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Live/Real Time Three-Dimensional Transthoracic Echocardiographic Assessment of Left Ventricular Volumes, Ejection Fraction, and Mass Compared with Magnetic Resonance Imaging

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Due to reliance upon geometric assumptions and foreshortening issues, the traditionally utilized transthoracic two-dimensional echocardiography (2DTTE) has shown limitations in assessing left ventricular (LV) volume, mass, and function. Cardiac magnetic resonance imaging (MRI) has shown potential in accurately defining these LV characteristics. Recently, the emergence of live/real time three-dimensional (3D) TTE has demonstrated incremental value over 2DTTE and comparable value with MRI in assessing LV parameters. Here we report 58 consecutive patients with diverse cardiac disorders and clinical characteristics, referred for clinical MRI studies, who were evaluated by cardiac MRI and 3DTTE. Our results show good correlation between the two modalities. (ECHOCARDIOGRAPHY, Volume 24, February 2007)

real time three-dimensional echocardiography, *transthoracic echocardiography*, *cardiac MRI*, *left ventricle*

It is well established that left ventricular (LV) hypertrophy and ejection fraction (EF) are themselves prognostic factors for cardiac events. Traditionally two-dimensional transthoracic echocardiography (2DTTE) and M-mode echocardiography have been the means used to assess LV dynamics, but their limited test-retest reliability is well known. LV volume and mass measurements with 2DTTE rely on geometric assumptions of uniform chamber size that have proven only accurate and reproducible with normal ventricles.[1] Image plane positioning for correct long-axis views from apical windows is often not possible. Hence, foreshortened views of the apex that underestimate measurements are often obtained.[2] Thus the accurate assessment and reassessment of diseased myocardium is difficult. Cardiac MRI has proven an alternative for accurate LV assessment but the cost and availability of MRI is largely impractical for routine clinical use.[1] The emergence of live/real time 3DTTE (RT-3DTTE) provides the ability to achieve the accuracy of MRI and improve the clinical utility of 2DTTE.

RT-3DTTE improves the accuracy of determining LV volumes and mass compared with 2DTTE because geometric assumptions are eliminated. As a result, these measurements correlate well with those of direct MRI measurements.[1–14] This has proven especially important in clinical population with structurally

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abnormal hearts.[14] RT-3DTTE has been studied in the evaluation of patients with hypertrophic cardiomyopathies, dilated cardiomyopathies, and in adults and children with known congenital heart disease.[15–18] RT-3DTTE is comparable to MRI for the determination of LV mass with great accuracy and reproducibility providing for serial assessment of LV mass and mass changes.[7–14]

The objectives of this study were to assess LV volumes, EF, and mass by RT-3DTTE, and compare with an MRI reference standard for accuracy. Our goal was to extend the comparison of RT-3DTTE with cardiac MRI, in a more clinically diverse and slightly larger patient population than previous studies, in order to further validate and support growing knowledge that RT-3DTTE provides accurate assessment of these important clinical variables.

Methods

Fifty-eight consecutive patients (40 men, 18 women; mean age 59 years, range 21–83) with various cardiac disorders referred for clinical MRI studies were evaluated by MRI and RT-3DTTE. Our patient population included 23 individuals with the diagnosis of coronary artery disease (CAD), 14 normals, 7 individuals with dilated cardiomyopathy, 3 individuals with atrial or ventricular septal defects, and 3 patients with valvular heart disease. Exclusion criteria were atrial fibrillation, pacemaker or defibrillator implantation, claustrophobia, and contraindications to MRI. Patients with cardiac arrhythmias, left bundle-branch block, and prior sternotomy were also excluded. RT-3DTTE data acquisition was performed on the same day as the MRI study. Institutional IRB approval was obtained prior to initiation of the study and all patients gave informed consent.

Live/Real Time Three-Dimensional Echocardiography

RT-3DTTE imaging was performed from the apical window of the LV with patients in the left lateral decubitus position by use of a commercial scanner (iE33, Philips Medical Systems, Andover, MA, USA) equipped with a 4X matrix array transducer. To encompass the complete LV into the 3D dataset, a full volume scan was acquired. For this purpose, a pyramidal volume of 93° × 84° was scanned, which was divided into four conical subvolumes. The acquisition of the subvolumes was steered electronically by the ultrasound system while the transducer was kept in a stable position. A full cardiac cycle was acquired for each subvolume. To accomplish the correct spatial registration of each subvolume, the acquisition was performed in an end-expiratory breath-hold lasting 6 to 8 seconds (depending on the heart rate). The 3D datasets were stored digitally for off-line analysis.

Data Analysis

LV MASS

The 3D dataset was analyzed offline using the TomTec Echoview version 5.2 (TomTec GmbH, Munich, Germany). We selected the anatomically correct 2- and 4-chamber views with the largest long-axis dimension. Around this user-defined LV long axis, the software generated 8 uniformly spaced apical images 22.5 degrees apart for each LV mass calculation. In each view, epicardial and endocardial contours, including the trabeculations and papillary muscles in the LV cavity, were traced manually at end-diastole. The traced contours were then used to calculate a myocardial volume. This volume was multiplied by the density of myocardial tissue (1.05 g/ml).

LV Volumes and EF

In each dataset end-systolic and end-diastolic frames were identified. End diastole was defined as the frame in the cardiac cycle in which the cardiac dimension was largest. End systole was defined as the frame in the cardiac cycle in which the cardiac dimension was smallest. Around a user-defined LV long axis, the software generated eight uniformly spaced apical images 22.5 degrees apart for each volume. The systolic and diastolic images were manually traced. LV trabeculations and papillary muscles were also included within the traced area. Subsequently, LV end-systolic volume (ESV) and LV end-diastolic volume (EDV) were calculated by the system automatically, as described in the instruction manual of the TomTec Echoview version 5.2 (TomTec GmbH, Munich, Germany). LV EF was calculated as (EDV-ESV)/EDV × 100%.

Magnetic Resonance Imaging and Analysis

Cardiac MRI examinations were done on a whole body 1.5 T scanner (Magnetom Symphony, Siemens, Erlangen, Germany) using a body-array coil for signal detection. After localizing scout images, True fast-imaging steadystate procession (TrueFISP) cine sequences with prospective ECG gating were acquired as previously described[18] in short-axis orientation, covering the entire heart, with an echo time (TE) of 1.86 ms, a repetition time (TR) of 55.65 ms, slice thickness of 5 mm, field of view of 320 mm and a matrix size of 148 × 256. Image analysis was performed on short-axis cine images. For contour tracing and evaluation of the end-systolic and end-diastolic short-axis views, an evaluation program (ARGUS, Siemens Medical System, Erlangen, Germany) on an independent satellite console was used. The window and level settings of a representative mid-ventricular image were optimized for best image contrast between the myocardium and ventricular lumen and consecutively applied to all images. The window and level settings were optimized for individual images, if necessary. The end-diastolic images were always the images immediately after the R-wave. The LV end-systolic images were selected as the images with the smallest area of the left cardiac chamber as visually assessed by displaying slow movie frames at several mid-ventricular levels. Afterwards LV ESV, LV EDV, and LV EF were calculated automatically.

Interobserver and Intraobserver Variability

To determine the interobserver variability in the RT-3DTTE evaluations of LV mass, LV EDV, LV ESV, and LV EF, a randomly selected subgroup of patients (n = 20) was analyzed a second time by a second observer blinded to the values obtained by the first observer and MRI measurements. To assess the intraobserver variability in LV mass, LV EDV, LV ESV, and LV EF measurements from RT-3DTTE, a randomly selected subgroup of patients (n = 20) was analyzed a second time after two weeks by the same observer, blinded to the previous results and MRI measurements.

Statistical Analysis

All values are expressed as means ± SD. The 3DTTE measurements were compared with MRI values using a linear regression analysis for the comparison of LV mass, LV EDV, LV ESV, LV EF, and the results of two independent observations. Pearson correlation coefficient and standard error of the estimate (SEE) were also computed. Agreements between 3DTTE and MRI reference standard were evaluated using Bland–Altman analysis. Interobserver and intraobserver variability was expressed relative to the average values plus 2 SDs by Bland–Altman analysis. A P value <0.05 was considered significant.

Results

RT-3DTTE Versus MRI

Data were collected from 58 patients using the methodology indicated above in which image quality was judged as optimal for comparison. Population descriptive statistics are shown graphically in Tables I and II. Paired sample statistics from the two groups are shown in Tables III and IV expressing mean values, standard deviation, and standard error of means. Overall the high correlation coefficients between RT-3DTTE and MRI support the reliability we sought to find in this study.

The linear regression curves for the three LV volume parameters are shown in Figures 1–3. Linear correlation analysis of EDV is shown in Figure 1A with a correlation coefficient of $r = 0.92$ and standard error of the estimate (SEE) of 21 ml. The Bland–Altman analysis displayed in Figure 1B, shows a bias of −22 ml and standard deviation (SD) of 23 ml for the comparison of RT-3DTTE with MRI. Comparisons of ESV is shown in the linear regression Figure 2A, with $r = 0.94$, SEE = 16 ml. Bland–Altman analysis for the RT-3DTTE to MRI comparison of ESV, shown in Figure 2B, revealed a bias of −15 ml and SD of 20 ml. The comparison of EF has a correlation coefficient of $r = 0.92$, SEE of 10%, and Bland–Altman bias of +5% with SD of 10% displayed in Figures 3A and 3B. All the three volume parameters showed high correlations with $r > 0.9$. Negative bias for both EDV and ESV, showed an underestimation for 3DTTE compared with the MRI modality used in our study. Notably, in evaluating these parameters, our study population contained three individuals with markedly dilated ventricles associated

TABLE I

Population Descriptive Statistics

	N	Minimum	Maximum	Mean	Standard Deviation
Sex	58	1	2	1.69	0.467
Age	58	21	83	58.97	16.932
Height	58	143	186	163.31	8.794
Weight	58	39	106	65.71	13.898
BSA	58	1.27	2.23	1.7091	0.20520

BSA = body surface area.

TABLE II

Descriptive Statistics

	N	Minimum	Maximum	Mean	Standard Deviation
Age	58	21	83	58.97	16.932
D-mass	58	51.14	301.46	124.9464	48.70693
D-index	58	30.44	143.67	72.8778	25.47407
D-EDV	58	45.40	396.00	117.3603	53.24439
D-ESV	58	16.90	310.80	64.3017	46.79865
D-EF	58	19.00	66.90	48.9897	12.99225
MRI-mass	58	39.49	299.81	116.8000	47.43754
MRI-index	58	26.15	134.44	67.7899	24.31525
MRI-EDV	58	60.00	426.97	139.4510	59.18294
MRI-ESV	58	19.00	357.59	79.7460	57.26137
MRI-EF	58	11.55	71.10	47.3241	16.86189

D = RT-TTE values; MRI = cardiac MRI values; mass = LV mass; index = mass index; EDV = end diastolic volume; ESV = end systolic volume; EF = ejection fraction.

with the clinical diagnosis of dilated cardiomyopathy. Inclusion or exclusion of the largest of these did not significantly affect correlations between RT-3DTTE and MRI for LV EDV and LV ESV.

Evaluation of LV mass revealed a similarly high correlation between RT-3DTTE and MRI, with r = 0.933 and SEE = 18 (Fig. 4A). Bland–Altman analysis, displayed in Figure 4B, had a bias of +8.14 with SD of 17.6%. Mass index was also compared between RT-3DTTE and MRI with correlations r = 0.916, SEE 10.30 with Bland–Altman analysis bias of +5.08 with SD of 10%.

Interobserver and intraobserver variability was expressed relative to the average values ± 2 SDs and displayed by Bland–Altman analysis. Pearson correlation coefficients and SEE are displayed in Tables V and VI. Results of the interobserver variability showed no significant difference between the two observers. The results for intraobserver variability had volume parameters of significant correlation with EDV r = 0.947, SEE 11.84 ml, ESV r = 0.982, SEE 5.95 ml, and EF r = 0.948, SEE 3.55%. LV mass also had limited variability with correlation r = 0.952 and SEE 11.34.

Discussion

The results of this study indicate that RT-3DTTE has good agreement with the reference standard MRI in assessing LV parameters and further validates this technology in a diverse patient population. Correlation of all clinical indices was acceptable in our patient group with a wide range of cardiac disease and resulting LV dynamics. Based on Bland–Altman

TABLE III

Paired Samples Statistics

		N	Standard Deviation	Standard Error Mean
D-mass	124.9464	58	48.70693	6.39553
MRI-mass	116.8000	58	47.43754	6.22885
D-index	72.8778	58	25.47407	3.34491
MRI-index	67.7899	58	24.31525	3.19275
D-EDV	117.3603	58	53.24439	6.99133
MRI-EDV	139.4510	58	59.18294	7.77110
D-ESV	64.3017	58	46.79865	6.14496
MRI-ESV	79.7460	58	57.26137	7.51879
D-EF	48.9897	58	12.99225	1.70597
MRI-EF	47.3241	58	16.86189	2.21408

D = RT-TTE values; MRI = cardiac MRI values; mass = LV mass; index = mass index; EDV = end diastolic volume; ESV = end systolic volume; EF = ejection fraction.

TABLE IV

Descriptive Statistics

	N	Minimum	Maximum	Mean	Standard Deviation
DIF-mass	20	−24.04	20.16	−1.795	11.554
DIF-EDV	20	−24.50	24.0	−4.29	13.31
DIF-ESV	20	−13.30	13.90	−2.51	6.856
DIF-EF	20	−6.5	8.4	−0.260	3.703

Mass = LV mass; index = mass index; EDV = end diastolic volume; ESV = end systolic volume; EF = ejection fraction; DIF = differences.

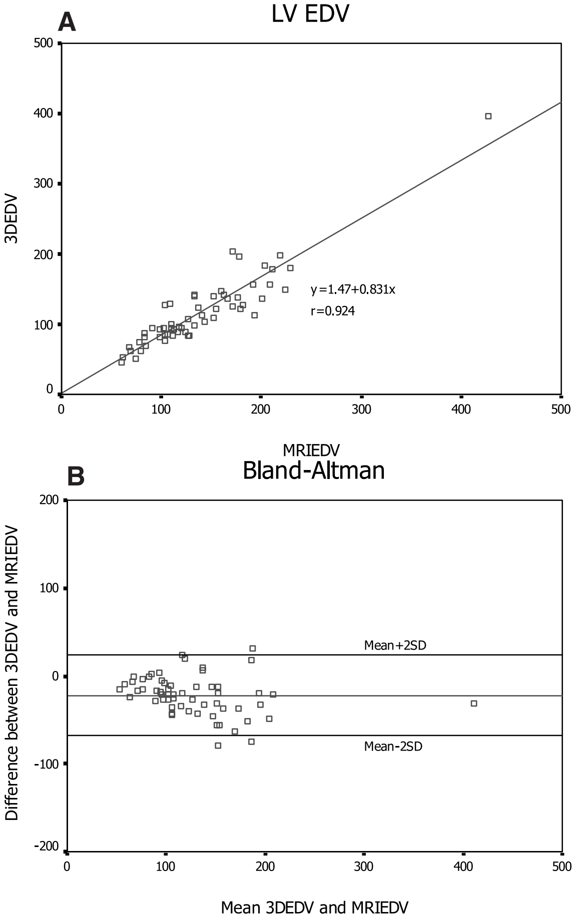

Figure 1. *Comparison of three-dimensional echocardiographic (3D) and MRI derived measures of left ventricular end-diastolic volumes (LV EDV).*

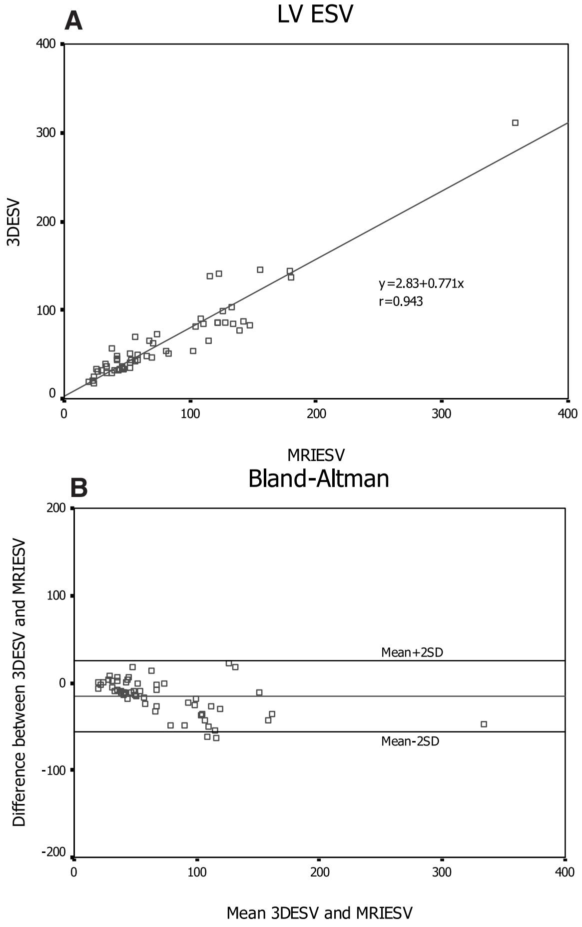

Figure 2. *Comparison of three-dimensional echocardiographic (3D) and MRI derived measures of left ventricular end-systolic volumes (LV ESV).*

analysis there was a slight tendency toward overestimation with respect to mass values and a small underestimation with respect to ventricular volumes. Due to limitations of RT-3DTTE and of cardiac MRI that was used as reference standard, we do not think an exact one to one correlation is possible or is of clinical significance. These limitations specifically include difficulty with 3DTTE acquisition of the entire ventricle in the largest cases, and the technical limitations of acquiring the MRI dataset at irregular heart rates with certain arrhythmias and during a breath hold. Also, 3D echo estimation of volumes is based on the rotation of apical planes and surface reconstruction of the 3D surface, while MRI estimation is derived from traced areas and known slice thickness and utilizes Simpson's rule. These algorithms are fundamentally different and have different partial volume effects and may contribute to differences between 3D echo and MRI estimations. However, the narrow limits of agreement shown by the Bland–Altman analysis reflect the high accuracy between the two modalities. To further strengthen the assessment, intraobserver and interobserver variabilities were limited as measurement variability was low between two independent observers.

The progression of RT-3DTTE to becoming a utility of everyday noninvasive cardiology was first supported by multiple studies that established its accuracy and reproducibility over standard 2DTTE.[1–4,9,12,18,19] Several studies have since gone on to show its accuracy and reproducibility to be comparable to cardiac MRI or CT.[9,10,14,18–20] Most studies have been done in small and generally diseased populations.[6,10,13] Although each differed in study size

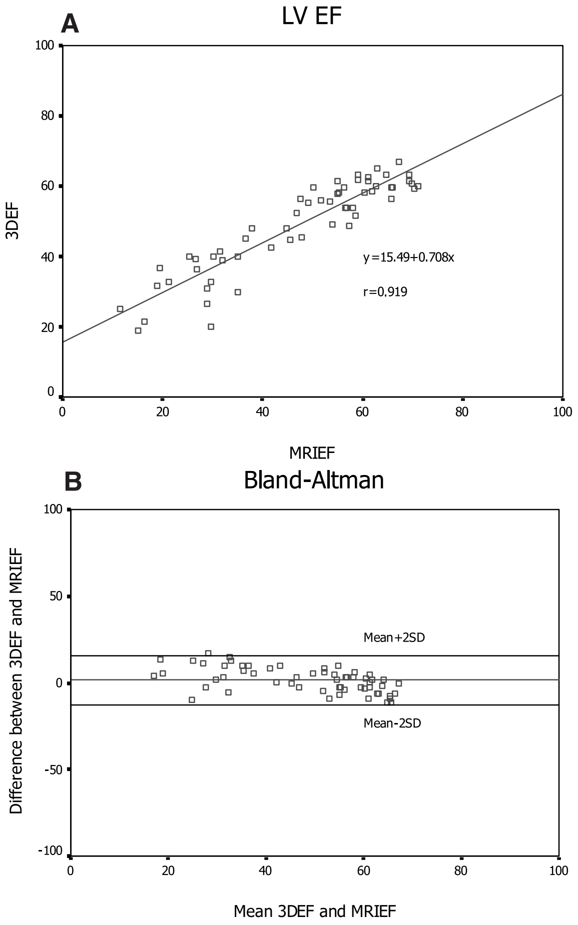

Figure 3. *Comparison of three-dimensional echocardiographic (3D) and MRI derived measures of left ventricular ejection fraction (LV EF).*

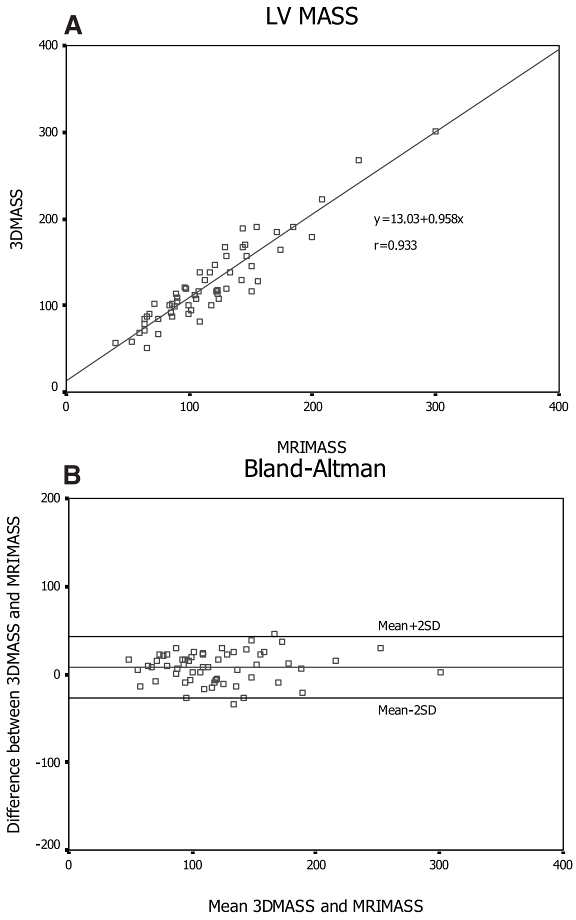

Figure 4. *Comparison of three-dimensional echocardiographic (3D) and MRI derived measures of left ventricular mass (LV MASS).*

and in variability of the studied patient population, all have shown similar results. Caiani et al. compared 2DTTE, RT-3DTTE, and MRI for LV volume measurements alone.[19] Similar to our study correlation coefficients were used to express reproducibility. In the areas of ESV, EDV, and EF correlation coefficients (r value) greater that 0.9 were seen in the group comparing 3DTTE and MRI. They also demonstrated no significant bias by Bland–Altman analysis. Lee et al. compared RT-3DTTE to MRI in a small population of patients with known cardiac disorders and found no statistical difference between each group with correlation values greater than 0.92.[6] With respect to LV mass, Mor-Avi et al. published a study of 21 patients comparing 2DTTE, 3DTTE, and cardiac MRI.[10] Their study reported that the lack of foreshortening with 2 and 4 chamber apical views using RT-3DTTE produced correlation results reaching 0.90 compared to cardiac MRI whereas the 2DTTE correlations were less than 0.80. Sugeng et al. extended the RT-3DTTE and cardiac MRI comparison to include cardiac CT (CCT). In their 31 patient dataset both CCT

TABLE V

Correlation of Intraobserver Variability

	R Value	Regression Equation	SEE
EDV	0.947	Y = 12.85 + 0.841x	11.84
ESV	0.982	Y = 3.48 + 0.894x	5.956
EF	0.948	Y = 5.61 + 0.894x	3.55
Mass	0.952	Y = 7.25 + 0.919x	11.34

Mass = LV mass; EDV = end diastolic volume; ESV = end systolic volume; EF = ejection fraction.

TABLE VI

Correlation of Interobserver Variability between Observer 1 and Observer 2

	R Value	Regression Equation	SEE
EDV	0.995	Y = 0.974× − 0.66	6.631
ESV	0.998	Y = 0.995× − 3.591	3.597
EF	0.980	Y = 0.99 − 0.605x	2.701
Mass	0.973	Y = 7.83 + 0.872x	11.27

Mass = LV mass; EDV = end diastolic volume; ESV = end systolic volume; EF = ejection fraction.

and RT-3DTTE measurements resulted in high correlation compared with MRI.[13] Interestingly CCT significantly overestimated end-diastolic and end-systolic volumes resulting in a small but significant bias in ejection fraction whereas RT-3DTTE underestimated end-diastolic and end-systolic volumes only slightly with no significant bias. Our current research serves to further validate these and other studies and expand the application of RT-3DTTE to a larger and more diverse clinic population with respect to cardiac disease state, gender, and age.

Conclusion

This study demonstrates the comparable accuracy of RT-3DTTE and cardiac MRI to quantify LV volume, mass, and EF. We feel that there is an important need for continued validation studies on larger and more diverse patient populations as the one we present to establish the use of RT-3DTTE in clinical cardiology.

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