

# Quantification of left ventricular volumes using three-dimensional echocardiographic speckle tracking: comparison with MRI

Hans-Joachim Nesser<sup>1</sup>, Victor Mor-Avi<sup>2</sup>, Willem Gorissen<sup>3</sup>, Lynn Weinert<sup>2</sup>, Regina Steringer-Mascherbauer<sup>1</sup>, Johannes Niel<sup>1</sup>, Lissa Sugeng<sup>2</sup>, and Roberto M. Lang<sup>2\*</sup>

<sup>1</sup>Public Hospital Elisabethinen, Linz, Austria; <sup>2</sup>University of Chicago, MC5084, 5841 S. Maryland Ave., Chicago, IL 60637, USA; and <sup>3</sup>Toshiba Medical Systems, Zoetermeer, the Netherlands

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## Aims

Although the utility of two-dimensional (2D) speckle tracking echocardiography (STE) to quantify left ventricular (LV) volume has been demonstrated, this methodology is limited by foreshortened views, geometric modelling, and the assumption that speckles can be tracked from frame to frame, despite their out of plane motion. To circumvent these limitations, a three-dimensional (3D) speckle tracking algorithm was recently developed. Our goal was to evaluate the accuracy of the new 3D-STE side by side with 2D-STE using cardiac magnetic resonance (CMR) as a reference.

## Methods and results

Apical two- and four-chamber views (A2C and A4C) and real-time 3D datasets (Toshiba Artida 4D System) obtained in 43 patients with a wide range of LV size and function were analysed to measure LV end-systolic and end-diastolic volumes (ESV and EDV) using 2D and 3D-STE techniques. Short-axis CMR images (Siemens 1.5T scanner) acquired on the same day were analysed to obtain ESV and EDV reference values using the method of disks approximation. Reproducibility of both STE techniques was assessed using repeated measurements. While 2D-STE correlated well with CMR ( $r$ : 0.72–0.88), it underestimated LV volumes with relatively large biases (10–30 mL) and wide limits of agreement (SD: 36–51 mL), with A2C-derived measurements being worse than A4C values. The 3D-STE measurements showed higher correlation with CMR (0.87–0.92), and importantly smaller biases (1–16 mL) and narrower limits of agreement (SD: 28–37 mL). In addition, 3D-STE showed lower inter- and intra-observer variability (11–14% and 12–13%), than 2D-STE (16–17% and 12–16%, respectively).

## Conclusion

This is the first study to validate the new 3D-STE technique for LV volume measurements and demonstrate its superior accuracy and reproducibility over previously used 2D-STE technique.

## Keywords

Echocardiography • Magnetic resonance imaging • Left ventricle

## Introduction

The recognition of the subjective nature of visual interpretation of left ventricular (LV) dynamics from echocardiographic images has sparked the development of a variety of techniques for quantitative evaluation of global and regional LV function. Currently, tissue Doppler imaging (TDI) is most frequently used for the assessment

of LV mechanics. Because of the known limitations of this technique, mostly associated with its angle dependency, it has been increasingly replaced by the more recently developed speckle tracking echocardiography (STE), which intrinsically circumvents most of the shortcomings of TDI. This latter technique is based on tracking local image details from frame to frame throughout the cardiac cycle.<sup>1</sup> Multiple investigators applied this approach to

\* Corresponding author. Tel: +1 773 702 1842, Fax: +1 773 702 1034, Email: rlang@bsd.uchicago.edu

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two-dimensional (2D) echocardiographic images to assess global and regional LV function using parameters such as myocardial strain<sup>2–16</sup> and rotational motion (twist/untwist) patterns,<sup>17–32</sup> and ventricular dyssynchrony.<sup>8–13,15,33,34</sup> 2D-STE was also used for tracking of the endocardial boundary and favourably tested for the quantification of LV<sup>35</sup> and atrial<sup>36</sup> volume and function.

However, like all 2D echocardiographic techniques used for LV volume quantification, 2D-STE quantification is likely to be affected by the use of foreshortened apical views<sup>37</sup> and geometric assumptions. Moreover, an additional limitation of this methodology is its 2D nature which limits its ability to track motion occurring within the imaging plane, while motion in and out of plane can only be detected as features appearing and disappearing from the image, resulting in noise and interfering with tracking.<sup>38,39</sup> With the three-dimensional (3D) anatomy of the LV and the complex 3D patterns of wall motion, the inability to quantify one of the three components of the local displacement vector is a major limitation. This inability precludes accurate evaluation of the true magnitude of the displacement vector and affects the accuracy of the evaluation of the derived indices of local dynamics. The newly developed 3D speckle tracking in real-time 3D echocardiographic (RT3DE) datasets has the potential to circumvent these limitations because: (i) it does not rely on 2D views that can be foreshortened, and (ii) it tracks motion of speckles within the scan volume, irrespective of its direction.<sup>40</sup>

Although this 3D technique promises to allow more accurate assessment of the regional ventricular dynamics, it requires rigorous testing and validation against other accepted techniques on different levels. One test of the ability of this new technique to correctly detect and accurately track the endocardial surface throughout the cardiac cycle is to determine how accurately it can quantify LV volumes. Accordingly, the aim of this study was to compare side-by-side 2D- and 3D-STE dynamic measurements of LV volumes against cardiac magnetic resonance (CMR) reference values in patients with a wide range of LV size and function.

## Methods

### Population

Forty-three subjects (28 males and 15 females, age:  $59 \pm 16$  years) were studied. These 43 subjects were selected from 47 who were scanned for transthoracic 2D acoustic windows that allowed adequate endocardial visualization throughout the cardiac cycle. Additional exclusion criteria were: dyspnoea precluding a 10–15 s breath-hold, atrial fibrillation, or other cardiac arrhythmias, pacemaker or defibrillator implantation, claustrophobia, and other known contraindications to CMR imaging. Of these 43 patients, 9 were normal volunteers, 17 had coronary artery disease (including 6 post myocardial infarction), 10 had dilated cardiomyopathy, 4 had myocarditis, and 3 had valvular disease. In each patient, RT3DE and CMR imaging were performed on the same day. The protocol was approved by the Institutional Review Board, and written informed consent was obtained in all patients.

### Echocardiographic imaging

Imaging was performed from the apical window with the patient in the left lateral decubitus position using a commercial scanner (Artida 4D, Toshiba Medical Systems) in the tissue harmonic mode. Before each acquisition, images were optimized for endocardial visualization by

modifying the gain, compress, and time-gain compensation controls. First, 2DE images were obtained using the PST-30SBT transducer in apical two- and four-chamber (A2C and A4C) views, while making an effort to avoid foreshortening. Then, RT3DE imaging was performed from the same apical position using the fully sampled matrix array transducer (PST-25SX). A wide-angled acquisition ‘full-volume’ mode was used, in which six wedge-shaped sub-volumes were acquired over six consecutive cardiac cycles during a single breath-hold, resulting in this study in temporal resolutions between 11 and 23 frames per cardiac cycle (mean  $18 \pm 3$ ), depending on heart rate. No medication was given to control the heart rate. Special care was taken to include the entire LV cavity within the pyramidal volume. Both 2DE and RT3DE images were stored digitally for off-line analysis.

### Two-dimensional speckle tracking analysis

Apical two- and four-chamber views were analysed using wall motion tracking software (Toshiba Medical Systems). Following manual initialization of the LV endocardial border, endocardial contours were tracked automatically frame by frame, with the papillary muscles included in the LV cavity. Endocardial contours were manually adjusted when necessary to optimize the boundary position. All measurements were performed by an investigator experienced in the interpretation of echocardiographic images, who was blinded to the results of both the 3D-STE and CMR measurements. Left ventricular volume was automatically calculated throughout the cardiac cycle and the resulting volume curve was analysed to obtain end-diastolic and end-systolic volumes (EDV and ESV) that were identified as the maximum and minimum values, respectively.

### Three-dimensional speckle tracking analysis

Pyramidal RT3DE datasets were analysed using the 3D wall motion tracking software (Toshiba Medical Systems) by an investigator experienced with STE analysis who was blinded to the results of both the 2D-STE and CMR measurements. First, six-chamber views as well as three short-axis views at different levels of the left ventricle from base to apex were automatically selected from the RT3DE pyramidal dataset in the first time frame of the dataset, i.e. end-diastole. Then the anatomically correct, non-foreshortened apical views were identified by finding the largest long-axis dimensions. In these two planes, LV endocardial boundaries were manually initialized, while including the papillary muscles in the LV cavity. Then, the 3D endocardial surface was automatically reconstructed and tracked in 3D throughout the cardiac cycle. Finally, the endocardial surface was manually adjusted when necessary in the above five planes until best match was visually verified. For each consecutive time frame, voxel count inside the detected endocardial surface was used to calculate LV volume. End-diastolic volume and ESV were then obtained from the LV volume curves as the maximum and minimum values, respectively.

### Cardiac magnetic resonance imaging

CMR images were obtained using a 1.5 Tesla scanner (Siemens, MAGNETOM Sonata, Erlangen, Germany) with a phased-array cardiac coil. Electrocardiogram-gated localizing spin-echo sequences were used to identify the long axis of the heart. Steady-state free precession (true FISP) dynamic gradient-echo mode was then used to acquire images using retrospective ECG gating and parallel imaging techniques (mSENSE) during 10 to 15 s breath-holds with a temporal resolution of 30 frames per cardiac cycle. In all patients, cine-loops of 8 mm thick short-axis slices with 2 mm gaps and  $2.0 \times 2.0$  mm in-plane

spatial resolution were obtained from just above the ventricular base to just below the apex. Images were stored digitally for off-line analysis.

### Cardiac magnetic resonance image analysis

CMR images were analysed using commercial software (Argus, Siemens, Erlangen, Germany). Analysis included slices from the first basal slice that showed the mitral annulus through the last apical slice that showed LV cavity. Left ventricular endocardial boundary was semi-automatically traced with the papillary muscles and trabeculae included in the LV cavity in every slice at end-diastole (first frame in the sequence) and end-systole (smallest LV cavity, as visually determined from two to three different slices), and manually adjusted when necessary. All tracings were performed by investigators experienced in CMR analysis of LV volume, who had no knowledge of any prior measurements. End-systolic volume and EDV were calculated using the disk-area summation method. These values were used as a reference for comparison with the 2D- and 3D-STE data.

### Reproducibility analysis

To determine the reproducibility of LV volume measurements for both STE techniques and CMR, image analysis was repeated in a random sample of 15 patients by an additional investigator as well as by the same primary reader at least 1 week later. During these repeated analyses, the investigators were blinded to the results of all prior measurements. Inter- and intra-observer variability was calculated as the absolute difference of the corresponding pair of repeated measurements in percent of their mean in each patient and then averaged over the 15 patients.

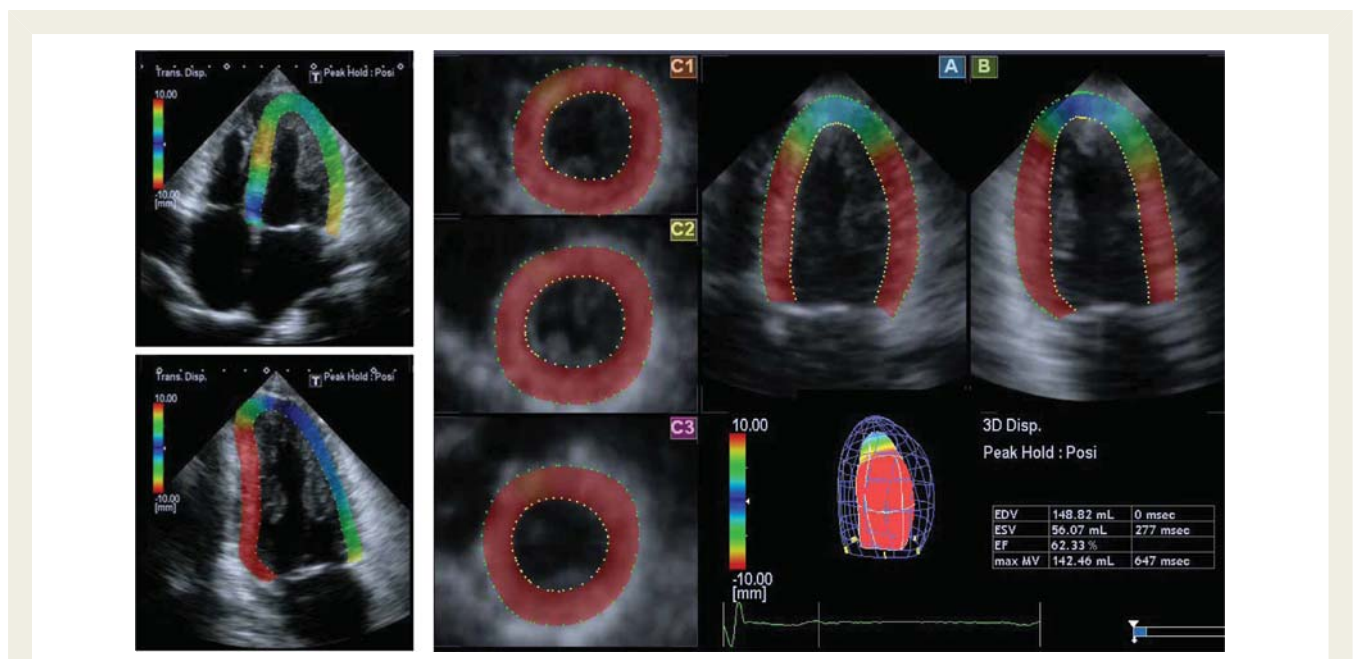
### Inter-technique comparisons and statistics

Both 2D- and 3D-STE-derived LV volumes were compared with the CMR reference values. The comparisons included linear regression, intra-class correlation, and Bland–Altman analyses to assess the bias and limits of agreement with the CMR reference. The significance of the biases between the STE and CMR measurements was tested using paired *t*-tests. *P*-values <0.05 were considered significant.

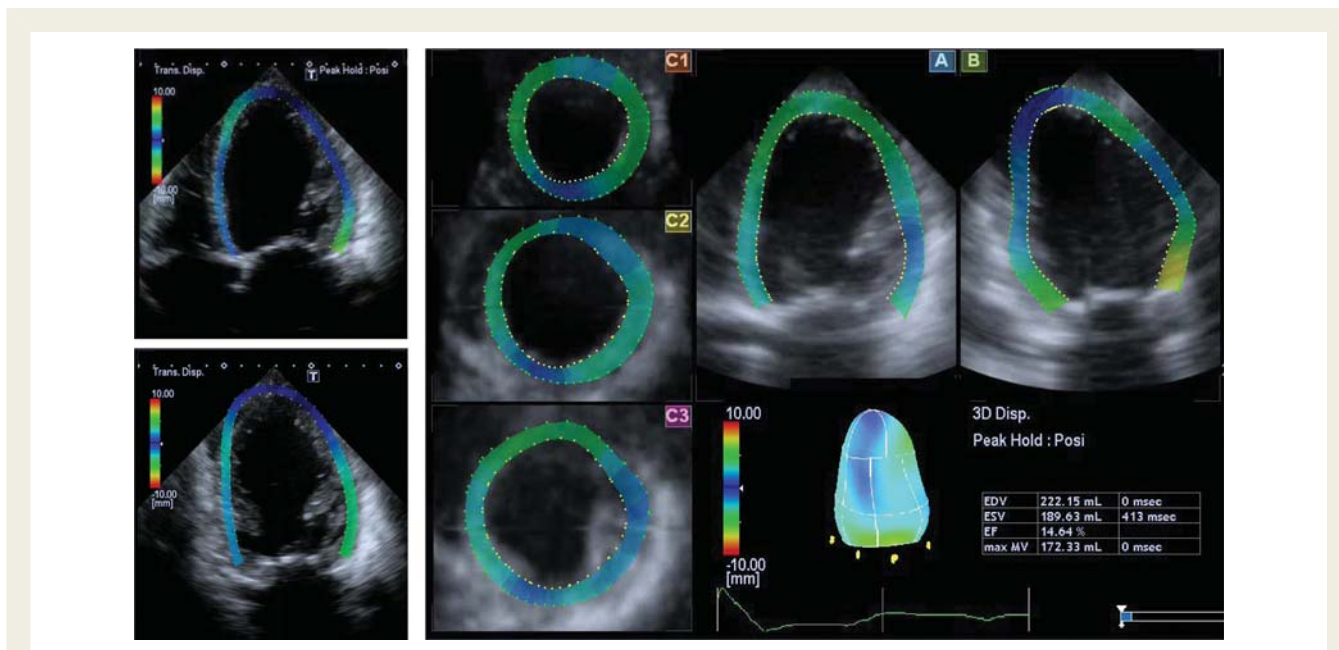
### Results

Both 2D- and 3D-STE were feasible in all study subjects, including the enlarged ventricles of the cardiomyopathic patients (CMR-derived EDV ranged from 99 to 441 mL and ESV ranged from 39 to 383 mL). The time required for 3D-STE image analysis, including surface detection throughout the cardiac cycle, manual adjustments, and the computation of LV volumes, less than 5 min on a Pentium 4 personal computer.

Figure 1 shows an example of 2D-STE (left) and 3D-STE (right) images obtained at end-systole in a patient with normal LV wall motion and concentric hypertrophy (EF = 62%), with endocardial displacement information shown in semi-transparent colour overlays superimposed on the gray-scale images. The colour patterns in both 2D A4C and A2C views showed considerable variability in the measured regional displacement, as reflected by different colours, despite the normal LV function, reflecting out of plane motion of the speckles. In contrast, the 3D slices extracted from the RT3DE datasets showed considerably more uniform colour patterns, consistent with normal LV wall motion, in the short-axis



**Figure 1** Example of images obtained at end-systole in a patient with normal left ventricular function and concentric hypertrophy: Left: two-dimensional speckle tracking echocardiography (top: A4C view; bottom: A2C view); and three-dimensional speckle tracking echocardiography views extracted from the RT3DE pyramidal dataset [right: (A) and (B)—A4C and A2C views, and C1, C2, C3—short-axis views from apex to base]. Displacement information is shown in semi-transparent colour overlays superimposed on the grey-scale images and a colour-coded 3D cast. See text for details.



**Figure 2** Example of two-dimensional and three-dimensional speckle tracking echocardiography images obtained at end-systole in a patient with dilated cardiomyopathy, shown in the same format as in Figure 1. See text for details.

views and also in the apical long-axis views, where one can also appreciate the gradual decrease in endocardial displacement towards the LV apex: from 8–9 mm represented by the red colour down to 2–6 mm range represented by the blue to green colours.

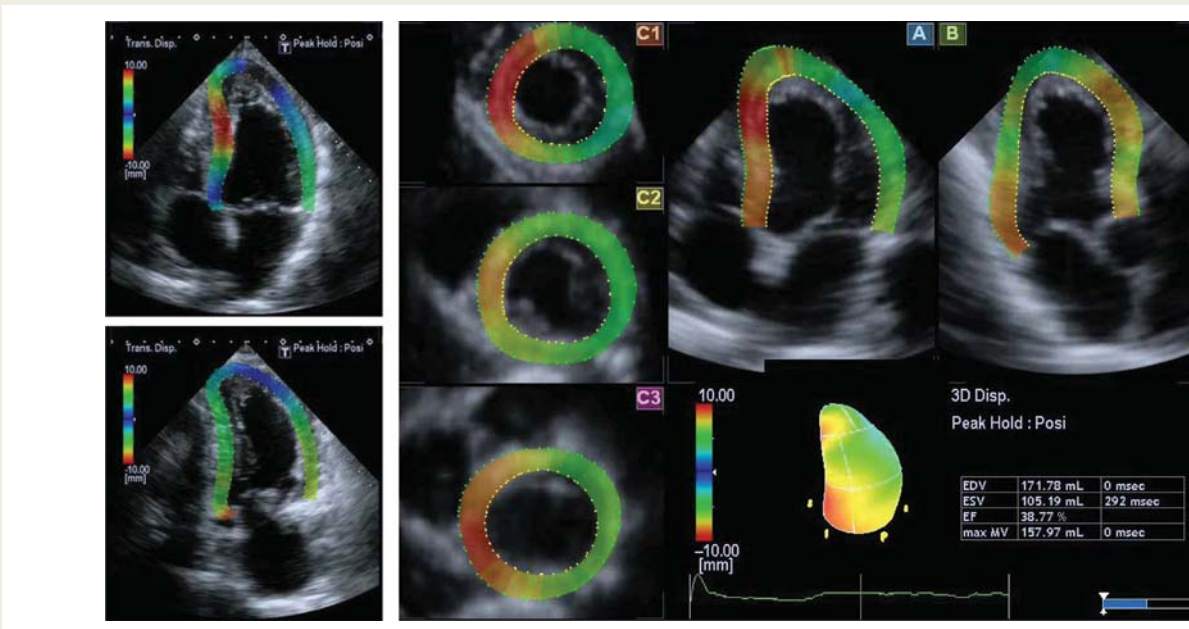
Figure 2 shows in the same format an example of images obtained at end-systole in a patient with dilated cardiomyopathy (EF = 15%). In both 2D and 3D images, the myocardial wall is thinned (narrowed colour band) and the motion is reduced, as reflected by minimal end-systolic endocardial displacement (mostly blue and green colours) throughout all ventricular walls.

Figure 3 shows an example of images obtained in a patient post infero-lateral myocardial infarction. While the colour patterns in the 2D-STE images were not clearly different from those of the normal ventricle shown in Figure 1, short-axis slices extracted from the RT3DE dataset clearly depicted reduced displacement in the infero-lateral and antero-lateral walls (reflected by the green colour), accompanied by myocardial thinning (narrowed colour band) in the infero-lateral wall, both consistent with the history of infarction in this region. Both reduced displacement and reduced myocardial thickness were also evident in the lateral wall in the A4C view.

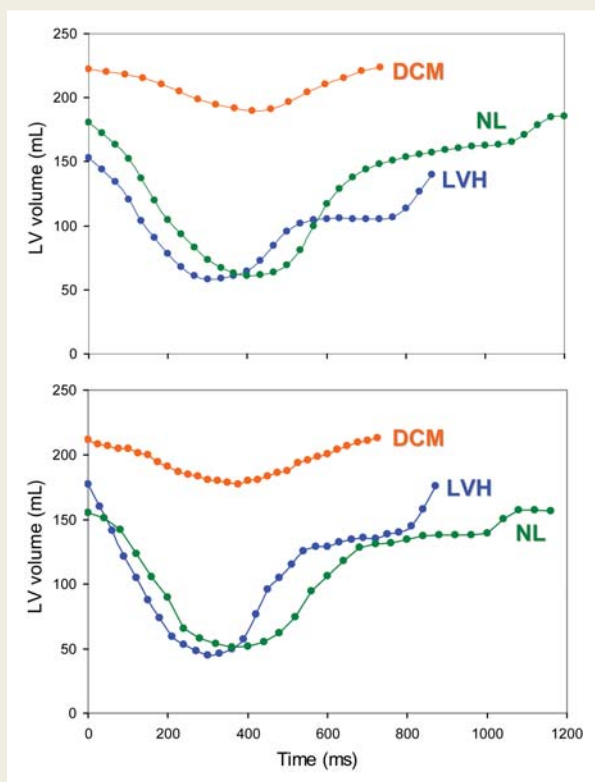
Figure 4 shows three examples of volume over time curves obtained using 3D-STE and CMR in a patient with normal LV function, a patient with dilated cardiomyopathy, and a patient with concentric LV hypertrophy. In each of the three patients, these curves are similar between the two modalities and have the well-known morphology of the LV volume time curves and clearly depict the differences between the three patients specific to their pathology.

Figures 5 and 6 show the results of linear regression and Bland–Altman analyses between the 2D- and 3D-STE against CMR reference values for ESV and EDV, respectively. Table 1 shows the summary of results of these comparisons, including intra-class correlation coefficients, biases, and limits of agreement. Although the 2D-STE measurements showed good agreement with CMR as reflected by the high-correlation coefficients for both ESV and EDV, the 3D-STE values showed even higher correlation with CMR for both the volumes. In addition, the slope was considerably closer to 1.0 and the intercept was smaller for the 3D compared with the 2D measurements (Figure 5 and 6). Moreover, the 2D-STE volume measurements of both volumes were underestimated compared with CMR values (negative biases between 10 and 30 mL) with relatively wide limits of agreement (SD between 36 and 51 mL). In contrast, the bias in 3D-STE measurements of ESV was essentially eliminated and the bias in EDV was approximately half of the corresponding EDV measurements by 2D-STE. Finally, the limits of agreement of the 3D-STE measurements were tighter than the average of the single-plane measurements. Of note, within the 2D-STE measurements, both LV volumes obtained from the A4C view were superior to those obtained from the A2C view, as reflected by higher correlation coefficients with CMR reference, smaller biases, and tighter limits of agreement.

Table 2 summarizes the reproducibility data for 2D- and 3D-STE as well as CMR measurements of LV volumes obtained in a subgroup of 15 patients. As expected, for most measurements, the inter-observer variability was slightly higher for both volumes than the corresponding intra-observer variability values. Both inter- and intra-observer variability were lower and less spread among patients for the 3D compared with the 2D measurements,



**Figure 3** Example of two-dimensional and three-dimensional speckle tracking echocardiography images obtained at end-systole in a patient with prior infero-lateral myocardial infarction, shown in the same format as in Figures 1 and 2. See text for details.



**Figure 4** Examples of volume over time curves obtained using three-dimensional speckle tracking echocardiography (top) and CMR (bottom) in three patients: a patient with normal LV function (NL), a patient with dilated cardiomyopathy (DCM), and a patient with concentric LV hypertrophy (LVH). See text for details.

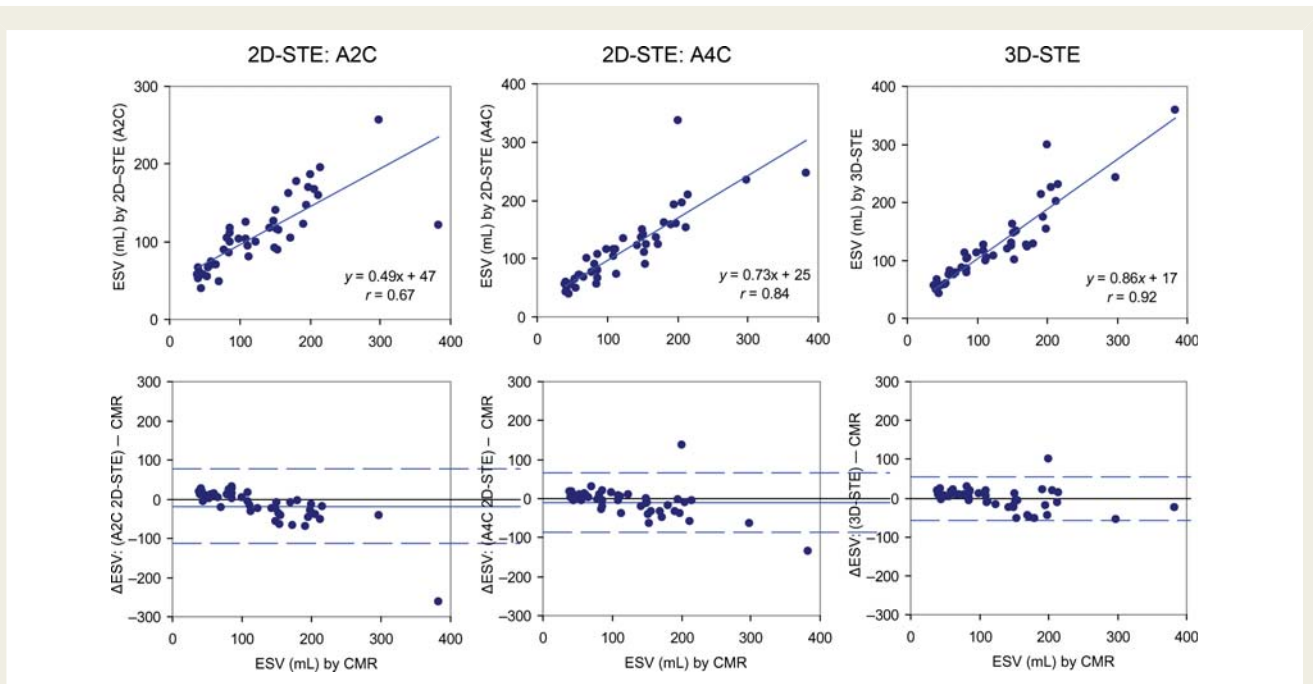
but several times higher than the variability in the CMR measurements.

## Discussion

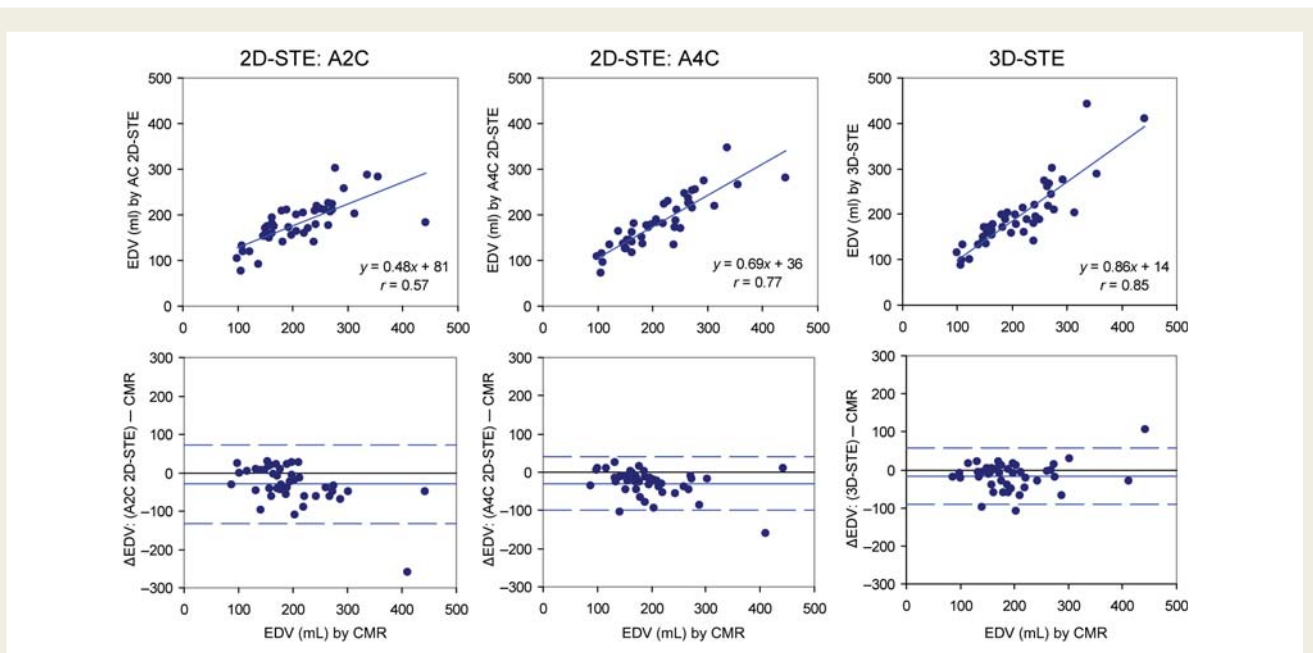
Although the ability of 2D speckle tracking to estimate LV volume throughout the cardiac cycle with relatively high accuracy was recently demonstrated,<sup>35</sup> this methodology, like any 2D echocardiographic technique, relies on geometric modelling to convert LV cross-sectional area into the volume and is affected by inadvertent use of foreshortened apical views of the ventricle. Three-dimensional echocardiographic imaging has resolved many of the limitations associated with the evaluation of LV volume and function from 2D images and significantly improved the accuracy of these measurements, mostly by eliminating the need for geometric modelling and the errors caused by the use of foreshortened views.<sup>41,42</sup>

In addition, unlike most previous 2D techniques, speckle tracking heavily relies on the assumption that morphological details can be tracked from one frame to the next, i.e. that they can be identified in consecutive frames. For this assumption to be true, it is mandatory that the objects being tracked remain within the scan volume. While for 2D imaging this could only be true if the motion occurred only within the imaging plane, this assumption should hold for 3D imaging as long as the ventricle fits into the pyramidal scan volume. Accordingly, we hypothesized that the newly developed 3D-STE technique could allow more accurate and more reproducible measurements of LV volumes.

We found that in individual patients, 3D-STE results in more homogeneous colour distribution in the normal ventricle, consistent with normal patterns of LV function, compared with 2D-STE used in the same patient (Figure 1). This observation remained true also in patients with dilated cardiomyopathy, in whom



**Figure 5** Results of comparisons between two-dimensional and three-dimensional speckle tracking echocardiography measurements of left ventricular end-systolic volume (ESV) against cardiac magnetic resonance (CMR) reference values: linear regression (top) and Bland–Altman (bottom) analyses. In each Bland–Altman plot, solid blue horizontal line represents the bias (mean difference from CMR reference) and dashed blue horizontal line depicts the 95% limits of agreement (2 SD around the mean difference).



**Figure 6** Results of comparisons between two-dimensional and three-dimensional speckle tracking echocardiography measurements of left ventricular end-diastolic volume (EDV) against CMR reference values shown in the same format as in Figure 5.

colours representing reduced endocardial displacement were uniformly distributed over the entire ventricle irrespective of cut-plane (Figure 2). In contrast, inhomogeneity in the colour

distribution was noted in patients with regional wall motion abnormalities, with colours representing reduced displacement in areas of hypokinesia (Figure 3).

**Table 1** Agreement between two- and three-dimensional echocardiographic speckle tracking (STE) measurements of left ventricular end-systolic and end-diastolic volumes (ESV, EDV) with cardiac magnetic resonance reference values

	ESV (mL)			EDV (mL)		
	2D-STE		3D-STE	2D-STE		3D-STE
	A2C	A4C		A2C	A4C	
<i>r</i>	0.67	0.84	0.92	0.57	0.77	0.85
Bias	-18	-10	-1	-30	-29	-16
SD	47	38	28	51	36	37

A2C, A4C—single-plane apical six-chamber measurements, *r*—intra-class correlation coefficient.

**Table 2** Inter- and intra-observer variability of two- and three-dimensional speckle tracking echocardiography (STE) as well as cardiac magnetic resonance (CMR) measurements of left ventricular end-systolic and end-diastolic volumes (ESV, EDV) obtained in a subgroup of 15 patients

	ESV				EDV			
	2D-STE		3D-STE	CMR	2D-STE		3D-STE	CMR
	A2C	A4C			A2C	A4C		
Inter-observer	17 ± 12	16 ± 15	14 ± 11	6 ± 3	17 ± 11	17 ± 12	11 ± 8	3 ± 3
Intra-observer	12 ± 12	16 ± 16	12 ± 11	3 ± 4	14 ± 9	15 ± 10	13 ± 7	2 ± 2

A2C, A4C—single-plane apical six-chamber measurements.

These observations imply that the main clinical utility of the 3D-STE is likely to be in the assessment of regional indices, such as regional volumes, strain, and twist. Up to date, these parameters have been assessed using tissue Doppler techniques, which are known to be limited by their angle dependence, of which speckle tracking is completely devoid. In addition, TDI in three dimensions is not available. The new 3D-STE technology is likely to become the method of choice for the assessment of regional LV function, replacing TDI. However, for this to happen, 3D-STE needs to be validated against an established reference technique. But because there is no non-invasive 'gold standard' technique that can be used in human subjects to validate regional ventricular function in three dimensions, it is essential to test the accuracy of 3D-STE using a global index, such as LV volume, against the current standard CMR reference. This is the first study designed to address this need.

One important feature of the speckle tracking technology in the context of LV volume measurements is its dynamic nature, which allows automated evaluation of LV volume throughout the cardiac cycle without tracing endocardial boundaries in multiple consecutive frames.<sup>43</sup> This is an important advantage over CMR measurements based on the method of disks approximation, which rely on tedious and time-consuming frame-by-frame tracing or adjustments in multiple planes to obtain the same dynamic information (Figure 4). In addition, LV volume time curves can potentially be used to calculate additional indices of systolic and diastolic LV function, such as rates of ejection and filling, as well as percent ejection and filling at any phase

of the cardiac cycle. In addition, the dynamic nature of STE volume measurements eliminates errors in ESV measurements associated with inaccurate identification of the timing of end-systole.

One limitation of the 3D-STE technique is its dependency on the quality of image RT3DE images, in particular the endocardial definition. Also, the ability to track fine anatomic details from frame to frame is affected by the random noise in the image and the relatively low temporal resolution of the RT3DE imaging. All these factors are likely to be responsible for the differences in the reproducibility of echocardiographic and CMR measurements, with the latter being derived from images of superior spatial and contrast resolution. Future technological developments geared towards the improvement of RT3DE image quality and higher temporal resolution are likely to further improve the clinical utility of 3D-STE and its dissemination into standard clinically used imaging equipment. Despite this limitation, our results showed that in patients with adequate transthoracic 2D acoustic windows, 3D-STE measurements of LV volumes were in close agreement with the CMR reference values, and that the levels of agreement were higher than for 2D-STE measurements obtained in the same patients, as reflected by higher correlation coefficients, smaller biases, and tighter limits of agreement. In addition, 3D-STE measurements were more reproducible than the corresponding 2D-STE measurements, as reflected by lower inter- and intra-observer variability levels.

These findings may have important implications regarding the potential use of 3D-STE technology in a variety of clinical

scenarios, even beyond simple LV volume measurements. Such potential applications may include analysis of regional function either for detection of wall motion abnormalities, or for quantitative evaluation of LV dyssynchrony in patients with heart failure, both to optimize the selection of patients for cardiac resynchronization therapy<sup>8,11–13,15</sup> and to assess its effectiveness.<sup>8,11,13,15,34</sup> These data may prove particularly useful in patients with congenital abnormalities, where such additional information on LV performance obtained during serial studies is more likely to affect the choice of treatment. The clinical value of the 3D-STE technology in these clinical scenarios needs to be tested in future studies.

In summary, this is the first study to validate LV volume measurements obtained using the new 3D-STE technology against CMR reference in a group of patients over a wide range of LV size and function, and demonstrate its advantages over 2D-STE measurements obtained in the same patients, including improved accuracy and reproducibility. Pending further validation of the ability of 3D-STE to accurately evaluate regional LV mechanics, this methodology may become the new standard for the evaluation of global and regional LV function.

## Funding

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**Conflict of interest:** none declared.

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## CARDIOVASCULAR FLASHLIGHT

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### Ischaemic mitral regurgitation

Raban V. Jeger\* and Hans Peter Brunner-La Rocca

Department of Cardiology, University Hospital Basel, Petersgraben 4, Basel, Switzerland

\*Corresponding author. Tel: +41 61 265 2525, Fax: +41 61 265 4598, Email: rjeger@uhbs.ch

A 79-year-old woman with a history of treated hypertension and permanent atrial fibrillation was referred because of increasing shortness of breath at minimal exercise. Blood pressure was 110/49 mmHg, heart rate 80 b.p.m. (peak exercise rate 146 b.p.m.), and brain natriuretic peptide 86 pg/mL. Myocardial perfusion scan [Panel A: stress (upper rows) and resting (lower rows) single photon emission computed tomography images (left: short-axis views, right: long-axis views)], spirometry, and chest computer tomography were unremarkable. Resting transthoracic echocardiography revealed slight concentric hypertrophy of both ventricles, no wall-motion abnormalities, diastolic left-ventricular dysfunction grade 2, no valvular disease, and moderate pulmonary hypertension. Resting right heart catheter showed mildly elevated filling pressures and only mild pulmonary hypertension [Panel B: resting right heart catheter with pulmonary capillary wedge pressure (PCWP) mean 14 mmHg, v-wave 18 mmHg (arrow; caliper 40 mmHg)]. However, with minimal exercise (handgrip), PCWP increased significantly with marked v-waves, suggestive of exercise-induced mitral regurgitation [Panel C: exercise right heart catheter (hand grip): PCWP mean 30 mmHg, v-wave 46 mmHg (arrow; caliper 100 mmHg)]. Subsequent coronary angiography showed a severe stenosis of the left circumflex artery [Panel D: coronary angiography (ap view): high-grade stenosis of the left circumflex artery (arrow)] that was treated by percutaneous coronary intervention including stent implantation [Panel E: coronary angiography (ap view): left circumflex artery after implantation of a bare-metal stent (arrow)]. After the intervention, the symptoms disappeared. Two months later, the patient still does not report any shortness of breath. In conclusion, shortness of breath may be caused by various pathologies related to myocardial ischaemia.

