Comparison between three-dimensional speckle-tracking echocardiography and cardiac magnetic resonance imaging for quantification of left ventricular volumes and function

Sebastiaan A. Kleijn1,2*, Wessel P. Brouwer1,2, Mohamed F.A. Aly1, Iris K. Rüssel3, Gerben J. de Roest1, Aernout M. Beek1, Albert C. van Rossum1,2, and Otto Kamp1,2

1Department of Cardiology 5F 003, Institute for Cardiovascular Research (ICaR-VU), VU University Medical Center, De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands; 2Interuniversity Cardiology Institute of the Netherlands (ICIN), Utrecht, The Netherlands; and 3Department of Clinical Physics, Hagaziekenhuis, The Hague, The Netherlands

Received 4 October 2011; accepted after revision 23 January 2012; online publish-ahead-of-print 17 February 2012

Aims
We evaluated the accuracy of three-dimensional speckle-tracking echocardiography (3DSTE) to evaluate left ventricular (LV) volumes, ejection fraction (EF), and global circumferential strain (CS) in comparison with cardiac magnetic resonance imaging (MRI) in a healthy population.

Methods and results
A total of 45 out of 50 consecutive healthy subjects (38 males, age 45 ± 15 years) successfully underwent both 3DSTE and MRI on the same day. Three-dimensional echocardiography data sets were analysed using speckle tracking to measure LV end-diastolic and end-systolic volumes, EF, and global CS. With MRI, the method of discs approximation was used to obtain volumes and the EF, whereas CS was acquired using myocardial tissue tagging. Inter-technique comparisons included regression and the Bland–Altman analysis. For quantification of LV volumes, 3DSTE correlated well with MRI (r: 0.75–0.81), but volumes were significantly underestimated with relatively large biases (13–34 mL) and wide limits of agreement (SD: 11–25 mL). However, excellent accuracy was revealed for measurement of EF by 3DSTE with a good correlation (r: 0.91), minimal bias, and narrow limits of agreement (0.6 ± 1.7%) compared with MRI. For measurement of CS, a large mean bias was found between techniques (10.0%), despite narrow limits of agreement (SD: 1.7%) and a good correlation between techniques (r: 0.80).

Conclusion
Although 3DSTE-derived LV volumes are underestimated in most patients compared with MRI, measurement of the LVEF revealed excellent accuracy. Measurements of CS were systematically greater (i.e. more negative) with 3DSTE than MRI, which likely reflects various inter-technique differences that preclude direct comparability of their measurements.

Keywords
Three-dimensional echocardiography • Speckle tracking • Cardiac magnetic resonance imaging • Left ventricular function

Introduction
Cardiac magnetic resonance imaging (MRI) is widely considered as the most accurate non-invasive imaging modality for quantitative assessment of left ventricular (LV) volumes and function. In addition, MRI was demonstrated to have superior reproducibility over two-dimensional (2D) echocardiography.1 Nevertheless, echocardiography remains the first-line imaging technique for assessment of the LV due to its ease of use and wide availability. By obviating limitations such as foreshortened views and geometric assumptions, three-dimensional echocardiography (3DE) has demonstrated to be a more accurate and reproducible echocardiographic technique for assessment of LV volumes and the ejection fraction (EF) when compared with MRI1,2. However, these results were derived from 3DE methods based on direct volumetric quantification. Recently, 3D speckle-tracking echocardiography

* Corresponding author. Tel: +31 20 444 2244; fax: +31 20 444 2446, Email: s.kleijn@vumc.nl
Published on behalf of the European Society of Cardiology. All rights reserved. © The Author 2012. For permissions please email: journals.permissions@oup.com
(3DSTE) was introduced to provide fast and highly automated LV chamber quantification, including global and regional myocardial strain assessment. An initial study demonstrated that the accuracy of LV volume measurements by 3DSTE is superior to 2DSTE when compared with MRI. In addition, 3D direct volumetric and speckle-tracking methods were recently shown to give comparable quantification of LV volumes and function, making interchangeable application a viable option in daily clinical practice. Finally, we recently demonstrated that good intra-observer, inter-observer, and test–retest reliability support the use of 3DSTE for routine evaluation of LV volumes, EF, and circumferential strain (CS). However, at present the accuracy of 3DSTE-derived measurements of functional parameters such as EF and myocardial strain has not been reported. Accordingly, the aim of this study was to validate measurements of LV volumes, EF, and global CS by 3DSTE against MRI in healthy subjects.

Methods

Subjects
A total of 50 healthy subjects were included in the study. The healthy subjects (38 males and 12 females, mean age 45 ± 15 years) satisfied the following criteria: no history of cardiac symptoms or disease, no other significant pathologies such as respiratory or renal disease or diabetes mellitus, no hypertension, obesity or current smoking, no use of medication and normal physical examination, electrocardiogram, and echocardiogram. 3DSTE and MRI were consecutively performed on the same day in each patient to minimize differences in physiological conditions in study subjects between both acquisitions. Written informed consent was obtained from all subjects according to our institutional guidelines.

Echocardiographic imaging and analysis
3DSTE imaging was performed from an apical position using a commercial scanner (Artida 4D, Toshiba Medical Systems, Tokyo, Japan) with a fully sampled matrix array transducer (PST-2SSX). In the tissue harmonic mode, wide-angled acquisitions were recorded consisting of six wedge-shaped sub-volumes acquired over seven consecutive cardiac cycles during a single breath-hold. While retaining the entire LV within the pyramidal volume, depth and sector width were decreased as much as possible to improve the temporal and spatial resolution of the images, resulting in a mean temporal resolution of 20 ± 3 volumes/s. 3DSTE images were analysed online. Analysis by 3DSTE involved the reader to set three markers on two orthogonal apical views, namely two markers at the edges of the mitral valve ring and one marker at the LV apex. The LV endocardial border was then automatically detected by the 3D wall motion tracking software (Toshiba Medical Systems, Tokyo, Japan), after which the reader could manually adjust the endocardial border and myocardial thickness if necessary. The system then automatically performed the analysis through the entire cardiac cycle, providing values of LV end-diastolic volume (EDV), end-systolic volume (ESV), EF, and global CS.

Cardiac magnetic resonance imaging and analysis
MRI was performed using a 1.5 Tesla scanner (Magnetom Sonata, Siemens, Erlangen, Germany). After survey scans in three orthogonal planes, standard long-axis images were acquired using a retro-triggered, steady-state, free precession (SSFP) gradient-echo sequence for cine imaging. Short-axis axis cine images were planned perpendicular on the long-axis of the heart and totally covered the LV, allowing quantification of LV volumes and EF. The number of phases within the cardiac cycle was set at 20, temporal resolution was <40 ms, slice thickness and slice gap were 5 mm, and typical in-plane spatial resolution was 1.3 × 1.6 mm. For quantification of CS, sinusoidal complementary high-temporal tagged (CSPAMM) MRI images of the LV were acquired using a retrospectively triggered SSFP sequence with a multiple brief expiration breath-hold scheme as previously described. Images were acquired in three short-axis planes, evenly distributed over the LV as measured on an end-systolic four-chamber cine image. Imaging parameters were: temporal resolution of ~15 ms, field of view of 300 × 300 mm², flip angle of 20°, repetition time of 3.6 ms, echo time of 1.8 ms, receiver bandwidth of 850 Hz/pixel, 256 × 78 matrix size, slice thickness of 6 mm, and tag-line distance of 7 mm. In addition, a high-temporal resolution cine imaging of a three-chamber view was acquired to assess opening and closure times of the mitral and aortic valves. Images were stored digitally for off-line analysis. Including the papillary muscles and trabeculae in the LV cavity, semi-automated endocardial border tracing was performed using MASS software (version 5.1b, MEDIS, Leiden, the Netherlands), providing measurements of LV volumes and the EF with the disc-area summation method. Global CS was obtained using the harmonic phase (HARP) method from the MRI-tagged images and calculated over the entire thickness of the LV wall.

Statistical analysis
Inter-technique comparisons between 3DSTE- and MRI-derived LV volumes, EF, and peak CS included linear regression and Bland–Altman analyses. The significance of differences between both techniques was tested using paired t-tests. Continuous data are presented as mean ± SD. Categorical data are presented as a count and percentage. Statistical significance was defined as a probability value <0.05. Data were analysed using SPSS version 15.0 (SPSS, Inc., Chicago, IL, USA).

Results
Of the 50 healthy subjects consecutively enrolled in the study, five subjects had to be excluded due to either poor echocardiographic image quality (n = 2) or failure to acquire appropriate cine-loops with MRI due to frequent extra-systoles (n = 2) and claustrophobia (n = 1). Therefore, results of comparison between 3DSTE and MRI for quantification of LV volumes and function were available in 45 healthy subjects (35 males and 10 females, mean age 39 ± 15 years). Figure 1 shows an example of 3DSTE (Figure 1A) and MRI (Figure 1B) images obtained at end-diastole in a healthy subject, whereas Figure 2 shows complementary horizontally and vertically tagged CSPAMM images at end-systole in the same individual, used for MRI-derived measurements of CS. The time required for 3DSTE acquisition and analysis of all studied LV parameters was generally ~5 min, whereas acquisition and analysis by MRI required ~15 min for LV volumes and EF, and more than an hour for CS.

Figure 3 shows results of linear regression and Bland–Altman analyses of LV volume measurements by 3DSTE compared with MRI reference values. Although measurements of LV EDV and ESV correlated well between both techniques (r: 0.75 and 0.81, respectively), 3DSTE significantly underestimated LV volumes...
with relatively large biases (13–34 mL) and wide limits of agreement (SD: 11–25 mL).

Regarding parameters of LV function (Figure 4), an excellent correlation was found for the LVEF (r: 0.91), while the Bland–Altman analysis demonstrated a small bias (0.6%) and relatively narrow limits of agreement (SD: 1.7%) between both techniques. For measurement of CS, a large systematic difference was found between 3DSTE and tagged MRI (10.0%), despite minimal variability (SD: 1.7%) and a good correlation (r: 0.80). Correlations between the LVEF and CS as functional parameters were good with MRI (r: −0.68) and excellent with 3DSTE (r: −0.88).

Discussion

Validation of novel techniques is often performed through comparative studies with reference techniques that are considered the ‘gold standard.’ For quantification of LV volumes and EF, cardiac MRI is the most accurate and reproducible imaging technique currently available. For quantification of LV mechanics, such as myocardial strain, however, expert consensus is that currently there is no true non-invasive ‘gold standard’ technique that can be used in humans. Although multiple studies have demonstrated that MRI tagging is both accurate and reliable for myocardial strain assessment, limited availability and expertise with this technique have significantly hampered its use in comparative research with echocardiographic techniques. The limited data that exist on comparison of myocardial strain measurements by 2D-echocardiographic techniques with MRI tagging demonstrated mixed results, suggesting that inter-technique differences between echocardiography and MRI may preclude adequate comparability. Therefore, in the present study comparisons of measurements of LV volumes, EF, and CS between 3DSTE and
Figure 3 Comparison of left ventricular volume measurements by 3D speckle-tracking echocardiography with cardiac magnetic resonance imaging. Results of linear regression (top) and Bland–Altman (bottom) analyses for left ventricular end-diastolic (left) and end-systolic volume (right). \( r \): Pearson’s correlation coefficient.

Figure 4 Comparison of left ventricular function measurements by 3D speckle-tracking echocardiography with cardiac magnetic resonance imaging. Results of linear regression (top) and Bland–Altman (bottom) analyses for the left ventricular ejection fraction (left) and global circumferential strain (right). \( r \): Pearson’s correlation coefficient.
MRI were performed in healthy subjects to specifically focus on potential inter-technique differences. Results show that 3DSTE-derived measurements of the LVEF were very accurate, despite significant underestimation of LV volumes compared with MRI. In contrast, measurements of global CS were systematically greater (i.e. more negative) with 3DSTE than with MRI tagging. To provide potential reasons for these findings, a critical appraisal of the strengths and limitations of each technique as well as inter-technique differences is warranted.

As thoroughly established by Mor-Avi et al., 18 3DE-derived LV volumes are underestimated in most patients because 3DE at present cannot differentiate between myocardium and trabeculae. In contrast, the excellent spatial resolution of current SSFP sequences allows clear differentiation between myocardium and trabeculae by MRI, although this also introduces difficulties with adequate endocardial border detection. Since automated border detection algorithms are currently insufficient to trace the small indentations between trabeculae and manual tracing is simply too labour intensive and time consuming, general consensus is to include the papillary muscles and trabeculae in the LV cavity. This does not only introduce potential overestimation of EDV, but of stroke volume as well, since the compacted trabeculae become indistinguishable from regularly compacted myocardium at end-systole. 19 Furthermore, it is known that SSFP sequences somewhat overestimate LV volumes compared with turbo gradient-echo sequences. 20 Finally, the choice to include a basal slice based on the criterion of at least 50% of the circumference being surrounded by LV myocardial tissue remains subjective, difficult to apply with confidence due to partial volume artefacts, and may significantly affect both the accuracy and reproducibility of LV volume measurements. 18 On the other hand, 3DSTE suffers from low frame rates, which could cause underestimation of EF by missing the actual end-systolic frame. Interestingly, however, measurements of the LVEF were highly comparable between 3DSTE and MRI. Although the accuracy of LVEF measurements by 3DE direct volumetric methodologies has been extensively validated with MRI, 1 this is the first study validating 3DSTE for this functional assessment. This finding has important clinical consequences, since determination of the LVEF is the most frequently performed echocardiographic assessment and many clinical decisions depend on accurate measurement of this parameter, such as when to place an implantable cardioverter-defibrillator or give cardiac resynchronization therapy.

Besides accurate quantification of LV chamber indices such as volumes and EF, assessment of myocardial strain is gaining clinical importance. 6,21 One of the issues still impedng its clinical application is lack of consensus on what should be measured and how to perform these measurements. This is also related to the use of different equipment and analysis software, which can result in substantial differences in measurements of myocardial strain between and within techniques. The large systematic bias found between measurements of CS by 3DSTE and MRI in the present study clearly demonstrates the consequences of this lack of standardization, e.g. both techniques have different reference values of CS in healthy volunteers. Nevertheless, the standard deviation of the inter-technique difference was quite small, reflecting a relatively consistent difference in the magnitude of CS measurements between both techniques. Together with the good correlation found for CS measurements between 3DSTE and MRI, this suggests that, even though their measurements are not directly interchangeable, quantification of CS by both techniques reflects LV myocardial deformation in a very similar fashion.

Some inter-technique differences may explain why CS measurements are systematically greater with 3DSTE than with MRI tagging. First of all, it is important to note that strain is deformation of an object relative to its original dimension, i.e. for CS the change in circumference during the cardiac cycle relative to its length at end-diastolic time. This relative change will be larger when the initial circumference is smaller as reflected by the gradual increase in CS from LV base to apex. Owing to the inability of 3DSTE to differentiate between myocardium and trabeculae, measured circumferences will be smaller using 3DSTE compared with MRI, thereby causing not only underestimation of absolute volume measurements, but also greater CS, even when both techniques measure equal myocardial thickening. However, it is additionally known that measurements of maximal myocardial thickening are generally larger with echocardiographic techniques compared with MRI, which would increase differences in strain measurements between both techniques exponentially. 21–23 Finally, 3DSTE was compared with 2D MRI tagging, which theoretically may be unable to accurately evaluate the true magnitude of the intrinsically 3D displacement vector. However, 2D and 3D CS using MRI tagging have previously been demonstrated to give comparable results in healthy subjects. 24

Although MRI should be considered the gold standard for accurate and reliable evaluation of LV volumes and EF and remains important in patients with poor echocardiographic image quality or with an indication for additional assessments such as viability, 3DSTE could become the ideal approach for clinical evaluation of LV size and function in daily routine. However, current limitations such as moderate image quality, low temporal resolution, and limited experience of clinicians with this novel technique will still need to be addressed. In addition, inter-vendor variability of 3DSTE-derived measurements of LV volumes, EF, and strain has recently been studied, demonstrating good comparability for LV volumes and EF measurements, but large inter-vendor variability for strain measurements. 6,25 This issue needs to be resolved to provide clinicians with the confidence to interpret their findings.

Conclusions

Although 3DSTE-derived LV volumes are underestimated in most patients compared with MRI, measurement of the LVEF revealed excellent accuracy. Measurements of CS were systematically greater with 3DSTE than with MRI, which likely reflects various inter-technique differences that preclude direct comparability of their measurements. With the understanding of these inter-technique differences, further studies should establish normal reference values of 3DSTE-derived strain measurements in a larger healthy population and determine their added usefulness over current clinical standards of LV function assessment in different clinical scenarios.
Funding
Equipment grant from Toshiba Medical Systems.

Conflict of interest: none declared.

References
3. Shimada YJ, Shiot A. A meta-analysis and investigation for the source of bias of left ventricular volumes and function by three-dimensional echocardiography in comparison with magnetic resonance imaging. Am J Cardiol 2011;107:126–38.