Real-Time 3-Dimensional Echocardiography
An Integral Component of the Routine Echocardiographic Examination in Adult Patients?

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One of the most significant developments of the last decade in ultrasound imaging of the heart was the evolution of 3-dimensional (3D) imaging from slow and labor-intense offline reconstruction to real-time volumetric imaging. This imaging modality provides valuable clinical information that empowers echocardiographers with new levels of confidence in the diagnosis of heart disease. We have previously described the technological milestones in the development of real-time 3D echocardiographic (RT3DE) imaging and its major advantages over conventional 2-dimensional echocardiography (2DE) and reviewed the published literature that supported the use of this new methodology in clinical practice. Since 2006, the growing availability of RT3DE technology, its ease of use, and its multiple attractive features have sparked significant interest in the research community, resulting in a large number of publications, most of which have endorsed RT3DE imaging for clinical use by demonstrating its unique capabilities in different scenarios. In parallel, the clinical acceptance of this new tool has broadened significantly. The most recent clinically significant addition is matrix-array transesophageal echocardiography (TEE), which provides images of unprecedented quality that aid surgeons and interventional cardiologists in planning and guiding procedures and evaluating their outcomes.

The purpose of the present article is to review the most recent RT3DE literature and provide readers with an update on the latest developments and the current status of this noninvasive imaging tool. Because different potential applications of RT3DE imaging have been explored to various extents, they are described here separately, and each is discussed with an emphasis on the scientifically established facts, along with the known stumbling blocks and difficulties.

Quantification of LV Volumes and Function
A firmly established advantage of 3D imaging over cross-sectional slices of the heart is the improvement in the accuracy of the evaluation of left ventricular (LV) volumes and ejection fraction (EF) by eliminating the need for geometric modeling, which is inaccurate in the presence of aneurysms, asymmetrical ventricles, or wall motion abnormalities, and the errors caused by foreshortened views even in symmetrical ventricles. The value of RT3DE imaging in this context has been demonstrated by multiple studies that compared RT3DE volume measurements with widely accepted reference techniques, including radionuclide ventriculography and cardiac magnetic resonance (CMR). These studies and others have demonstrated higher levels of agreement between the RT3DE approach and the respective reference technique compared with conventional 2DE methodology. Additionally, RT3DE measurements were found to be more reproducible than 2DE and, in some studies, even as reproducible as CMR. Interestingly, in a recent study in patients after myocardial infarction (MI), RT3DE-derived LV volumes were more accurate and more reproducible than those obtained with 201Tl-gated single-photon emission computed tomography compared with a CMR reference.

The improved accuracy and reproducibility of RT3DE-based LV volume and EF measurements are of vital importance because clinical decision making relies heavily on these measurements in multiple clinical scenarios. In addition, these findings translate into smaller numbers of patients required to test a hypothesis, promising to result in significant savings in future studies aimed at assessing the effects of new drugs. Indeed, this trend was demonstrated by a recent follow-up study in patients after MI in which, similar to CMR, serial RT3DE measurements had low test-retest variability and were thus able to detect with confidence subtle changes in LV volumes over time that were not detectable by 2DE. Similar findings were described in another study aimed at risk stratification in patients after MI and patients with heart failure. However, despite the high correlation with the CMR reference values and the high reproducibility, several studies have reported that RT3DE-derived LV volumes were significantly underestimated.

Different possible explanations have been offered that focused mostly on intertechnique acquisition and analysis differences, but none of the studies were able to conclusively identify the main sources of error. Importantly, the degree of underestimation varied widely between these single-center studies from a few milliliters to considerable biases as high as 30% of the measured values. One possible explanation for the...
variable degrees of underestimation is that RT3DE data sets were analyzed differently by different investigators. Indeed, 2 approaches are commonly used for LV quantification from RT3DE data sets (Figure 1). One approach is based on selecting from a pyramidal RT3DE data set 2 anatomically correct nonforeshortened 2D views of which LV volume is calculated using a biplane approximation,\textsuperscript{7,17} the same as that used with 2D imaging (Figure 1, left). Although this 3D-guided biplane technique can minimize LV foreshortening, it still relies on geometric modeling to calculate volumes and is thus likely to be inaccurate in distorted ventricles. In an attempt to minimize this problem, investigators used larger number of planes to interpolate LV endocardial surface\textsuperscript{16,18} with partial success. Another approach to quantify LV volumes from RT3DE data sets, which was recently implemented in commercial analysis software, is based on semi-automated detection of LV endocardial surface\textsuperscript{16,18} with partial success. Another approach to quantify LV volumes from RT3DE data sets, which was recently implemented in commercial analysis software, is based on semi-automated detection of LV endocardial surface\textsuperscript{16,18} with partial success. Another approach to quantify LV volumes from RT3DE data sets, which was recently implemented in commercial analysis software, is based on semi-automated detection of LV endocardial surface\textsuperscript{16,18} with partial success.

Nevertheless, even direct volumetric analysis, which is the more accurate of the 2 techniques, was found to significantly underestimate LV volumes, threatening to undermine the usefulness of RT3DE evaluation of LV size and function. To investigate this issue in depth, we recently conducted a multicenter study designed to identify the potential sources of error and to determine their relative contributions to the underestimation of RT3DE-derived LV volumes.\textsuperscript{20} RT3DE and CMR reference data obtained in a large group of patients with a wide range of LV function were used to test several hypotheses that allowed us to resolve this controversy. RT3DE images were analyzed at 5 sites by experienced echocardiography investigators who had received various levels of instruction with prototype software for direct volumetric analysis (Figure 2, right) without being informed that the level of experience was one of the variables in the study design. Despite the high correlations with the CMR reference values at all sites (mostly >0.90), the biases progressively increased with decreasing level of specific experience, reaching 2 to 3 times those noted by the most experienced site.

In the search for additional sources of error, CMR images were reformatted into 3D data sets and analyzed with the same software used for analysis of RT3DE date sets. These measurements resulted in virtually the same volume values and thus ruled out analysis-related differences as a significant source of error. Thereafter, several in vitro experiments were performed, including volume measurements in a phantom, which revealed that a barely visible 1-mm difference in the position of the endocardial surface resulted in a 10% difference in volume (Figure 3, top). Subsequent measurements in water-filled latex balloons showed that tracing along what appeared to be the water-latex interface resulted in volume measurements that were \textsuperscript{10} below the true volume, whereas tracing further out, along the middle of the latex layer, yielded accurate volumes (Figure 3, bottom), even without the complicating effects of the papillary muscles and endocardial trabeculae. From these findings and the fact that biases in measured LV volumes in humans were related to image quality,\textsuperscript{6} we hypothesized that the spatial resolution of RT3DE images is not sufficiently high to differentiate between myocardial tissue and trabeculae (Figure 4, top) and that the more experienced investigators in the multicenter...
study traced the endocardium beyond the visible interface to compensate for this limitation, which resulted in larger LV volumes. To test this hypothesis, CMR images were reanalyzed with trabeculae excluded from the LV cavity (Figure 4, bottom). The use of these nonconventional reference values essentially eliminated the bias.

The results of this multicenter study underscored the need for unified guidelines for tracing LV endocardial boundary to obtain RT3DE measurements of LV volumes comparable to the current standard reference CMR technique. Moreover, this study demonstrated that this reference technique relies on the user’s decision about which short-axis slices (basal and apical) should be included in LV volume calculation. This decision is subjective, depends on the choice of criteria, and significantly affects the reference values. In this regard, volumetric analysis based on detection of endocardial surface avoids these limitations and thus is more reproducible and potentially more accurate, assuming that the endocardial boundary can be well visualized, including clear differentiation between the myocardium and the trabeculae.

In this respect, multiplane 2D imaging or 3D-guided triplane analysis may provide a practical solution for LV volume measurements in patients with suboptimal endocardial visualization in 3D data sets, which may be particularly useful in the setting of a busy clinical laboratory. This approach offers superior image quality because of improved line density while preserving the benefits of knowing the precise location and relationship of the image planes with respect to each other (Figure 5).

**RT3DE Evaluation of LV Mass**

As opposed to LV volume measurements, which require accurate identification of the endocardial boundaries, LV mass measurements rely on epicardial visualization, which is known to be even more challenging. This difficulty is in addition to inaccurate modeling and foreshortening. Nevertheless, in our initial studies aimed at RT3DE evaluation of LV mass by either the 3D-guided biplane technique or the volumetric analysis, the accuracy and reproducibility of RT3DE estimates were higher than those of the traditional M-mode and 2D techniques. More recently, these observations were confirmed without significant differences between techniques in a large group of patients with concentric LV hypertrophy. Moreover, volumetric measurements of LV mass were found to correlate highly with CMR reference values in patients with wall motion abnormalities and in patients with abnormally shaped ventricles secondary to congenital heart disease. Although the former study described a considerable negative bias, the latter reported only minimal biases. Similar to the inconsistencies with LV volume measurements, these differences are likely to be due to differences in strategies for identifying and tracing the endocardial and epicardial boundaries.

**RT3DE Assessment of Regional Wall Motion**

Furthermore, the ability of RT3DE imaging to almost simultaneously capture the entire heart into a data set that contains the complete dynamic information on LV chamber, from
which the ventricle can be viewed in any arbitrary plane, suggested that RT3DE data sets are suitable for simultaneous analysis of regional wall motion in all LV segments. In a recent study, RT3DE-derived regional EF was validated against a CMR reference, and the feasibility of its use as an index of regional LV function was tested for objective detection of wall motion abnormalities. The methodology described in this study indicated that RT3DE-based analysis of regional LV function may also be potentially useful in different clinical applications, including stress testing and guidance of resynchronization therapy. Indeed, the fast volumetric imaging of the entire heart has indicated its potential usefulness in the context of exercise stress testing in which speed of acquisition of multiple views is crucial. Another study highlighted the advantages of using RT3DE imaging over 2DE during dobutamine stress testing (Figure 6). A more recent study demonstrated that RT3DE data sets contained sufficient information for the interpretation of dobutamine stress tests, which allowed accurate diagnosis of myocardial ischemia compared with single-photon emission computed tomography myocardial perfusion imaging, which was similar to conventional 2D methodology. However, an important advantage of the RT3DE approach, in addition to faster acquisition, was its ability to extract offline multiple short- and long-axis views of the ventricle that can help in determining the extent of wall motion abnormality and in ruling out artifacts frequently noted in standard imaging planes caused by limited endocardial visualization. Another study demonstrated high levels of agreement with 2DE-based wall motion scores.

Contrast-Enhanced RT3DE Imaging

Recently, LV triplane imaging with contrast enhancement was reported to be accurate and reproducible for the calculation of LV EF compared with CMR imaging. Although numerous previous studies have demonstrated contrast-related improvement in endocardial visualization on 2DE images, this does not automatically mean that similar improvements would be seen on RT3DE images. A probable reason is the increased microbubble destruction caused by an increase in ultrasound energy that is delivered into the entire scan volume during RT3DE imaging rather than into a thin slice, as in the case of 2D imaging. This problem can be minimized either by selective dual triggering at end systole and end diastole or by using low mechanical indexes with continuous harmonic imaging. One may speculate that alternative contrast-targeted imaging modes such as pulse inversion and power modulation may be useful in this context, but this remains to be tested in future studies.

Contrast enhancement was found not only to improve the accuracy and reproducibility of LV volume measurements in
patients with poor image quality but also to enhance the assessment of regional wall motion from RT3DE data sets. We found that with the use of selective dual triggering to minimize bubble destruction by ultrasound energy, contrast enhancement increased the accuracy of RT3DE-based analysis of regional LV function against CMR reference and its reproducibility to levels similar to those noted in patients with optimal image quality.33 Several other studies that used contrast enhancement with dobutamine stress have demonstrated that it improved segmental endocardial visualization34 and resulted in high levels of agreement with 2DE-based wall motion scores.35 Although the results of these studies may have important implications on the use of contrast for volumetric quantification of both global and regional LV function, no studies published to date have demonstrated the ability of contrast enhancement to improve the diagnostic accuracy of stress testing. Such studies are necessary for contrast-enhanced RT3DE imaging to become part of routine pharmacological stress testing.

LV Shape Analysis
In patients after MI or patients undergoing cardiac resynchronization therapy, evaluation of LV remodeling has traditionally been performed with 2DE-derived LV volumes. It is well known, however, that as LV function worsens, ventricular size increases and the ventricle becomes more globular than elliptical. Until now, these changes have been assessed with a 2D-derived sphericity index, which does not reflect discrete changes in regional LV shape. It has been postulated that RT3DE-based characterization of the LV endocardium may better reflect global and regional LV shape. Mannaerts and colleagues36 described a new 3DE-based sphericity index that was shown to be an earlier and more accurate predictor of LV remodeling in patients after an acute MI than other clinical ECG and echocardiographic parameters. The development of software for dynamic LV shape analysis from RT3DE data sets (Figure 7) promises to make the assessment of LV remodeling with this approach clinically useful.37

RT3DE Evaluation of LV Dyssynchrony
Tissue Doppler imaging (TDI) is currently considered the standard technique for selecting patients for cardiac resynchronization therapy because of its ability to quantify intraventricular dyssynchrony. Despite the excellent temporal resolution of TDI, this methodology has several limitations, including an inability to assess multiple myocardial segments in different planes simultaneously, an angle dependency that translates into the evaluation of the timing of longitudinal motion only, and an inability to reliably depict wall motion in the apical segments. In addition, despite the wealth of TDI-based dyssynchrony research, different investigators have used different approaches to quantify dyssynchrony, resulting in inconsistent conclusions. Although there is currently no accepted reference standard technique for LV dyssynchrony measurements, no TDI-based technique has been proved to reliably measure dyssynchrony in large clinical trials. Accordingly, other techniques for the quantification of intraventricular dyssynchrony are required.

With its capability to quickly capture the 3D dynamics of the entire left ventricle, including the timing of regional wall motion independent of its direction, RT3DE imaging has emerged as an alternative approach for the quantification of LV dyssynchrony.38 Most RT3DE dyssynchrony studies have used the SD of the regional ejection times (interval between the R wave and minimum systolic LV volume) as an index of
dyssynchrony. Recent attempts to compare this index against TDI have resulted in disparate results that ranged from fair intertechnique correlation to poor agreement, which was explained by the angle dependency of TDI and by the fact that these 2 techniques measure different parameters. RT3DE assessment of LV dyssynchrony has the potential advantage of measuring the timing of the longitudinal, radial, and circumferential motion as opposed to the longitudinal motion only, which is measured by TDI. Of note, the RT3DE dyssynchrony index was recently compared against phase analysis of gated single-photon emission computed tomography images and showed good intertechnique correlation.

RT3DE was used in patients with heart failure, low EF, and wide QRS complex to predict the acute response to cardiac resynchronization therapy. It was shown that approximately two thirds of patients with high RT3DE-derived dyssynchrony index responded to biventricular pacing with a decrease in dyssynchrony and acute improvement in global LV function (Figure 8, left). Recent studies have shown a direct relationship between overall LV performance and synchronicity. In these studies, RT3DE assessment of LV dyssynchrony identified patients with heart failure, low EFs, and asynchronous LV contraction who could theoretically benefit from cardiac resynchronization therapy but would not be considered candidates because of their narrow QRS duration. Interestingly, contrary to expectations, biventricular pacing did not result in significant long-term benefits in this subgroup of patients with narrow QRS and increased intraventricular dyssynchrony as reflected by tissue Doppler parameters. One explanation for the failure of cardiac resynchronization therapy to improve long-term outcomes in approximately one third of the patients selected on the basis of established criteria could be that placement of the pacing electrodes was not optimized because of the lack of sufficiently accurate tools to guide the pacing catheter to the site of latest activation. RT3DE imaging also may prove useful in this regard because RT3DE-based mapping of the distribution of regional contraction times (Figure 8, right) shows which LV myocardial segments are the latest to contract. One of the emerging technological advancements in this context is the fusion of RT3DE-derived dyssynchrony maps with coronary vein computed tomography to guide the placement of the pacing catheter.

**Figure 8.** Assessment of the improvement in synchrony of LV contraction with pacing. Regional volume-time curves (left) obtained in a patient with LV dyssynchrony without (top) and with (bottom) biventricular pacing. Endocardial surfaces reconstructed from each data set are shown with segmentation and color coding according to regional time to end ejection (middle) along with the bull’s-eye representation of the same data (right). Note the changes in colors with pacing reflecting the effects of resynchronization therapy in this parametric display.

**RT3DE Evaluation of Right Ventricular Volumes and Function**

The ability to measure right ventricular (RV) volumes and function accurately is important in the management of congenital heart disease and primary pulmonary hypertension. Because of the complex geometrical crescent shape of this chamber, the estimation of RV volumes based on geometric modeling from 2D images has been extremely challenging. As a result, in clinical practice, tricuspid annular plane systolic excursion has traditionally been used as a surrogate for RV performance. Theoretically, the intrinsic ability of RT3DE imaging to directly measure RV volumes without the need for geometric modeling could be expected to result in improved accuracy and reproducibility compared with traditional 2DE measurements. Surprisingly however, the first study to compare these 2 techniques side by side against a
CMR reference found that RT3DE measurements offered no significant advantage. A subsequent RT3DE study reported only slightly better levels of agreement with CMR. Similar to LV volume measurements, there are several ways to explain these findings, but the major sources of errors, which may be different for the 2 chambers, have not yet been identified for the right ventricle. Indeed, RV volume measurements were affected by multiple factors, including gain settings and thickness and orientation of disks used by the disk summation technique.

Another potential source of intermodality discordance is that the complex 3D shape of the right ventricle may affect the ability of CMR imaging to accurately quantify RV volumes. In particular, the identification of RV boundaries near the RV outflow tract may be quite challenging from short-axis slices perpendicular to the long axis of the left ventricle, which is the standard for CMR image acquisition. It is likely that a different acquisition strategy is necessary for accurate RV volume measurements. Indeed, 2 more recent studies using new software designed specifically for volumetric analysis of the right ventricle from RT3DE data sets (Figure 9A) and from a combination of short- and rotated long-axis CMR views found high levels of agreement between the 2 techniques. Moreover, the RT3DE measurements were both more accurate and more reproducible than several 2DE-based measurements.

**RT3DE Evaluation of Atrial Volumes**

Left atrial (LA) enlargement is a marker of both the severity and long-term elevation of LA pressures. It is known to be associated with increased incidence of atrial fibrillation, ischemic stroke, and poor cardiovascular outcomes, including increased risks of overall mortality in patients after MI. When LA size is measured, volume determinations should be preferred over linear dimensions because they allow accurate assessment of the asymmetrical remodeling of the left atrium. Consequently, LA volume calculations from 2D cut planes are recommended as a standard technique instead of linear measurements. However, both the proposed area-length technique and the biplane method of disks are dependent on the selection of the location and direction of the LA minor axis, the ability to clearly visualize and accurately trace the LA boundaries, and geometric modeling. With its independence of geometrical assumptions, RT3DE imaging has the potential to provide more accurate LA volume measurements (Figure 9B). However, there is no consensus on the specific methods that should be used for data acquisition and analysis aimed at LA quantification.

Until recently, most studies have compared RT3DE measurements of LA volume against traditional 2DE measurements and reported good agreement between these techniques. Although these results are of limited value in the absence of an independent reference technique, these studies demonstrated several findings that support the superiority of RT3DE imaging for LA volume measurements. First, RT3DE-derived LA volume was more sensitive to volume changes than the 2DE indexes. Second, it was demonstrated for the first time that RT3DE-derived maximum LA volume is a major predictor of cardiac events in patients with severe LV dysfunction. Similar to previous 2DE studies, a progressive increase in RT3DE-derived maximum LA volume directly correlated with age, LV mass, and LV diastolic function and inversely correlated with LV systolic function. Recently, RT3DE imaging was shown to be useful for the evaluation of the LA appendage with and without thrombi.

The feasibility of RT3DE evaluation of right atrial (RA) volume and its superiority over 2DE measurements also were recently demonstrated. Nevertheless, RT3DE measurements of either LA or RA volumes have yet to be validated against an independent reference technique such as CMR. Importantly, these studies require CMR acquisition to be specifically targeted to LA or RA quantification, including appropriate imaging planes and sufficient number of slices, to provide accurate CMR reference values.

**Real-Time 3D TEE**

Three-dimensional echocardiography provides unique visualization and better understanding of the relationship between cardiac structures than 2D imaging, as well as accurate measurements of valvular and ventricular function. Although transthoracic 3D imaging is currently performed in real time with matrix-array transducers, transesophageal 3D imaging has, until recently, relied on lengthy sequential multiplane acquisition gated to ECG and respiration. Because this method is time consuming, is prone to artifacts, and requires offline processing to obtain rendered images, it has never been embraced in clinical practice. An alternative approach based on a combination of miniaturized transducers mounted on a rotating cylinder was recently proposed to obtain transesophageal images in real time.
Recent advances in ultrasound transducer technology have allowed the miniaturization of matrix-array transducers, which was achieved by fitting thousands of piezoelectric elements into the tip of the TEE transducer and using integrated circuits that perform most of the beam forming within the transducer. These technological advances have simplified the connection between the transducer and the imaging system, resulting in a reduction in the size of the connecting cable and significantly lowering power consumption, thus allowing real-time 3D TEE imaging.

We have recently described our initial experience with this new technology and tested its feasibility and clinical utility for real-time 3D imaging of different cardiac structures, including mitral, aortic, and tricuspid valves; interatrial septum; LA appendage; and pulmonic veins. One of the major findings of this study was that real-time 3D TEE consistently provided excellent quality of volume-rendered images of the mitral valve apparatus, including the anterior and posterior leaflets, as well as annulus and subvalvular structures. This finding suggests that matrix TEE (MTEE) imaging may become one of the modalities of choice for perioperative planning of mitral valve surgery (Figures 10 and 11). Similar to previous 3D TEE acquisition methods, the views of the mitral valve from both the LA and LV perspectives are unique to 3D imaging, but what distinguishes MTEE from rotational 3D acquisition is the consistency of superb quality of visualization of the mitral valve, the absence of rotational artifacts, and the immediate online display of volume-rendered views. With the unparalleled level of anatomic detail, these volume renderings allow detailed volumetric analysis of the geometry and dynamics of the mitral valve (Figure 12).

It is anticipated that with the ability of real-time acquisition, online adjustments of rendering, and cropping capabilities, this modality will be used routinely in perioperative planning of mitral valve surgery and guidance of percutaneous interventions. It is easy to predict that the ease and speed of data acquisition, coupled with the ability to display cardiac structures using unique 3D views, are likely to result in rapid integration of MTEE into clinical practice and have an impact on echocardiographic diagnosis of valve disease.

**RT3DE Evaluation of Valvular Heart Disease**

**Mitral Valve**

The availability of transthoracic RT3DE technology has enabled real-time volumetric imaging of the mitral valve from the transthoracic approach, the feasibility of which was demonstrated in 70% of consecutive patients, resulting in optimal visualization of both mitral leaflets, commissures, and the orifice. Importantly, the anterior mitral leaflet was visualized better than the posterior leaflet, probably because of its larger size. In addition, the posterior leaflet was best visualized from the parasternal window, whereas the anterior mitral leaflet was seen equally well from either the parasternal or apical windows. Similar to improved visualization of native valves by obtaining unique en face views, RT3DE was recently reported as a useful tool in the evaluation of prosthetic valve endocarditis.

The accuracy of RT3DE in the evaluation of mitral valve orifice area in mitral stenosis has been established in several earlier studies, which demonstrated that perpendicular en face views of the mitral valve depicting the tips of the mitral leaflets allow the most accurate measurements of mitral valve area. Compared with traditional 2D and Doppler measurements such as 2D planimetry, pressure half-time, and flow convergence, 3DE best agreed with mitral orifice area calculations derived from the Gorlin formula during cardiac catheterization. Accordingly, this approach has been validated in several clinical settings.
suggested as the new standard for mitral valve orifice measurements in patients with mitral stenosis. In addition, these 3D measurements have the advantage of lower intraobserver and interobserver variability.

RT3DE estimates of annular size were compared with magnetic resonance measurements and were found to be similar. A recent study compared segmental analysis of mitral prolapse from transthoracic RT3DE images against TEE findings and found that these 2 techniques yield similar comparative accuracy for precise anatomic localization of prolapsing mitral valve segments. Interestingly, the study by De Castro and colleagues reported higher concordance between 3D TEE and surgery than 2D TEE in the evaluation of prolapsing mitral valve scallops. The diagnostic accuracy of RT3DE evaluation of functional anatomy of mitral regurgitation also was demonstrated recently against surgical findings. The more complex the mitral lesion is, the more valuable 3D echocardiography is compared with 2D TEE.

An important technological advancement in the last 3 years was the development of dedicated software to allow advanced 3D rendering of the valves and quantitative analysis of mitral apparatus geometry (Figure 12). The availability of this

Figure 12. Volume renderings of the mitral valve obtained with quantitative analysis software in 4 patients showing different mitral apparatus measurements: annular diameter (top left, green line); the height of the saddle-shaped mitral valve (top right, the height of the green box); prolapse height and volume and leaflet angles, surfaces, and lengths (bottom left; the surface of the anterior leaflet is represented by the green grid); and the aortic orifice to mitral plane angle, as well as the position of the papillary muscles in 3D space (bottom right, green lines). Abbreviations as in Figure 11.
Recent studies characterizing the mitral valve apparatus in nonischemic and ischemic cardiomyopathy have demonstrated geometric differences in mitral annular deformation with increased intercommissural and anteroposterior dimensions compared with healthy individuals, coupled with increased leaflet tenting and cordal tethering.79–81 Similarly, in patients with MI, the mitral annulus was found to be more dilated and flattened and further deformed in anterior versus posterior infarction.75 Studies in patients with mitral regurgitation and ischemic cardiomyopathy have demonstrated that the regurgitation occurs in parallel with LV remodeling rather than as an intrinsic valve disorder.82,83

Most recently, we and others have demonstrated that analysis of RT3DE images of the mitral valve can provide information on dynamic changes in mitral valve annular surface area and annular longitudinal displacement throughout the cardiac cycle, as well as define the position of the papillary muscles in 3D space.84–86 Specifically, in patients with dilated cardiomyopathy and mitral regurgitation, symmetrical papillary muscle displacement with simultaneous enlargement of the mitral annulus leads to progressive cordal tethering and leaflet tenting, resulting in predominantly central mitral regurgitation, as a result of decreased leaflet coaptation.84–86 These changes were associated with a relatively nonpulsatile mitral annulus that displaces minimally toward the apex during systole. In contrast, in patients with ischemic mitral regurgitation, LV remodeling caused by abnormal inferior wall motion results in uneven papillary muscle displacement and asymmetrical localized tethering associated with eccentric mitral regurgitation.78,84 In addition, the characteristics of the mitral annular function were compared between patients with hypertrophic cardiomyopathy and LV hypertrophy secondary to hypertension or aortic stenosis.87 Annular function in the LV hypertrophy group was similar to that of normal control subjects, whereas annular apical-basal motion and annular area changes were reduced in hypertrophic cardiomyopathy.87 All of these observations have important implications in the planning of mitral valve repair.

3D Color Flow

Current noninvasive methods for measurements of cardiac output and stroke volume are limited by dependence on geometric assumptions, which can be overcome by the use of quantitative volumetric color flow imaging. This approach was initially validated in an in vitro setup and in open-chest animals88 and more recently in human subjects.89–91 The feasibility of visualizing valvular regurgitant jets with RT3DE color flow imaging also has been demonstrated, and the quantification of mitral and tricuspid regurgitation jet volumes was shown to correlate well with 2D flow convergence methods.92 RT3DE-derived ratio of mitral regurgitant jet volume to LA volume has been proposed as a new method to assess the severity of regurgitant lesions, although these ratios were smaller than those measured with 2DE.92

Having the advantage of volumetric imaging of the geometry of the flow convergence surface without the assumption of rotational symmetry, RT3DE color flow imaging can quantify mitral regurgitation more reliably than 2DE.93 Indeed, it was shown that the true proximal flow convergence region is more hemielliptical than hemispheric as previously believed.94 Based on these observations, a hemielliptical approach was proposed for improved 2DE quantification of mitral regurgitation.94 Direct assessment of the vena contracta with RT3DE imaging revealed significant asymmetry in functional compared with organic mitral regurgitation, resulting in poor estimation of the effective regurgitant orifice area with single-plane vena contracta measurements.95

Tricuspid Valve

The utility of 3D echocardiography in the evaluation of tricuspid valve disease has not been explored in depth. Numerous case reports have described tricuspid abnormalities such as tricuspid stenosis, cleft tricuspid valve, and a flail tricuspid leaflet.96 A recent study has found that RT3DE measurements of the tricuspid annulus are comparable to those obtained from magnetic resonance images,97 which may have important implications in tricuspid valve surgical planning. Several studies have subsequently explored the 3D geometry of the normal tricuspid annulus and compared it with the mitral annulus using RT3DE imaging combined with the newly developed quantitative analysis software.98 The tricuspid annulus was found to have a less nonplanar saddle shape compared with the mitral annulus, with a round or oval shape.98 In patients with functional tricuspid regurgitation, the annulus is even larger, more planar, and more circular.99 In patients with tricuspid regurgitation secondary to pulmonary hypertension, in addition to annular dilatation, an enlargement in tenting volume was reported.100 The severity of tricuspid regurgitation was found to be determined mainly by septal leaflet tethering, septal-lateral annular dilatation, and the severity of pulmonary hypertension.101 Characterization of the tricuspid annulus and leaflets in patients with rheumatic heart disease with mitral stenosis and severe tricuspid regurgitation also was performed recently with RT3DE imaging, which allowed, in addition to tricuspid valve planimetry, separate evaluation of each tricuspid valve leaflet with regard to thickness, mobility, and calcification, as well as the commissural width at the time of maximal tricuspid valve opening.102

Aortic Valve

RT3DE imaging of the aortic valve from either the transthoracic or transesophageal approach is challenging, probably because of the oblique angle of incidence of the ultrasound beam combined with the thinner leaflets. RT3DE imaging has recently been used to improve the accuracy of the quantification of aortic stenosis. Planimetry of the aortic valve with RT3DE images showed good agreement with the standard 2D TEE technique, flow-derived methods, and cardiac catheterization data with the advantage of improved reproducibility.103

Analysis of RT3DE images in a small group of normal subjects revealed that in half of the subjects, the LV outflow tract cross section is not round but rather elliptical. Incorrectly assuming a round LV outflow tract geometry during
assessment of aortic stenosis may significantly underestimate the measurements of aortic valve area. This hypothesis was subsequently confirmed in an animal model of upper septal hypertrophy, the severity of which correlated with the discrepancy between the traditional 2DE and RT3DE measurements of aortic valve area. This experimental work also showed that the continuity equation based on RT3DE color Doppler–derived estimates of stroke volume correlated better than 2DE measurements with that based on invasive outflow tract flow measurements. An alternative approach based on direct volumetric measurements of stroke volume using semiautomated LV endocardial border detection was compared in humans side by side with the Doppler continuity equation and Simpson’s 2D technique against Gorlin’s invasive formula. This study showed that volumetric evaluation from RT3DE images is more accurate than traditional non-invasive techniques.

The diagnostic value of epicardial RT3DE imaging during cardiac surgery has been recently described. Qualitative evaluation determined epicardial RT3DE superiority over 2D TEE in depicting aortic cusp morphology lesions, LV outflow tract spatial relationships with the mitral apparatus and aortic root, and both anterior and posterior mitral leaflet scallops.

**RT3DE Guidance and Evaluation of Intracardiac Interventions**

The recent increase in the use of less invasive interventional therapies for a variety of cardiac disease states created a need for improved image guidance. Both transthoracic and transesophageal RT3DE imaging holds promise in addressing this increasing need because both provide improved visualization of device location and spatial orientation relative to the surrounding anatomic structures. This imaging modality has been used to visualize the RV bioptome along its entire course, as opposed to only partial views with 2DE, to guide RV endomyocardial biopsies.

Successful transcatheter closure of secundum atrial septal defects is dependent on accurate assessment of atrial septal defect location and size and of the surrounding rim tissue of the atrial septum (Figure 13A). These atrial septal defect features are important to determine the appropriateness of transcatheter closure, device selection, and guidance of device deployment (Figure 13B). This assessment can be accomplished with RT3DE imaging from either the transthoracic or transesophageal approach (Figure 13A). Historically, atrial septal defect closure device selection and placement have been guided by fluoroscopy and 2D TEE.
Intracardiac echocardiography has since emerged as the preferred method in the United States because of shorter procedure times and the lack of need for general anesthesia. However, because intracardiac transducers are costly and not universally available, RT3DE TEE, which allows dynamic en face visualization of the atrial septum and related cardiac anatomy in 3 dimensions in real time, has been used as an alternative to intracardiac imaging. Similarly, RT3DE imaging may be used to guide transcatheter closure of perimembranous ventricular septal defects with an Amplatzer occluder, for which RT3DE provided information on defect size, rims, and device position and profile.113

Real-time 3D MTEE has been shown to consistently provide excellent-quality volume-rendered images of the mitral valve components, including the anterior and posterior leaflets, as well as the annulus and subvalvular structures.6 Not surprisingly, 3D MTEE imaging has been used to guide percutaneous balloon mitral valvuloplasty in patients with rheumatic mitral stenosis (Figure 13C and 13D), percutaneous closures of mitral and aortic perivalvular leaks, percutaneous mitral valve repair using the edge-to-edge technique in patients with mitral regurgitation, and percutaneous mitral annuloplasty for ischemic mitral regurgitation.114

Atrial fibrillation is increasing in prevalence and currently is a major public health concern. Although the combination of rate control and anticoagulation is an effective treatment for atrial fibrillation, not all patients are candidates for anticoagulation. LA appendage occluder devices constitute a novel treatment option for patients with atrial fibrillation at risk for stroke who have contraindications to warfarin. Accurate real-time quantification of the LA appendage, which is essential to ensure correct sizing and placement of occluder devices, has been achieved by 3D MTEE imaging (Figure 13E).115 The role of 3D MTEE for the guidance of catheter placement during electrophysiology procedures (Figure 13,F) remains to be established. In the future, developments in intracardiac 3D ultrasound may address the challenges of acquiring high-quality 3D visualization of the left atrium and pulmonic veins.

Current Practice and Future Developments

Currently, many laboratories perform a complete 2DE study, followed by a focused 3D examination, in patients with specific pathologies in which RT3DE imaging could potentially provide additional diagnostic information. It can be anticipated that a full-volume acquisition of the left ventricle will be performed in every patient to obtain LV volumes and EF. The 3D images should be stored in a digital archiving system with the 2D study to allow integrated interpretation of all images and incorporation of 3D findings into the report. Future advances in transducer and computer technology will result in several important improvements that will further enhance the clinical application of RT3DE imaging. One highly desirable improvement is the ability to acquire wider-angle pyramid of data with and without color flow in a single cardiac cycle. This will shorten data acquisition and eliminate stitching artifacts. Furthermore, future improvements in both spatial resolution and temporal resolution of the transthoracic RT3DE imaging, which are still below those of 2DE, will broaden the spectrum of patients who can be imaged with this modality. Further miniaturization of the 3D MTEE technology will allow 3D TEE imaging in pediatric patients and the development of real-time 3D imaging intracardiac catheters. Future software developments will allow new types of sophisticated quantitative analysis of the cardiovascular anatomy and function, including the fusion of RT3DE data with other 3D imaging modalities such as magnetic resonance and computed tomography.

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Mor-Avi et al
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