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**Aim:** The aim of this study was to investigate the feasibility and accuracy of using symmetrically rotated apical long axis planes for the determination of left ventricular (LV) volumes with real-time three-dimensional echocardiography (3DE).

**Methods and Results:** Real-time 3DE was performed in six sheep during 24 haemodynamic conditions with electromagnetic flow measurements (EM), and in 29 patients with magnetic resonance imaging measurements (MRI). LV volumes were calculated by Simpson’s rule with five 3DE methods (i.e. apical biplane, four-plane, six-plane, nine-plane (in which the angle between each long axis plane was 90°, 45°, 30° or 20°, respectively) and standard short axis views (SAX)). Real-time 3DE correlated well with EM for LV stroke volumes in animals (r-values=0·68–0·95) and with MRI for absolute volumes in patients (r-values=0·93–0·98).

However, agreement between MRI and apical nine-plane, six-plane, and SAX methods in patients was better than those with apical four-plane and bi-plane methods (mean difference= −15, −18, −13, vs. −31 and −48 ml for end-diastolic volume, respectively, P<0·05).

**Conclusion:** Apically rotated measurement methods of real-time 3DE correlated well with reference standards for calculating LV volumes. Balancing accuracy and required time for these LV volume measurements, the apical six-plane method is recommended for clinical use.

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**Key Words:** left ventricular function; magnetic resonance imaging; three-dimensional echocardiography.

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**Introduction**

Accurate evaluation of left ventricular (LV) volume and ejection fraction (EF) has important diagnostic, prognostic and therapeutic implications; therefore, a rapid, accurate, reproducible and non-invasive method of calculating these indices is important¹.² While magnetic resonance imaging (MRI) is an accepted method for determining LV volume and EF³,⁴, the equipment is expensive, not mobile, and requires special facilities.

Although conventional two-dimensional echocardiography (2DE) is a widely used technique for clinical evaluation of LV volumes, it has several limitations, including the necessity for left ventricular geometric assumptions. However, these assumptions are invalid in patients with distorted LV geometry and impaired LV function. LV EFs calculated from apical single and biplane views from 2DE have correlated well with values from radionuclide angiography in asymmetric modelled hearts⁵, but even the biplane disk method represents only an approximation of the true dimensions of the ventricle. Therefore, it has been suggested that more than two planes be used to determine LV volumes⁶. Reconstruction of the LV by three-dimensional
Echocardiography (3DE) can be used to determine LV volume with more than two planes, mitigating the limitations of 2DE and allowing for quantification of LV volume without these geometric assumptions. Nosir et al.\[5\] recommended the use of a series of 15-mm-thick short axis (SAX) slices for accurate and rapid measurement of LV volume and EF. However, previously reported 3DE methods involve complicated systems, require ECG/respiratory gating, and involve prolonged imaging times\[7\]-[11], all of which limit clinical applicability.

Real-time 3DE has the potential to overcome these problems. The 3DE images obtained by a new real-time system consist of two independent B-mode and two or three C-mode scan images simultaneously acquired in variable orientations. C-scans are planes parallel to the transducer face that cannot be imaged in real time by conventional ultrasound systems. Standard B-scans, which originate at the centre of the transducer aperture, can be obtained in any direction within the volume. Because the real-time 3DE apical long axis images (standard B-scans) are of higher quality than the corresponding SAX views (C-scans), they may yield more accurate LV volume measurements.

The aim of this study was to determine the feasibility and accuracy of LV volume measured by a series of apical long axis planes compared to those by SAX with real-time 3DE, using electromagnetic flow meters (EM) for validation in an animal study and MRI as a reference standard in a clinical study. In addition, LV volumes and EF were assessed by using different numbers of apical long axis planes to determine the minimum number of planes required without loss of accuracy.

**Methods**

**Animal Study**

**Animal preparations**

Six sheep with previously surgically created chronic aortic regurgitation, weighing 30–60 kg, were anaesthetized with pentobarbital (30–50 mg/kg IV), intubated and ventilated. A sternotomy was performed, the heart was suspended in a pericardial cradle. To measure LV stroke volumes (LV SV), an EM probe (model EP455, Carolina Medical Electronics, Inc, King, NC, U.S.A.) was placed snugly around the skeletonized ascending aorta distal to the coronary ostia.

**Experimental protocol**

Each sheep was studied under four different haemodynamic conditions: (i) baseline; (ii) after 500 ml blood infusion; (iii) during nitroprusside infusion; and (iv) during angiotensin II infusion. At each stage, real-time 3DE images were obtained epicardially from the apex without respiratory and ECG gating by a newly developed real-time 3DE system (Volumetrics Medical Imaging Inc., Durham, NC, U.S.A.) and a 2.5 MHz phased array hand-held transducer (14 mm in diameter). All images were digitally stored onto optical discs of off-line analysis. For validation, aortic flow rates measured by EM were recorded simultaneously with real-time 3DE. All operative and animal management procedures were approved by the Animal Care and Use Committee of the National Heart, Lung and Blood Institute.

**Patient Study**

**Population**

Real-time 3DE was performed in 32 consecutive patients (22 men, 54 ± 11 years old) undergoing MRI for evaluation of LV volume and EF. Among them, six patients had right ventricular dysplasia, nine had aortic regurgitation, four had dilated cardiomyopathy, and 12 had ischaemic cardiomyopathy. All patients included in this study were in sinus rhythm.

**Magnetic resonance imaging**

MRI was performed as a reference standard for LV volumes. All images were obtained using a commercially available 1.5-Tesla whole-body scanner (Siemens Vision, Erlangen, Germany) with a phased-array chaser coil. ECG-gated localizing spin-echo sequences were used to identify the intrinsic long axis of the heart. For all patients, short-axis MRI images were started at the mitral valve plane with a slice thickness of 8–10 mm. These images were manually segmented using commercially available image analysis software (Argus, Siemens Medical Systems, Isklin, NJ, U.S.A.), using Simpson’s algorithm to determine total LV volumes at end-diastole (EDV) and end-systole (ESV) and to calculate EF. These measurements were all performed by an investigator experienced in cardiac MRI and without knowledge of the 3DE measurements.

**Real-time 3D ultrasound**

All ultrasound imaging was performed within 1 h of MRI imaging. Real-time 3DE images were obtained from a transthoracic apical view, while the patients were placed in a left lateral decubitus position. Thus, the apical four-chamber view, apical two-chamber view (standard B-scans), and a series of short axis images (C-scans) were acquired simultaneously without the need for respiratory and ECG gating (Fig. 1). After the highest quality image was obtained, the entire LV volumetric data set for one cardiac cycle was stored onto an optical disc. Care was taken to include the entire left ventricle in the real-time pyramidal volumetric data set for the entire cardiac cycle.

A personal computer equipped with a recently developed software (3D EchoTech, Echo Tech...
America, Lafayette, CO, U.S.A.) was used to display the images of the 3DE data set and to measure LV volumes.

This protocol was approved by the Institutional Review Board of the Cleveland Clinic Foundation and all patients provided informed written consent prior to enrolment.

**Quantitative 3DE Measurements**

LV volumes were calculated using a series of symmetrically rotated apical long axis planes (standard B-scans). After the 3DE data sets were transferred to the 3D EchoTech computer system, the LV common long axis was defined from the centre of the mitral annulus to the apex by the observer. Then, the computer displayed the 3DE images along the long axis as apical biplane, apical four-plane, apical six-plane, and apical nine-plane images. The cavity of the left ventricle in each apical view was manually traced. For the apical biplane method, the LV cavities were traced in apical four-chamber and two-chamber views. For the apical four-plane method, the LV cavities were traced in four apical planes separated by 45°. For the apical six-plane method, this angle of separation was 30°. For the apical nine-plane method, the LV planes were separated by 20° (Fig. 2). Finally, the LV volumes were automatically calculated using the biplane Simpson’s rule for apical biplane imaging and using the multiplanar Simpson’s rule for the other apical methods. The LV volume was also calculated from a stack of parallel SAX views (C-scans)\textsuperscript{[12]}. The LV cavity in each SAX view was manually traced and the cavity area calculated using the same analysis software. After multiplying each LV cavity area by the slice thickness (10 mm), the data were consecutively added to obtain the entire LV cavity volume. The time required for 3DE volume measurements was determined with a stopwatch. The peak of the QRS wave from the ECG was used for selecting the largest LV volume (i.e. the EDV) and the end of the T wave for selecting the smallest LV volume (i.e. the ESV). For each subject, both EDV and ESV were determined and the SV was obtained by subtracting ESV from EDV; EF was determined as SV divided by EDV. For both diastolic and systolic measurements, the LV papillary muscles were excluded from the LV cavity contour.
Interobserver Variability

In order to evaluate the effect of observational variability on the measurement of LV volumes, the real-time 3DE images obtained from 10 patients were analysed randomly at different times with the same 3D EchoTech system for LV EDV and ESV by two independent observers, each without knowledge of the results obtained by the other, or MRI.

Statistical Analysis

Values are expressed as mean ± S.D. for continuous variables. Linear regression analysis was used to obtain the relationships between the real-time 3DE and the EM for LV SV in the animal study, and between real-time 3DE and MRI for LV EDV, ESV and EF in the clinical study. Agreements between the real-time 3DE and the EM for LV SV in the animal study, and between real-time 3DE and MRI for LV EDV, ESV and EF in the clinical study, were evaluated using the Bland and Altman method\textsuperscript{[13]}. Paired Student’s t-testing was performed to compare the different 3DE methods and reference standards for LV volume, SV, EF and to compare time required for LV volume measurement by 3DE methods. A value of $P<0.05$ was considered statistically significant.

Results

Feasibility

Real-time 3DE image acquisition was performed without difficulty for all 24 haemodynamic conditions in the animal study. However, in the clinical study, three patients were excluded because the quality of 3DE images was suboptimal for quantitative analysis. Among the remaining 29 patients, 3DE revealed that nine patients had segmental wall motion abnormalities, four had global hypokinesis, and 16 had normal wall motion. In each case the examination required 3–8 min, including storage of the data on optical discs. Off-line image post-processing and analysis were performed immediately after data transfer to the 3D EchoTech computer.

Animal Study

LV SVs determined by EM ranged from 27 to 66 ml. LV EDVs, ESVs and SVs measured by 3DE are displayed in

Figure 2. The LV volume measurements by the apical nine-plane method. Using as an axis of rotation a line from the apex to the centre of the mitral valve annulus, the 3D EchoTech system obtained nine consecutive longitudinal planes rotated 20° from each adjacent plane. The LV cavity in each of the planes was traced manually, and the LV volume then calculated by multiplanar Simpson’s rule automatically.
was excellent (the apical nine-plane method and the EM for LV SVs; Table 2). There were excellent correlations in the measurements of LV EDVs, ESVs and SVs obtained by the apical nine-plane method and the SAX view method (r=0.94, 0.85 and 0.88, respectively). No significant differences existed between these two methods (SAX view method–apical nine-plane method) for LV EDVs (−1 ± 5 ml), ESVs (1 ± 5 ml) or SVs (−1 ± 4 ml, all P<0.05). However, significant differences existed for LV SVs obtained by the apical four-plane and biplane methods compared with that by the apical nine-plane method, (Δ=−3 ± 7 ml for four-plane vs. nine-plane, Δ=−4 ± 8 ml for biplane vs. nine-plane, each P<0.05). However, there was no significant difference between the apical six-plane and nine-plane methods for LV SV measurements (Δ=1 ± 4 ml, P>0.05). Hence, the apical six-plane method appeared to be sufficient for accurate estimation of LV SVs.

**Patient Study**

**Comparison of MRI and real-time 3DE**

The mean ± S.D. values of LV volumes and EFs obtained by MRI and real-time 3DE using the apical nine-plane method are presented in Table 3. There were excellent correlations and agreements in the measurements of LV EDVs, ESVs and EFs obtained by MRI and real-time 3DE; r-values were 0.98, 0.98 and 0.94, respectively (Fig. 4). No significant difference existed in the mean difference between the average values of LV EF obtained by MRI and real-time 3DE (P>0.05), but real-time 3DE slightly underestimated the LV volumes obtained by MRI (P<0.05).

**Comparison of the use of apical long axis planes and short axis views in 3DE**

There was both excellent correlation and agreement between the conventional SAX and the apical nine-plane
measurements of LV EDV, ESV and EF values (r=0.98, 0.96 and 0.90, respectively, and Δ (SAX–apical)=2±17 ml, −5±19 ml, 2±7%, respectively, all P>0.05).

Using a slice thickness of 10 mm, the average number of slices required to measure LV volumes with the SAX view in real-time 3DE was 10±1; 16 patients (55%) required more than nine slices.

**Table 3.** The correlation and agreement between magnetic resonance imaging (MRI) and real-time 3DE methods in the clinical study.

<table>
<thead>
<tr>
<th></th>
<th>MRI</th>
<th>Nine-plane</th>
<th>Six-plane</th>
<th>Four-plane</th>
<th>Biplane</th>
<th>SAX</th>
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<tr>
<td><strong>EDV (ml)</strong></td>
<td>Mean</td>
<td>188 ± 86</td>
<td>174 ± 76</td>
<td>171 ± 79</td>
<td>158 ± 72*</td>
<td>141 ± 57*</td>
</tr>
<tr>
<td></td>
<td>S.D.</td>
<td>86</td>
<td>76</td>
<td>76</td>
<td>79</td>
<td>57</td>
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<tr>
<td>r</td>
<td>0.98</td>
<td>0.98</td>
<td>0.97</td>
<td>0.93</td>
<td>0.98</td>
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<tr>
<td><strong>ESV (ml)</strong></td>
<td>Mean</td>
<td>102 ± 76</td>
<td>94 ± 64</td>
<td>91 ± 63</td>
<td>84 ± 60*</td>
<td>76 ± 56*</td>
</tr>
<tr>
<td></td>
<td>S.D.</td>
<td>76</td>
<td>64</td>
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<td>63</td>
<td>56</td>
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<tr>
<td>r</td>
<td>0.98</td>
<td>0.98</td>
<td>0.95</td>
<td>0.93</td>
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<tr>
<td><strong>EF (%)</strong></td>
<td>Mean</td>
<td>50 ± 16</td>
<td>50 ± 15</td>
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<td>51 ± 14</td>
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<tr>
<td></td>
<td>S.D.</td>
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<td>15</td>
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<tr>
<td>r</td>
<td>0.94</td>
<td>0.93</td>
<td>0.79</td>
<td>0.75</td>
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*P<0.05 when compared with apical nine-plane 3DE data. The abbreviations are the same with those in Tables 1 and 2.

**Figure 4.** The correlation and agreement between the apical nine-plane method of real-time 3DE and MRI for LV end-diastolic volume (EDV), end-systolic volume (ESV) and ejection fraction (EF) in the clinical study.
The times needed for LV volume measurements (both EDV and ESV) for each of the real-time 3DE methods were significantly different. LV volumes measured by SAX required the longest time: average $278 \pm 29$ s (240–345 s). The time required was $131 \pm 12$ s (110–160 s) for the nine-plane method, $93 \pm 11$ s (81–123 s) for the six-plane method, $58 \pm 6$ s (45–72 s) for the four-plane method, and $29 \pm 5$ s (21–40 s) for the biplane method, $P<0.0001$.

The minimum number of slices required for calculation of LV volumes (Table 3) The correlations between MRI and the different four real-time 3DE apical long axis plane methods were excellent, both for LV EDV and for LV ESV ($r=0.93-0.98$). The correlations between MRI and real-time 3DE for LV EF obtained by the apical nine-plane and six-plane methods were also excellent ($r=0.94$ and 0.93). However, the correlations were reduced for the apical four-plane and biplane methods ($r=0.79$ and 0.75). There were no significant differences for LV EDVs and ESVs obtained by the apical six-plane method compared with those obtained by the apical nine-plane method ($\Delta=3 \pm 9$ ml, $-2 \pm 7$ ml, respectively, both $P>0.05$), but there were significant differences for those obtained by the apical four-plane and biplane methods compared with those by the apical nine-plane method, ($\Delta=18 \pm 19$ ml, $-10 \pm 18$ ml, respectively, for four-plane vs nine-plane and $\Delta=-35 \pm 29$ ml, $-18 \pm 19$ ml, respectively, for biplane vs nine-plane, each $P<0.05$).

**Interobserver variability**

There was a strong agreement and correlation between the two independent observers’ measurements for real-time 3DE volumes included EDV and ESV (85 ± 45 ml vs. 87 ± 45 ml, $r=0.99$, $P<0.0001$, $\Delta=2 \pm 3 \pm 3$ ml).

**Discussion**

**Previous Studies**

Conventional 2DE is widely used, since it allows for assessment of cardiac anatomy and function expeditiously and non-invasively. Furthermore, when compared to MRI, 2DE is inexpensive and mobile. Although several methods for determining LV volumes with 2DE have been developed, including the ellipsoid method[14], area-length method[15,16], Simpson rule method[12] and the disk method[6,17] for single and biplane calculations, each has significant limitations. Most studies, even with symmetrical ventricles, demonstrate underestimation of LV volume because of the difficulty in positioning the probe on the true LV apex on the patient’s chest to obtain true apical four-chamber or two-chamber view images[18,19]. Erbel et al., therefore, suggested that more than two planes be used to determine LV volumes[6].

Our findings are in agreement with the study conducted by Buck and colleagues, who compared LV volumes and EF, calculated by MRI and 3DE reconstruction in 23 patients with chronic LV aneurysms. They obtained dynamic reconstructed 3DE image data sets from transthoracic apical views using a rotating probe with acquisition gated to control for ECG and respiration (Echoscan, TomTec, Boulder, CO, U.S.A.)[20]. LV volumes were calculated from the 3DE data sets by summing the volumes of multiple SAX parallel disks. Their results showed excellent correlation and agreement between 3DE and MRI for LV EDV ($r=0.97$, SEE=14.7 ml), for ESV ($r=0.97$, SEE=12.4 ml) and EF ($r=0.74$, SEE=5.6%), and better correlation and agreement than those provided by other techniques. Although these 3DE results correlated well with those by MRI, an underestimation existed. Apfel[21] who compared 3DE and MRI in young patients with pulmonary hypertension and compressed left ventricles, obtained similar results to ours, an underestimation of LV EDVs and ESVs by 3DE ($r=0.94$ and 0.87, $\Delta=-6 \pm 9 \pm 6$ ml and $-16 \pm 11$ ml, respectively) compared with MRI, while Siu et al[9] reported good correlation ($r=0.96$, SEE=2.99 ml) between LV SV obtained by 3DE and actual SV in dogs. However, these 3DE reconstruction methods are technically complicated, and therefore their applicability has not been widely clinically implemented.

**Advantages of Real-time 3DE for Measurement of LV Volume**

The real-time 3DE method has demonstrated the ability to determine right ventricular SVs accurately using SAX views[22]. In the current study, the real-time 3DE data sets were acquired directly from the apical long axis view (standard B-scans), so the image quality was consistently better than that of SAX views (C-scans). Thus, it was easier to identify the LV endocardial boundary from the apical long axis planes than that from the SAX views. Unlike other systems such as the TomTec system[20] that analyze reconstructed 3DE images from a series of 2DE images, the 3D EchoTech system simultaneously displays up to nine apical long axis plane images on the screen in one cine loop. Therefore, it was convenient to compare the LV endocardial boundary for each consecutive apical long axis plane image frame by frame.

In our group of patients, we found the use of the apical six-plane method for measurement of LV volumes gave similar accuracy to that of the apical nine-plane method. The use of the apical four-plane and biplane methods significantly underestimated the LV volumes compared to the apical nine-plane method. For accurate calculation of LV volumes, compared to the conventional SAX method, the apical long axis six-plane method analysis time was reduced from 278 ± 29 to 93 ± 11 s because fewer slices were needed. This provides a more rapid, easy to perform and accurate method for calculating LV volumes.
**Study Limitations**

The real-time 3DE system is based on a novel phased array transducer matrix that allows for rapid beam steering over three dimensions. The massive parallel processing system used currently permits the reception of 16 lines for each transmitted signal (16:1). From these, a pyramidal tissue volume measuring $60^\circ \times 60^\circ$ is imaged at a rate of 22 volumes/s at a depth of 12 cm, or for a depth of 16 cm, 17-1 volumes/s.

The major limitation of the current real-time 3DE system is image resolution, in part because of the limited channel elements and 16:1 parallel processing. For this reason, in our study, three of 32 patients were excluded because of suboptimal image quality.

An additional drawback is the low frame rate that may cause problems with capturing precise end-diastolic and end-systolic frames, especially in the presence of tachycardia. The limited angle of the pyramidal volume also makes it difficult to image patients with dilated hearts. High scan depths were often used to acquire real-time 3DE from dilated hearts, resulting in lower frame rates. Therefore, the underestimation observed in patients as compared to MRI may be explained as above.

On the other hand, the three-dimensional point-spread-function of this scanner has the shape of a water droplet with a constant length throughout the data pyramid. The volume of this will increase with depth and will increase towards the edges of the pyramid. In any cross-sectional plane, the effect will be a penetration of wall echo signals into the cavity of the ventricle that will result in an underestimation of the LV volume. However, the use of intravenous contrast agents may enhance the ability to visualize the endocardial boundary. Also, using higher frequency transducers, wider sector angles and higher frame rates could resolve some of these limitations with the next generation of real-time 3DE technology.

Real-time 3DE should have the greatest advantage in patients with asymmetric left ventricles. However, only nine patients with regional wall motion abnormalities and 20 patients without asymmetric left ventricles were studied in our present patient population. Hence, further studies are needed to compare the accuracy of real-time 3DE in patients with symmetrical versus asymmetrical ventricles.

**Conclusion**

Apical rotation measurement methods using real-time 3DE have an excellent correlation with reference standards for calculating LV volumes both experimentally and clinically. Balancing the accuracy and required time for LV volume and ejection fraction determination, the use of apical six-plane method is recommended clinically.

**Acknowledgments**

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