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Rapid Freehand Scanning Three-Dimensional Echocardiography: Accurate  
Measurement of Left Ventricular Volumes and Ejection Fraction Compared  
With Quantitative Gated Scintigraphy

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## ABSTRACT

This study was performed to assess clinical feasibility of rapid freehand scanning three-dimensional echocardiography (3DE) for measuring left ventricular end-diastolic (LVEDV) and end-systolic (LVESV) volumes and ejection fraction (LVEF) using quantitative gated myocardial perfusion single photon emission computed tomography (SPECT) as the reference standard. We performed transthoracic two-dimensional echocardiography (2DE) and magnetic freehand 3DE using a harmonic imaging system in 15 patients. 3DE data sets were collected by slowly tilting the probe (fan-like scanning) in the apical position. The 3DE data were recorded in 10-20 sec, and the analysis was performed within 2 min after transferring the raw digital ultrasound data from the scanner. For LVEDV and LVESV measurements, there was a high correlation and good agreement (LVEDV;  $r=0.94$ ,  $p<0.0001$ ,  $SEE=21.6$  mL,  $bias=6.7$  mL and LVESV;  $r=0.96$ ,  $p<0.0001$ ,  $SEE=14.8$  mL,  $bias=3.9$  mL) between gated SPECT and 3DE. There was an overall underestimation of volumes with greater limits of agreement by 2DE. For LVEF, regression and agreement analysis also demonstrated high precision and accuracy ( $y=0.82x+5.1$ ,  $r=0.93$ ,  $p<0.001$ ,  $SEE=7.6\%$ ,  $bias=4.0\%$ ) by 3DE compared to 2DE. Rapid 3DE using a magnetic-field system provides precise and accurate measurements of LV volumes and ejection fraction in humans.

Three-dimensional (3D) echocardiography has demonstrated superior accuracy and reproducibility over conventional two-dimensional (2D) echocardiography for measuring left ventricular (LV) volume, because no geometric assumptions are necessary about LV shape [1-3]. There are several methods for registering multiple 2D echo images in 3D space. However, only magnetic-field systems are able to track the position and orientation of a transthoracic scanhead during freehand scanning, allow acquisition of images from randomly oriented image planes [4]. The ultrasound probe is coupled to a sensor that registers the spatial coordinates inside a magnetic field. The introduction of a method for freehand dynamic echocardiographic acquisition and reconstruction using raw digital ultrasound data provides an alternative to the preserve high temporal resolution in the 3D reconstruction [5].

The purpose of this study was to assess clinical feasibility and the precision and accuracy of this system for measuring LV volumes. Quantitative gated myocardial perfusion single photon emission computed tomography (SPECT) was used as the reference standard [6, 7].

## METHODS

### Study Subjects

We performed a freehand 3D echocardiographic scanning in patients for

whom a standard transthoracic echocardiographic examination and rest Tc-99m-MIBI SPECT were clinically indicated. Patients with a variety of LV shapes were considered in an attempt to cover a large range of LV volumes. Exclusion criteria were cardiac arrhythmias, including patients with pacemaker and implantable cardioverter defibrillator. Fifteen patients (8 men; mean age, 65.2 years, 39 to 78 years) entered the study. Ten patients had previous myocardial infarction, two had severe mitral regurgitation, two had dilated cardiomyopathy and one had hypertrophic cardiomyopathy. All echocardiographic examinations were performed within 24 hours before or after SPECT study and no changes in clinical status occurred during that period. Informed consent was obtained before the study from all patients.

## 2D Echocardiographic Study

All patients had a complete 2D echocardiographic and Doppler study. LV end-diastolic (LVEDV) and end-systolic (LVESV) volumes were measured by using the modified biplane Simpson's rule with the apical four-chamber and two-chamber views [8]. The QRS wave from the ECG was used to select the largest volume (i.e. LVEDV), and the T wave was used to select smallest volume (i.e. LVESV). An experienced sonographer blinded to clinical and gated SPECT data measured 2D volumes. The total stroke volume of the LV

was calculated as the difference between these volumes. The derived LV ejection fraction (EF) was calculated directly as the ratio of stroke volume to end-diastolic volume.

### 3D Echocardiographic Study

The data were acquired using a Philips SONOS 5500 digital ultrasound scanner (Andover, Mass). For 3D data processing, a PC based 3D freehand system (3D EchoTech, Munich, Germany) was used (Figure 1A). The system utilizes an electromagnetic sensor device. The sensor device consists of an electromagnetic field transmitter and a field receiver (Figure 1B). The electromagnetic receiver (position sensor) was attached directly to the standard ultrasound probe with the frequency of 1.8/3.6 MHz in harmonic mode. The field transmitter generates an alternating spheric electromagnetic field in a strength of up to 5 times the earth magnetic field depending on the distance between transmitter and receiver. For 3D data acquisition, the ultrasound probe with the attached position sensor can be moved freely in a hemisphere of 60 cm around the transmitter. During data acquisition the electromagnetic sensor device generates with a frequency of about 100 Hz a set of 3 translation and 3 angulation values. These values describe the position of the ultrasound probe in space. Simultaneous to the calculation of the

position, the images of the ultrasound system are digitized and stored. The acquired ultrasound images are transformed into an isotropic rectangular (Cartesian) coordinate system with the help of the corresponding set of translation and angulation values. All other relevant scanner parameters, including the ECG signal from the patient, were recorded simultaneously. The precision of the system for locating a point target from any direction was tested using a calibration phantom consisting the nylon strings (calibration-operating instructions, 3D Echotech, March 1997).

For the data acquisition, the probe was placed apically between two ribs and then tilted slowly, covering the whole LV. The pace of this motion and the patient heart rate decided the sampling density for each volume (i.e. the distance between the 2-D frames). The total recording was done with normal respiration, and lasted typically for 10-20 cardiac cycles. The data were sampled continuously all the time, so the operator did not have to interact to start a recording. Acquisition was repeated 2 to 3 times to optimize image quality.

Analysis was performed by 2 independent observers. After 3D data sets were transferred to the computer system, the computer displayed rotating radial LV images around a center axis, as apical biplane, apical four-plane, apical six-plane and apical nine-plane images, respectively. The true long axis

was defined in the reconstructed cross section showing the maximal distance from mitral annulus to apex. Using equally spaced apical four-plane images (i.e., 45 degrees increments), LV endocardial borders were manually traced, including the LV outflow tract up to the aortic valve (Figure 2). The mitral valve plane was traced as the straight line between the boundaries of the mitral annulus. The LV volume was calculated using the multiplanar Simpson's method. The QRS wave from the ECG was used to select the largest volume (i.e. LVEDV), and the T wave was used to select smallest volume (i.e. LVESV), from which EF was calculated.

#### Gated SPECT Study

A single dose of technetium-99m methoxy isobutyl isonitile (MIBI, 600MBq) was administered intravenously at rest. ECG gated myocardial SPECT was initiated 60 minutes after tracer injection. Data acquisition was performed with a two-headed SPECT system (Millenium VG, GE Medical Systems, WI) with a low energy high resolution collimator. A total of 60 projections of 40 heart beats duration at 3° steps. LV volumes were calculated from the gated SPECT images using previously validated and commercially available automated software (Quantitative gated SPECT, QGS, Cedars-Sinai Medical Center, Los Angels, CA) [6].



## Statistical Analysis

All values of the LV and EF measurements were expressed as mean $\pm$ SD. To assess precision, LV volumes estimated from 3DE by 2 independent observers (J.K., K.T.) were averaged and compared to with those measured with gated SPECT by linear regression. Interobserver variability was expressed as the coefficient of variation between the 2 observers. To determine whether the difference in the values between the 2 methods was statistically significant, a paired t test was performed; the level of significance was set to  $p < 0.05$ . The bias was expressed as the mean difference between the 2 methods, and the limits of agreement as 2 SDs of the difference of the 2 methods [9].

## RESULTS

LV volumes and EF determined with gated SPECT were as follows: EDV ranged from 35.8 to 279.0 mL ( $135.1 \pm 69.8$  mL), ESV ranged from 3.8 to 236.0 mL ( $80.1 \pm 67.6$  mL), and EF ranged from 15.4 to 89.4 % ( $49.5 \pm 22.1$  %).

The 3D data were recorded in 10-20 sec, and the analysis was performed within 2 min after transferring the raw digital ultrasound data from the scanner. In the estimation of the LVEDV and LVESV values by 3D method, interobserver variability was 7.4 % and 5.6 %, respectively.

Regression analysis and Bland and Altman plots for LVEDV and LVESV measurements are shown in Figures 3 and 4. Linear regression indicated a high correlation ( $r=0.94$ ;  $p<0.0001$  for LVEDV and  $r=0.96$ ;  $p<0.0001$  for LVESV) between gated SPECT and 3D method, with standard error of estimates (SEE) of 21.6 mL for LVEDV and 14.8 mL for LVESV. The limits-of-agreement analysis demonstrated minimal mean differences (bias, 6.7 mL for LVEDV and 3.9 mL for LVESV). 2D method also showed similar correlations with gated SPECT for LVEDV and LVESV ( $r = 0.96$  and  $0.98$ , respectively) with a SEE of 12.8 and 7.9 mL, respectively. There was an overall underestimation of volumes with greater limits of agreement by 2D method.

The results of LVEF regression and agreement analysis, which are shown in Figure 5, demonstrated high precision and accuracy ( $y = 0.82x + 5.1$ ,  $r=0.93$ ;  $p<0.001$ ; SEE, 7.6%; bias, 4.0%) and no significant mean differences between gated SPECT and 3D method. Because the degree of underestimation was same for LVEDV and LVESV by 2D method, over all agreement was good ( $r=0.95$ ;  $p<0.001$ ; SEE, 4.5%; bias, -1.8%). However, the regression line of 2D method for LVEF was significantly different from the line of identity ( $y=0.59x + 22.2$ ).

## DISCUSSION

3D reconstructions of LV volumes with the use of either freehand scanning techniques [10, 11] or rotational data acquisition [12-14] have previously been reported. More recently, real-time acquisition of LV volume data has been introduced [15]. However, the clinical application of these techniques is not widespread because of compromised image quality, challenging technical design and prolonged acquisition or processing times. We demonstrated that, with a magnetic position sensor integrated with the harmonic imaging system, 3D acquisition and reconstruction can be performed in a considerably shorter time than previously described. The clinical value depends on the amount of quantitative information that can be extracted from the data, and the quality of the tissue rendering. Compared to video-based systems, both these factors were improved using raw digital tissue data [5]. In addition, tissue harmonic imaging has been introduced and overall image quality is improved with particular enhancement of endocardial borders [16, 17]. Thus, the time and subjectivity involved in manual identification of the LV endocardial borders are minimal.

Freehand scanning techniques are conceptually biased because the image planes are not uniformly arranged. Thus, we collected a series of 10 to 20 apical tomograms using fan-like scanning. Because the probe movement

was measured continuously, geometrical distortion was minimized. An important characteristic of apical geometry is that the slice resolution is unchanged along the imaging axis at the same radial distances and is particularly useful for reconstructing the whole LV. In addition, this system could sample sufficient 4D data for a dynamic analysis of LV function.

The M-mode and 2D echocardiographic methods of estimating LV volumes have two major limitations-image position errors and use of geometric assumptions. Erbel et al. [18] has shown in a large percentage of patients that in the apical view of the LV is foreshortened due to anterior displacement of the imaging transducer by rib interference, thus potentially leading to underestimation of LV volumes. The accurate assessment of LV remodeling is integral to the clinical evaluation of patients with LV overload or dysfunction. In normal ventricles, assessment of LV size and function using M-mode echocardiography is adequate [19]. Therefore, 3D echocardiographic assessment is not necessary in all patients undergoing echocardiography. It is an important addition for the appropriate measurement of LV volumes in patients in whom LV dilation or remodeling is suspected, such as in patients with cardiomyopathy, previous myocardial infarction or valvular heart disease.

## Limitations

For patients with severe arrhythmias, this method described will result in reconstruction errors. Nonrepresentative cardiac cycles need to be eliminated during acquisition. The accuracy of the magnetic-field system diminishes if the receiver is  $>60$  cm from the transmitter. The calibration procedure can be time consuming. However, if the sensor is firmly attached to the ultrasound scanhead, the calibration need to be done only once.

## Conclusions

Rapidly acquired 3D data sets of apical tomograms using a magnetic-field system provide precise and accurate measurements of LV volumes and ejection fraction in humans. Because of the short duration of acquisition and processing time, this technique is clinically feasible, and it allows, repeated collection of 3D data during the course of a routine clinical examination, further enhancing the results.

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## FIGURE LEGENDS

Figure 1 A, The data were acquired using a Philips SONOS 5500 digital ultrasound scanner (right). For 3D data processing, a PC based 3D freehand system (3D EchoTech, Munich, Germany) was used (left). B, The magnetic-field transmitter (above) and receiver. The receiver is mounted directly on the scanhead.

Figure 2 LV volume measurement using equally spaced apical four-plane images (i.e., 45 degrees increments).

Figure 3 Linear regression analysis (left) and limits of agreement analysis (right) for LVEDV measurements by 2D method (2DE) (upper) and 3D method (3DE) (lower) compared with gated SPECT (QGS).

Figure 4 Linear regression analysis (left) and limits of agreement analysis (right) for LVESV measurements by 2D method (2DE) (upper) and 3D method (3DE) (lower) compared with gated SPECT (QGS).

Figure 5 Linear regression analysis (left) and limits of agreement analysis (right) for LVEF measurements by 2D method (2DE) (upper) and 3D method

(3DE) (lower) compared with gated SPECT (QGS).