hozumi T, Arai K, Sugioka K, Ujino K, Takemoto Y, et al. Non-invasive assessment of myocardial ischaemia using new real-time three-dimensional dobutamine stress echocardiography: comparison with conventional two-dimensional methods. *Eur Heart J* 2005;26:1625-32.
47. Ahmad M, Xie T, McCulloch M, Abreo G, Runge M. Real-time three-dimensional dobutamine stress echocardiography in assessment stress echocardiography in assessment of ischemia: comparison with two-dimensional dobutamine stress echocardiography. *J Am Coll Cardiol* 2001;37:1303-9.
48. Papavassiliou DP, Parks WJ, Hopkins KL, Fyfe DA. Three-dimensional echocardiographic measurement of right ventricular volume in children with congenital heart disease validated by magnetic resonance imaging. *J Am Soc Echocardiogr* 1998;11:770-7.

49. Fujimoto S, Mizuno R, Nakagawa Y, Dohi K, Nakano H. Estimation of the right ventricular volume and ejection fraction by transthoracic three-dimensional echocardiography: a validation study using magnetic resonance imaging. *Int J Card Imaging* 1998;14:385-90.
50. Vogel M, Gutberlet M, Dittrich S, Hosten N, Lange PE. Comparison of transthoracic three-dimensional echocardiography with magnetic resonance imaging in the assessment of right ventricular volume and mass. *Heart* 1997;78:127-30.
51. Jiang L, Siu SC, Handschumacher MD, Luis Guererro J, Vazquez de Prada JA, King ME, et al. Three-dimensional echocardiography: in vivo validation for right ventricular volume and function. *Circulation* 1994;89:2342-50.
52. Pini R, Giannazzo G, Di Bari M, Innocenti F, Rega L, Casolo G, et al. Transthoracic three-dimensional echocardiographic reconstruction of left and right ventricles: in vitro validation and comparison with magnetic resonance imaging. *Am Heart J* 1997;133:221-9.
53. Shiota T, Jones M, Chikada M, Fleishman CE, Castellucci JB, Cotter B, et al. Real-time three-dimensional echocardiography for determining right ventricular stroke volume in an animal model of chronic right ventricular volume overload. *Circulation* 1998;97:1897-900.
54. Ota T, Fleishman CE, Strub M, Stetten G, Ohazama CJ, von Ramm OT, et al. Real-time, three-dimensional echocardiography: feasibility of dynamic right ventricular volume measurement with saline contrast. *Am Heart J* 1999;137:958-66.
55. Hubka M, Mantei K, Bolson E, Coady K, Sheehan F. Measurement of right ventricular mass and volume by three-dimensional echocardiography by freehand scanning. *Comput Cardiol* 2000;27:703-706.
56. Nabeel H. Optimal assessment of right ventricular size and function by real-time 3D echocardiography: comparison to cardiac magnetic resonance imaging. *Circulation* 2004;110(suppl III):III-570 [abstract].
57. Jiang L, Levine RA, Weyman AE. Echocardiographic assessment of right ventricular volume and function. *Echocardiography* 1997;14:189-206.
58. Jiang L, Handschumacher MD, Hibberd MG, Siu SC, King ME, Weyman AE, et al. Three-dimensional echocardiographic reconstruction of right ventricular volume: in vitro comparison with two-dimensional methods. *J Am Soc Echocardiogr* 1994;7:150-8.
59. Poutanen T, Jokinen E, Sairanen H, Tikanoja T. Left atrial and left ventricular function in healthy children and young adults assessed by three-dimensional echocardiography. *Heart* 2003;89:544-9.
60. Khankirawatana B, Khankirawatana S, Lof J, Porter TR. Left atrial volume determination by three-dimensional echocardiography reconstruction: validation and application of a simplified technique. *J Am Soc Echocardiogr* 2002;15:1051-6.
61. Keller AM, Gopal AS, King DL. Left and right atrial volume by freehand three-dimensional echocardiography: in vivo validation using magnetic resonance imaging. *Eur J Echocardiogr* 2000;1:55-65.
62. Bauer F, Shiota T, White RD, Lever HM, Qin JX, Drinko J, et al. Determinant of left atrial dilation in patients with hypertrophic cardiomyopathy: a real-time 3-dimensional echocardiographic study. *J Am Soc Echocardiogr* 2004;17:968-75.
63. Jenkins C, Bricknell K, Marwick TH. Use of real-time three-dimensional echocardiography to measure left atrial volume: comparison with other echocardiographic techniques. *J Am Soc Echocardiogr* 2005;18:991-7.
64. Levine RA, Triulzi MO, Harrigan P, Weyman AE. The relationship of mitral annular shape to the diagnosis of mitral valve prolapse. *Circulation* 1987;75:756-67.
65. Freed LA, Levy D, Levine RA, Larson MG, Evans JC, Fuller DL, et al. Prevalence and clinical outcome of mitral valve prolapse. *N Engl J Med* 1999;341:1-7.
66. Levine RA, Hung J, Otsuji Y, Messas E, Liel-Cohen N, Nathan N, et al. Mechanistic insights into functional mitral regurgitation. *Curr Cardiol Rep* 2002;4:125-9.
67. Flachskampf FA, Chandra S, Gaddipati A, Levine RA, Weyman AE, Ameling W, et al. Analysis of shape and motion of the mitral annulus in subjects with and without cardiomyopathy by echocardiographic 3-dimensional reconstruction. *J Am Soc Echocardiogr* 2000;13:277-87.
68. Kwan J, Shiota T, Agler DA, Popovic ZB, Qin JX, Gillinov MA, et al. Geometric differences of the mitral apparatus between ischemic and dilated cardiomyopathy with significant mitral regurgitation: real-time three-dimensional echocardiography study. *Circulation* 2003;107:1135-40.
69. Qin JX, Shiota T, McCarthy PM, Firstenberg MS, Greenberg NL, Tsujino H, et al. Real-time three-dimensional echocardiographic study of left ventricular function after infarct exclusion surgery for ischemic cardiomyopathy. *Circulation* 2000;102(suppl III):III101-6.
70. Messas E, Guerrero JL, Handschumacher MD, Conrad C, Chow CM, Sullivan S, et al. Chordal cutting: a new therapeutic approach for ischemic mitral regurgitation. *Circulation* 2001;104:1958-63.
71. Hung J, Guerrero JL, Handschumacher MD, Supple G, Sullivan S, Levine RA. Reverse ventricular remodeling reduces ischemic mitral regurgitation: echo-guided device application in the beating heart. *Circulation* 2002;106:2594-600.
72. Langer F, Rodriguez F, Ortiz S, Cheng A, Nguyen TC, Zasio MK, et al. Subvalvular repair: the key to repairing ischemic mitral regurgitation? *Circulation* 2005;112(suppl I):I383-9.
73. Tibayan FA, Rodriguez F, Langer F, Zasio MK, Bailey L, Liang D, et al. Annular or subvalvular approach to chronic ischemic mitral regurgitation? *J Thorac Cardiovasc Surg* 2005;129:1266-75.
74. Inoue M, McCarthy PM, Popovic ZB, Doi K, Schenk S, Neme H, et al. The Coapsys device to treat functional mitral regurgitation: in vivo long-term canine study. *J Thorac Cardiovasc Surg* 2004;127:1068-76.
75. Schwalm SA, Sugeng L, Raman J, Jeevanandam V, Lang RM. Assessment of mitral valve leaflet perforation as a result of infective endocarditis by 3-dimensional real-time echocardiography. *J Am Soc Echocardiogr* 2004;17:919-22.
76. Cheng TO, Xie MX, Wang XF, Li ZA, Hu G. Evaluation of mitral valve prolapse by four-dimensional echocardiography. *Am Heart J* 1997;133:120-9.
77. Ahmed S, Nanda NC, Miller AP, Nekkanti R, Yousif AM, Pacifico AD, et al. Usefulness of transesophageal three-dimensional echocardiography in the identification of individual segment/scallop prolapse of the mitral valve. *Echocardiography* 2003;20:203-9.
78. Acar P, Laskari C, Rhodes J, Pandian N, Warner K, Marx G. Three-dimensional echocardiographic analysis of valve anatomy as a determinant of mitral regurgitation after surgery for atrioventricular septal defects. *Am J Cardiol* 1999;83:745-9.

79. Barrea C, Levasseur S, Roman K, Nii M, Coles JG, Williams WG, et al. Three-dimensional echocardiography improves the understanding of left atrioventricular valve morphology and function in atrioventricular septal defects undergoing patch augmentation. *J Thorac Cardiovasc Surg* 2005;129:746-53.
80. Espinola-Zavaleta N, Vargas-Barron J, Keirns C, Rivera G, Romero-Cardenas A, Roldan J, et al. Three-dimensional echocardiography in congenital malformations of the mitral valve. *J Am Soc Echocardiogr* 2002;15:468-72.
81. Chauvel C, Bogino E, Clerc P, Fernandez G, Vernhet JC, Becat A, et al. Usefulness of three-dimensional echocardiography for the evaluation of mitral valve prolapse: an intraoperative study. *J Heart Valve Dis* 2000;9:341-9.
82. Delabays A, Jeanrenaud X, Chassot PG, Von Segesser LK, Kappenberger L. Localization and quantification of mitral valve prolapse using three-dimensional echocardiography. *Eur J Echocardiogr* 2004;5:422-9.
83. Macnab A, Jenkins NP, Bridgewater BJ, Hooper TL, Greenhalgh DL, Patrick MR, et al. Three-dimensional echocardiography is superior to multiplane transoesophageal echo in the assessment of regurgitant mitral valve morphology. *Eur J Echocardiogr* 2004;5:212-22.
84. Sitges M, Jones M, Shiota T, Qin JX, Tsujino H, Bauer F, et al. Real-time three-dimensional color Doppler evaluation of the flow convergence zone for quantification of mitral regurgitation: validation experimental animal study and initial clinical experience. *J Am Soc Echocardiogr* 2003;16:38-45.
85. Iwakura K, Ito H, Kawano S, Okamura A, Kurotobi T, Date M, et al. Comparison of orifice area by transthoracic three-dimensional Doppler echocardiography versus proximal isovelocity surface area (PISA) method for assessment of mitral regurgitation. *Am J Cardiol* 2006;97:1630-7.
86. Gilon D, Cape EG, Handschumacher MD, Jiang L, Sears C, Solheim J, et al. Insights from three-dimensional echocardiographic laser stereolithography: effect of leaflet funnel geometry on the coefficient of orifice contraction, pressure loss, and the Gorlin formula in mitral stenosis. *Circulation* 1996;94:452-9.
87. Cheng TO. Assessment of mitral valve volume by quantitative three-dimensional echocardiography in patients with rheumatic mitral valve stenosis. *Clin Cardiol* 1998;21:869-70.
88. Binder TM, Rosenhek R, Porenta G, Maurer G, Baumgartner H. Improved assessment of mitral valve stenosis by volumetric real-time three-dimensional echocardiography. *J Am Coll Cardiol* 2000;36:1355-61.
89. Xie MX, Wang XF, Cheng TO, Wang J, Lu Q. Comparison of accuracy of mitral valve area in mitral stenosis by real-time, three-dimensional echocardiography versus two-dimensional echocardiography versus Doppler pressure half time. *Am J Cardiol* 2005;95:1496-9.
90. Zamorano J, Cordeiro P, Sugeng L, Perez de Isla L, Weinert L, Macaya C, et al. Real-time three-dimensional echocardiography for rheumatic mitral valve stenosis evaluation: an accurate and novel approach. *J Am Coll Cardiol* 2004;43:2091-6.
91. Sebag IA, Morgan JG, Handschumacher MD, Marshall JE, Nesta F, Hung J, et al. Usefulness of three-dimensionally guided assessment of mitral stenosis using matrix-array ultrasound. *Am J Cardiol* 2005;96:1151-6.
92. Mannaerts HF, Kamp O, Visser CA. Should mitral valve area assessment in patients with mitral stenosis be based on anatomical or on functional evaluation? A plea for 3D echocardiography as the new clinical standard. *Eur Heart J* 2004;25:2073-4.
93. Zamorano J, Perez de Isla L, Sugeng L, Cordeiro P, Rodrigo JL, Almeria C, et al. Non-invasive assessment of mitral valve area during percutaneous balloon mitral valvuloplasty: role of real-time 3D echocardiography. *Eur Heart J* 2004;25:2086-91.
94. Applebaum RM, Kasliwal RR, Kanojia A, Seth A, Bhandari S, Trehan N, et al. Utility of three-dimensional echocardiography during balloon mitral valvuloplasty. *J Am Coll Cardiol* 1998;32:1405-9.
95. Ge S, Warner JG Jr, Abraham TP, Kon ND, Brooker RF, Nomeir AM, et al. Three-dimensional surface area of the aortic valve orifice by three-dimensional echocardiography: clinical validation of a novel index for assessment of aortic stenosis. *Am Heart J* 1998;136:1042-50.
96. Handke M, Jahnke C, Heinrichs G, Schlegel J, Vos C, Schmitt D, et al. New three-dimensional echocardiographic system using digital radiofrequency data: visualization and quantitative analysis of aortic valve dynamics with high resolution: methods, feasibility, and initial clinical experience. *Circulation* 2003;107:2876-9.
97. Kasprzak JD, Nosir YF, Dall'Agata A, Elhendy A, Taams M, Ten Cate FJ, et al. Quantification of the aortic valve area in three-dimensional echocardiographic data sets: analysis of orifice overestimation resulting from suboptimal cut-plane selection. *Am Heart J* 1998;135:995-1003.
98. Menzel T, Mohr-Kahaly S, Kolsch B, Kupferwasser I, Kopp H, Spiecker M, et al. Quantitative assessment of aortic stenosis by three-dimensional echocardiography. *J Am Soc Echocardiogr* 1997;10:215-23.
99. Nanda NC, Roychoudhury D, Chung SM, Kim KS, Ostlund V, Klas B. Quantitative assessment of normal and stenotic aortic valve using transesophageal three-dimensional echocardiography. *Echocardiography* 1994;11:617-25.
100. Haugen BO, Berg S, Brecke KM, Torp H, Stordahl SA, Skaerpe T, et al. Blood flow velocity profiles in the aortic annulus: a 3-dimensional freehand color flow Doppler imaging study. *J Am Soc Echocardiogr* 2002;15:328-33.
101. Mehwald PS, Rusk RA, Mori Y, Li XN, Zetts AD, Jones M, et al. A validation study of aortic stroke volume using dynamic 4-dimensional color Doppler: an in vivo study. *J Am Soc Echocardiogr* 2002;15:1045-50.
102. Acar P, Jones M, Shiota T, Masani N, Delabays A, Yamada I, et al. Quantitative assessment of chronic aortic regurgitation with 3-dimensional echocardiographic reconstruction: comparison with electromagnetic flowmeter measurements. *J Am Soc Echocardiogr* 1999;12:138-48.
103. Shiota T, Jones M, Tsujino H, Qin JX, Zetts AD, Greenberg NL, et al. Quantitative analysis of aortic regurgitation: real-time 3-dimensional and 2-dimensional color Doppler echocardiographic method: a clinical and a chronic animal study. *J Am Soc Echocardiogr* 2002;15:966-71.
104. Acar P, Aggoun Y, Saliba Z, Sidi D, Kachaner J. Effect of balloon dilatation on aortic stenosis assessed by 3-dimensional echocardiographic reconstruction. *Circulation* 1999;99:2598-9.
105. Dall'Agata A, Cromme-Dijkhuis AH, Meijboom FJ, Spitaels SE, McGhie JS, Roelandt JR, et al. Use of three-dimensional echocardiography for analysis of outflow obstruction in congenital heart disease. *Am J Cardiol* 1999;83:921-5.
106. Ge S, Warner JG Jr, Fowle KM, Kon ND, Brooker RF, Nomeir AM, et al. Morphology and dynamic change of discrete subaortic stenosis can be imaged and quantified with

- three-dimensional transesophageal echocardiography. *J Am Soc Echocardiogr* 1997;10:713-6.
107. Yamamoto Y, Shiraishi I, Yamagishi M, Hamaoka K. Mitral valve injury during balloon valvuloplasty for an infant with severe aortic stenosis: spatial evaluation using three-dimensional echocardiography. *Pediatr Cardiol* 2003;24:300-3.
108. Faletta F, La Marchesina U, Bragato R, De Chiara F. Three-dimensional transthoracic echocardiography images of tricuspid stenosis. *Heart* 2005;91:499.
109. Schnabel R, Khaw AV, von Bardeleben RS, Strasser C, Kramm T, Meyer J, et al. Assessment of the tricuspid valve morphology by transthoracic real-time 3D echocardiography. *Echocardiography* 2005;22:15-23.
110. Trocino G, Salustri A, Roelandt JR, Ansink T, van Herwerden L. Three-dimensional echocardiography of a flail tricuspid valve. *J Am Soc Echocardiogr* 1996;9:91-3.
111. Vogel M, Ho SY, Lincoln C, Anderson RH. Transthoracic three-dimensional echocardiography for the assessment of straddling tricuspid or mitral valves. *Cardiol Young* 2000;10:603-9.
112. Nekkanti R, Nanda NC, Ahmed S, Huang WY, Pacifico AD. Transesophageal three-dimensional echocardiographic demonstration of clefts in the anterior tricuspid valve leaflet. *Am J Geriatr Cardiol* 2002;11:329-30.
113. Citro R, Salustri A, Gregorio G. Images in cardiovascular medicine: three-dimensional reconstruction of pulmonary valve endocarditis. *Ital Heart J* 2001;2:938-9.
114. Wanitkun S, Rusk RA, Sahn DJ. Assessment of pulmonary artery stenosis using freehand "flock of birds" digital color three-dimensional echocardiographic reconstruction. *J Med Assoc Thai* 2002;85(suppl 4):S1259-65.
115. Marx GR, Sherwood MC. Three-dimensional echocardiography in congenital heart disease: a continuum of unfulfilled promises? No. A presently clinically applicable technology with an important future? Yes. *Pediatr Cardiol* 2002;23:266-85.
116. Balestrini L, Fleishman C, Lanzoni L, Kisslo J, Resai Bengur A, et al. Real-time 3-dimensional echocardiography evaluation of congenital heart disease. *J Am Soc Echocardiogr* 2000;13:171-6.
117. Sinha A, Nanda NC, Misra V, Khanna D, Dod HS, Vengala S, et al. Live three-dimensional transthoracic echocardiographic assessment of transcatheter closure of atrial septal defect and patent foramen ovale. *Echocardiography* 2004;21:749-53.
118. Dall'Agata A, Cromme-Dijkhuis AH, Meijboom FJ, McGhie JS, Bol-Raap G, Nosir YF, et al. Three-dimensional echocardiography enhances the assessment of ventricular septal defect. *Am J Cardiol* 1999;83:1576-9, A8.
119. Ishii M, Hashino K, Eto G, Tsutsumi T, Himeno W, Sugahara Y, et al. Quantitative assessment of severity of ventricular septal defect by three-dimensional reconstruction of color Doppler-imaged vena contracta and flow convergence region. *Circulation* 2001;103:664-9.
120. Nascimento R, Pereira D, Freitas A, Pereira E, Mendonca I, Dinis M. Comparison of left ventricular ejection fraction in congenital heart disease by visual versus algorithmic determination. *Am J Cardiol* 1997;80:1331-5.
121. Abd El Rahman MY, Abdul-Khaliq H, Vogel M, Alexi-Meskishvili V, Gutberlet M, Lange PE. Relation between right ventricular enlargement, QRS duration, and right ventricular function in patients with tetralogy of Fallot and pulmonary regurgitation after surgical repair. *Heart* 2000;84:416-20.
122. Heusch A, Rubo J, Krogmann ON, Bourgeois M. Volumetric analysis of the right ventricle in children with congenital heart defects: comparison of biplane angiography and transthoracic 3-dimensional echocardiography. *Cardiol Young* 1999;9:577-84.
123. Abraham TP, Warner JG Jr, Kon ND, Lantz PE, Fowle KM, Brooker RF, et al. Feasibility, accuracy, and incremental value of intraoperative three-dimensional transesophageal echocardiography in valve surgery. *Am J Cardiol* 1997;80:1577-82.
124. De Castro S, Salandin V, Cartoni D, Valfre C, Salvador L, Magni G, et al. Qualitative and quantitative evaluation of mitral valve morphology by intraoperative volume-rendered three-dimensional echocardiography. *J Heart Valve Dis* 2002;11:173-80.
125. George SJ, Al-Ruzzeh S, Amrani M. Mitral annulus distortion during beating heart surgery: a potential cause for hemodynamic disturbance. A three-dimensional echocardiography reconstruction study. *Ann Thorac Surg* 2002;73:1424-30.
126. Miller AP, Nanda NC, Aaluri S, Mukhtar O, Nekkanti R, Thimmarayappa MV, et al. Three-dimensional transesophageal echocardiographic demonstration of anatomical defects in AV septal defect patients presenting for reoperation. *Echocardiography* 2003;20:105-9.
127. Nash PJ, Agler DA, Shin JH, Qin J, Smedira NG, Lever HM, et al. Images in cardiovascular medicine: epicardial real-time 3-dimensional echocardiography during septal myectomy for obstructive hypertrophic cardiomyopathy. *Circulation* 2003;108:e54-5.
128. Suematsu Y, Takamoto S, Kaneko Y, Ohtsuka T, Takayama H, Kotsuka Y, et al. Beating atrial septal defect closure monitored by epicardial real-time three-dimensional echocardiography without cardiopulmonary bypass. *Circulation* 2003;107:785-90.
129. Yao J, Takeuchi M, Teupe C, Sheahan M, Connolly R, Walovitch RC, et al. Evaluation of a new ultrasound contrast agent (AI-700) using two-dimensional and three-dimensional imaging during acute ischemia. *J Am Soc Echocardiogr* 2002;15:686-94.
130. Yao J, De Castro S, Delabays A, Masani N, Udelson JE, Pandian NG. Bulls-eye display and quantitation of myocardial perfusion defects using three-dimensional contrast echocardiography. *Echocardiography* 2001;18:581-8.
131. Camarano G, Jones M, Freidlin RZ, Panza JA. Quantitative assessment of left ventricular perfusion defects using real-time three-dimensional myocardial contrast echocardiography. *J Am Soc Echocardiogr* 2002;15:206-13.
132. Toledo E, Lang RM, Collins KA, Lammertin G, Williams U, Weinert L, et al. Imaging and quantification of myocardial perfusion using real-time three-dimensional echocardiography. *J Am Coll Cardiol* 2006;47:146-54.
133. Takeuchi M, Otani S, Weihert L, Spencer KT, Lang RM. Comparison of contrast-enhanced real-time live 3D dobutamine stress echocardiography with contrast 2D echocardiography for detecting stress-induced wall motion abnormality. *J Am Soc Echocardiogr* 2006;19:294-9.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found, in the online version, at 10.1016/j.echo.2007.01.010.