



Real-Time 3D Fusion Echocardiography

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OBJECTIVES This study assessed 3-dimensional fusion echocardiography (3DFE), combining several real-time 3-dimensional echocardiography (RT3DE) full volumes from different transducer positions, for improvement in quality and completeness of the reconstructed image.

BACKGROUND The RT3DE technique has limited image quality and completeness of datasets even with current matrix transducers.

METHODS RT3DE datasets were acquired in 32 participants (mean age 33.7 ± 18.8 years; 27 men, 5 women). The 3DFE technique was also performed on a cardiac phantom. The endocardial border definition of RT3DE and 3DFE segments was graded for quality: good (2), intermediate (1), poor (0), or out of sector. Short-axis and apical images were compared in RT3DE and 3DFE, yielding 2,048 segments. The images were processed to generate 3DFE and then compared with cardiac magnetic resonance.

RESULTS In the heart phantom, fused datasets showed improved contrast to noise ratio from 49.4 ± 25.1 (single dataset) to 125.4 ± 25.1 (6 datasets fused together). In subjects, more segments were graded as good quality with 3DFE (805 vs. 435; $p < 0.0001$) and fewer as intermediate (184 vs. 283; $p = 0.017$), poor (31 vs. 265; $p < 0.0001$), or out of sector (4 vs. 41; $p < 0.001$) compared with the single 3-dimensional dataset. End-diastolic volume (EDV) and end-systolic volume (ESV) obtained from 3-dimensional fused datasets were equivalent to those from single datasets (EDV 118.2 ± 39 ml vs. 119.7 ± 43 ml; $p = 0.41$; ESV 48.1 ± 30 ml vs. 48.4 ± 35 ml; $p = 0.87$; ejection fraction [EF] $61.0 \pm 10\%$ vs. $61.8 \pm 10\%$; $p = 0.44$). Bland-Altman analysis showed good 95% limits of agreement for the nonfused datasets (EDV ± 46 ml; ESV ± 36 ml; EF $\pm 14\%$) and the fused datasets (EDV ± 45 ml; ESV ± 35 ml; EF $\pm 16\%$), when compared with cardiac magnetic resonance.

CONCLUSIONS Fusion of full-volume datasets resulted in an improvement in endocardial borders, image quality, and completeness of the datasets. (J Am Coll Cardiol Img 2010;3:682–90)
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Real-time 3-dimensional echocardiography (RT3DE) has been used as an alternative to the 2-dimensional (2D) technique for the assessment of left ventricular (LV) volumes and systolic function (1,2) in addition to stress tests and resynchronization studies (3,4).

The RT3DE technique allows 3-dimensional (3D) visualization of cardiac structures in multiple planes and can provide rapid analysis of cardiac function. However, despite these advantages, RT3DE is still not in routine clinical use; difficulties with image quality and complete coverage of the left ventricle owing to limited echocardiographic windows may have contributed to its nonuse.

We hypothesized that combining several full echocardiographic volumes (= datasets) from different scanning positions of the RT3DE matrix transducer would result in improved image quality and completeness of the 3D image. We developed a novel technique, 3-dimensional fusion echocardiography (3DFE), involving the merging of 3D datasets from different transducer positions, the technical details of which have been previously described (5–7). We aimed to validate the technique against cardiac magnetic resonance (CMR) of a cardiac phantom and in a group of human participants.

METHODS

For in vitro validation, we used an ultrasound heart phantom (model 067, CIRS Tissue Simulation Technology, Norfolk, Virginia). The phantom had increased thickness of the interventricular septum, mimicking hypertrophic cardiomyopathy.

The clinical study group consisted of 32 participants (mean age 33.7 ± 18.8 years; 27 men, 5 women), including 16 healthy volunteers and 16 patients referred for LV assessment with stable sinus rhythm, referred for echocardiographic assessment of LV function, with at least moderate image quality in 2D echocardiography. The only exclusion criteria were arrhythmia or clinical condition preventing breath holding for the time of full-volume acquisition (4 heartbeats). The study was approved by the local ethics committee, and all participants gave informed consent.

RT3DE. Full-volume RT3DE datasets were acquired using a commercially available ultrasound scanner (iE33, Philips, Andover, Massachusetts) with a broadband, matrix-array real-time 3D transducer (X3-1, frequency range 3 to 1 MHz). Datasets were recorded using different transducer positions (Fig. 1). For both the phantom and clinical

studies, the probe was located at the apex of the left ventricle for an optimal 4-chamber view (position 1), and a full-volume dataset was acquired. The probe was then positioned toward the lateral wall of the left ventricle (position 2) and then further to the left (position 3). Second and third full-volume datasets were acquired. After that, the probe was directed toward the interventricular septum (position 4), and another full volume was acquired. Finally, the probe was positioned above (position 5) and below (position 6) the optimal apical image. These positions led to inclusion of the left ventricle within all datasets from different transducer positions. The acquisition was performed with electrocardiogram gating and breath holding at end-expiration, with gain, compression, and depth settings standardized for all the views obtained in a given patient. A full-volume acquisition was obtained in 4 cardiac cycles by physicians (H.B., C.S.) using the designated protocol (Fig. 1). The datasets were then transferred via CD from the scanner to a separate workstation and processed offline, taking approximately 1 extra hour per analysis.

Alignment and fusion of multiple RT3DE datasets—generation of the 3DFE datasets.

The alignment methodology is described in detail in engineering references (5–7). Briefly, we used a voxel-based method that maximizes a voxel similarity measure, termed the normalized cross-correlation, which was chosen for its invariance to contrast changes between the images, common in echocardiographic acquisitions. Given 2 datasets, named *fixed* and *floating*, the registration procedure finds the translation and rotation that maximize the normalized cross-correlation value between the datasets (Fig. 2). The 3D alignment is divided into spatial and temporal components.

Spatial alignment is accomplished by calculating the optimal rigid alignment between the corresponding end-diastolic frames in the fixed and floating datasets. The same alignment is then applied individually to all frames of the floating dataset. No user interaction is required in this case, which is achieved by sequentially trying a range of different starting positions from which the algorithm automatically keeps the one providing the largest similarity value. The method is carried out within a multiresolution framework (5,8) so that alignment is performed first on downsampled versions of the fixed and floating datasets, with larger

ABBREVIATIONS AND ACRONYMS

2DE = 2-dimensional echocardiography

3DFE = 3-dimensional fusion echocardiography

EDV = end-diastolic volume

EF = ejection fraction

ESV = end-systolic volume

LV = left ventricle/ventricular

RT3DE = real-time 3-dimensional echocardiography

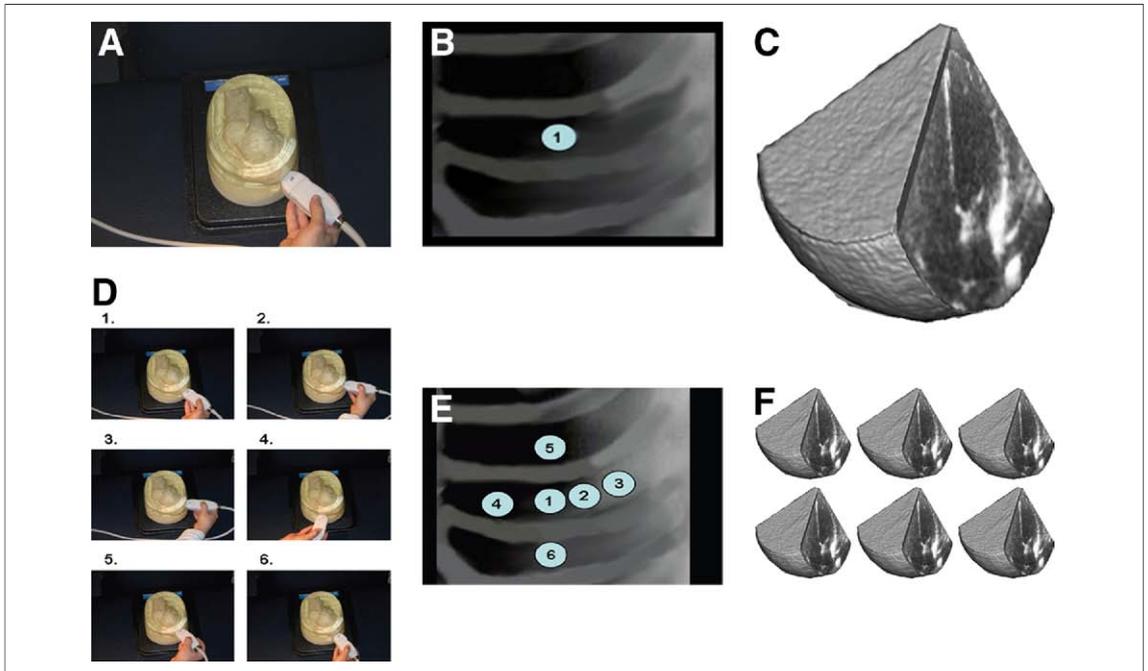


Figure 1. Acquisition Sites of Apical Full-Volume Datasets for 3DFE

(A) Single site of apical acquisition on the heart phantom. (B) Single site of apical acquisition on the patient, illustrated on a scheme of chest X-ray. (C) RT3DE single (source) full-volume dataset. (D) Multiple sites of acquisition from different transducer positions on the heart phantom. Six different positions of the transducer according to the protocol (1–6). (E) Multiple sites of acquisition from different transducer positions on the patient, illustrated on a scheme of a chest X-ray. Six different positions of the transducer according to the protocol (1–6). (F) RT3DE multiple, single full-volume datasets for fusion. 3DFE = 3-dimensional fusion echocardiography; RT3DE = real-time 3-dimensional echocardiography.

voxel size. The alignment results are then used as an initialization for the next level of resolution and so on until the original resolution level is reached. The multiresolution approach reduces computation time and increases the robustness of the algorithm. The Powell method was used for maximization of the similarity measure (9).

Temporal alignment was accomplished by manually identifying the end-systolic and end-diastolic frames on both floating and fixed data-

sets and then calculating intermediate frames using linear interpolation.

Once the alignment was performed, voxels of the aligned datasets were processed as follows. In the areas of overlap, the intensities of individual voxels were used, whereas in areas in which only one of the views contained image data, the intensities of these were directly copied to the final fused dataset. Algorithms were written using a combination of Matlab (The MathWorks,

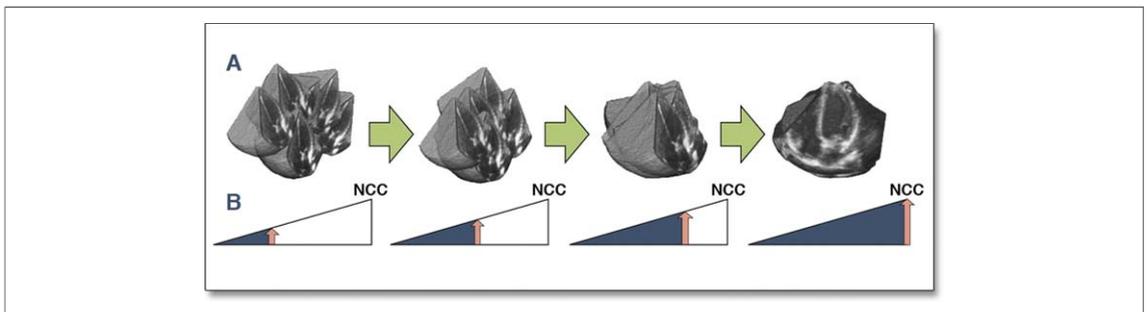


Figure 2. Schematic Presentation of the Fusion Process of Multiple, Apical, Single Full-Volume Datasets

(A) Fusion of multiple single full-volume datasets. (B) Similarity function (normalized cross-correlation [NCC]) increases with improvement in alignment of the multiple datasets.

Natick, Massachusetts) and the C++ programming language.

Contrast-to-noise ratio (CNR) as a quantitative measurement of image quality. The CNR is defined as the ratio of the signal intensity differences between image regions and the image noise. We manually selected 6 cubic regions of interest on corresponding slices in well-aligned 4-chamber views—3 contained in the middle of the interventricular septum (IVS) (12×20 , 12×16 , 10×15 voxels) and 3 in the LV cavity 1 cm from the endocardial border (12×27 , 17×27 , 14×21 voxels). The signal intensities S_{IVS} and S_{LV} were calculated as the average intensity value for all image voxels contained in the IVS/LV. The noise was estimated using the average of the variance of voxel values at the regions of interest, both at the septum and chambers. Finally, CNR was calculated as the ratio between $(S_{IVS} - S_{LV})^2$ and the estimated noise (Fig. 3).

Echocardiographic assessment of RT3DE and 3DFE. IMAGE QUALITY. For analysis, the American Heart Association 16-segment model was used (10). Standard RT3DE and new 3DFE datasets were used for reconstruction of routine echocardiographic imaging planes with imaging software (CardioView, TomTec Imaging Systems, Unterschleissheim, Germany). For standardized image analysis, 2D imaging planes were obtained by cropping 3D datasets, and the same planes were used for image comparison, including 3 short-axis planes (PSAX 1–3) and 3 apical planes (A4C, A3C, and A2C). Quality ratings were compared on a segment-wise analysis, and the data were paired. Cardiac segments were graded according to the quality of endocardial border definition and visualization of wall thickening—good [2], intermediate [1], and poor quality [0]. Out of sector segments were labeled as such. For a more extensive analysis, segments in the short-axis view and in apical views were studied separately, yielding 32 segments per patient. Image quality was assessed in a total of 2,048 cardiac segments (16 segments in PSAX + 16 segments in apical views \times 32 patients \times 2 assessments – 1 using the standard datasets and 1 using the fused datasets). For each segment, the difference in quality between the fused image and the standard ones was assessed. The number of segments in each quality grade was recorded and the percentage of each quality grade calculated.

VOLUMETRIC MEASUREMENTS: ECHOCARDIOGRAPHY—RT3DE AND 3DFE. LV volumes (end-diastolic volume [EDV] and end-systolic volume [ESV]) and

ejection fraction (EF) were calculated using 3D imaging software (CardioView) (11). In each dataset, ED and ES frames were identified as defined by the American Society of Echocardiography (12). Eight long-axis planes were created at 22.5° intervals around the central axis (13). Endocardial borders were traced manually in end-diastole and end-systole in all 8 planes. LV trabeculation and papillary muscles were included within the LV cavity according to the American Society of Echocardiography guidelines. Volumetric measurements (EDV and ESV) were computed, and EF was calculated ($(EDV - ESV)/EDV \times 100\%$). Measurements were performed independently by 2 readers (R.K. and C.S.).

CMR. For reference LV volumes, we performed CMR using a standard cardiovascular approach on a 1.5-T scanner (Siemens Sonata, Siemens Medical Solutions, Erlangen, Germany). For the study group, images were acquired following a standard protocol in horizontal and vertical LV long-axis views and multiple contiguous short-axis views parallel to the atrioventricular groove, covering the entire left ventricle. Steady-state free-precession cine sequences were used for all images (slice thickness 7 mm; gap 3 mm; temporal resolution 45 ms; echo time 1.54 ms; repetition time 3.08 ms; flip angle 50° to 60° ; field of view 380×380 mm). The volumes of the LV were calculated with dedicated

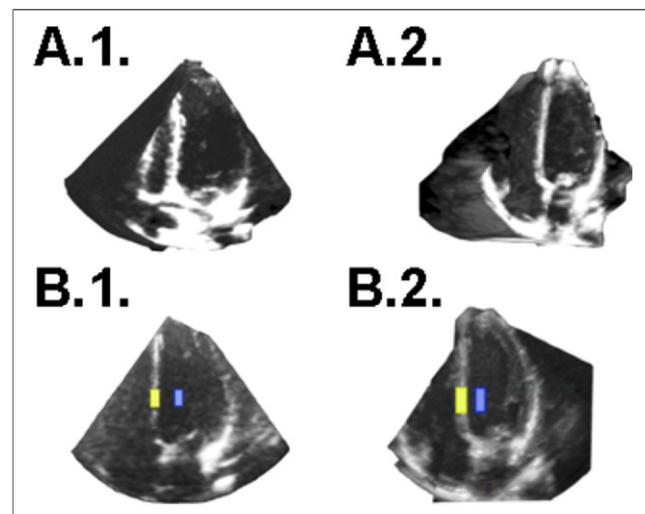


Figure 3. Examples of Images From RT3DE and 3DFE

(A1) The RT3DE single full-volume dataset. (A2) The 3DFE dataset. (B1) Two-dimensional apical 4-chamber view obtained from RT3DE. (B2) Two-dimensional apical 4-chamber view obtained from 3DFE. Markers represent regions of interest within interventricular septum and left ventricular cavity. Abbreviations as in Figure 1.

software (Argus, Siemens Medical Solutions) by summing the area of the left ventricle in each short-axis image, following the Simpson rule. For the cardiac phantom, T2-weighted turbo-spin echo images were used because these gave the greatest contrast between the phantom's "myocardium" and "blood" (echo time 90 ms; repetition time 750 ms; slice thickness 5 mm; gap 2.5 mm; field of view 160×270 mm).

STATISTICS. Measurements are expressed as mean \pm SD. Distribution of the variables was assessed using the Shapiro-Wilk test. Variables with normal distribution were compared using the paired Student *t* test (* in text). Variables with not normal distribution were compared using the Wilcoxon test (# in text). Limits of agreement between techniques were compared by the Bland-Altman method (14). Interobserver variability was controlled by calculating the intraclass correlation coefficient for a single measurement (average and 95% confidence intervals) of the results of 2 investigators. SPSS version 15.0 (SPSS Incorporated, Chicago, Illinois) was used for the analysis.

RESULTS

3DFE of subjects. IMAGE QUALITY. In patients, mean signal to noise ratio increased significantly from 11.90 ± 7.91 before fusion to 21.08 ± 12.89 after fusion ($p < 0.0001\#$) (Fig. 4). Significantly more segments were graded as good quality in the 3DFE datasets (805 vs. 435; $p < 0.0001\#$), and fewer were graded as intermediate (184 vs. 283; $p = 0.017\#$) or poor quality (31 vs. 265; $p <$

$0.0001\#$), in addition to fewer out of sector segments (4 vs. 41; $p = 0.001\#$) (Figs. 6 and 7; Online Videos 1, 2, 3, and 4).

VOLUMETRIC MEASUREMENTS. Mean values were similar for both RT3DE and 3DFE, suggesting no systematic bias (EDV 118.2 ± 39 ml vs. 119.7 ± 43 ml [$p = 0.41^*$]; ESV 48.1 ± 30 ml vs. 48.4 ± 35 ml [$p = 0.87^*$]; and EF $61.0 \pm 10\%$ vs. $61.8 \pm 10\%$ [$p = 0.44^*$], respectively). When compared with CMR volumes performed in the 16 healthy volunteers, volumetric measurements were higher with CMR (EDV 199.7 ± 33 ml; ESV 64.6 ± 19 ml; EF $67.8 \pm 7\%$), in keeping with the literature. However, Bland-Altman analysis showed small mean differences between ultrasound methods and CMR, also suggesting no significant systematic bias, and 95% limits of agreement were good for the nonfused datasets (EDV ± 46 ml; ESV ± 36 ml; EF $\pm 14\%$) and the fused datasets (EDV ± 45 ml; ESV ± 35 ml; EF $\pm 16\%$) (Fig. 8). The intraclass correlation coefficients were 0.92 for EDV and 0.92 for ESV.

3DFE of the cardiac phantom. RT3DE full volumes of the phantom were aligned and fused. Even with only 2 volumes for fusion, an improvement in the CNR was observed (1 volume CNR 49.4 ± 25.1 ; 2 volumes 74.3 ± 29.6), which was further enhanced with increasing numbers of fused volumes (3 volumes 92.1 ± 28.9 ; 4 volumes 106.0 ± 28.6 ; 5 volumes 116.8 ± 27.3 ; 6 volumes 125.4 ± 25.1) (Fig. 4). Phantom 3D full volumes were used to assess voxel intensities and their localization within the same imaging planes. Fusion also filled in

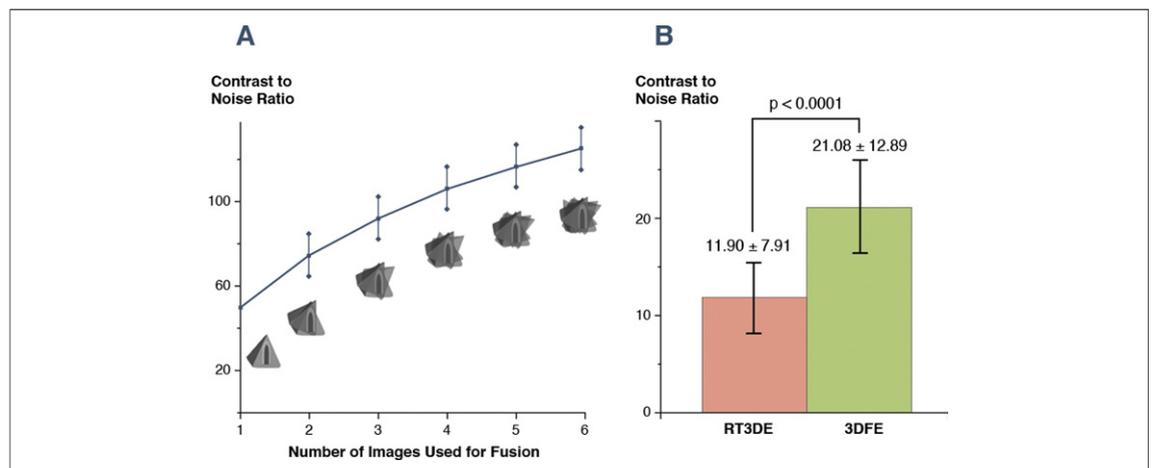


Figure 4. CNR Before and After Fusion

(A) Relationship between number of standard RT3DE full volumes used for fusion and CNR within fused 3DFE datasets in the heart phantom. (B) CNR in participants before and after fusion. CNR = contrast to noise ratio; other abbreviations as in Figure 1.

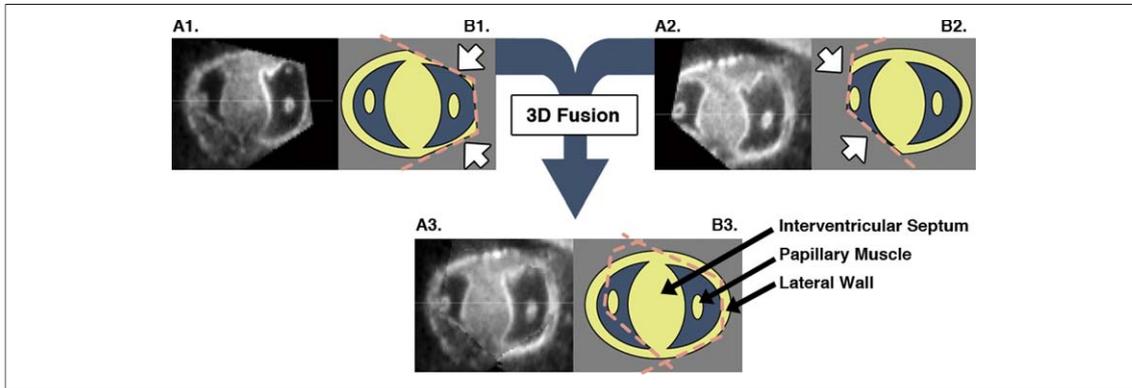


Figure 5. Short-Axis Images From the Phantom From the Standard RT3DE Datasets (A1, A2) and From the Fused Dataset (A3)

Dropout areas are also presented on the schematic drawings (B1, B2, B3) and shown with white arrows. Dashed lines show borders of the RT3DE sectors limiting full dataset acquisition. (A1, B1) Dropout on the right side of the short-axis view from standard RT3DE. (A2, B2) Dropout on the left side of the short-axis view from standard RT3DE. (A3, B3) Complete fused short-axis view from the 3DFE. Abbreviations as in Figure 1.

dropout areas of the phantom images and ensured greater completeness of the image set when compared with standard images (Fig. 5).

DISCUSSION

This study showed for the first time in a clinical setting how fusion of different apical RT3DE volumes yields improved image quality and completeness of the image.

Image quality is often a critical factor limiting 3D echocardiography, and significant improvements would aid uptake of this technique in clinical practice (15). In this study, participants included healthy volunteers and patients referred for LV assessment with at least moderate image quality on 2D echocardiography. Standard RT3DE images were suboptimal, and significant improvements in both border definition and general image quality were seen with the new fusion method (3DFE). In

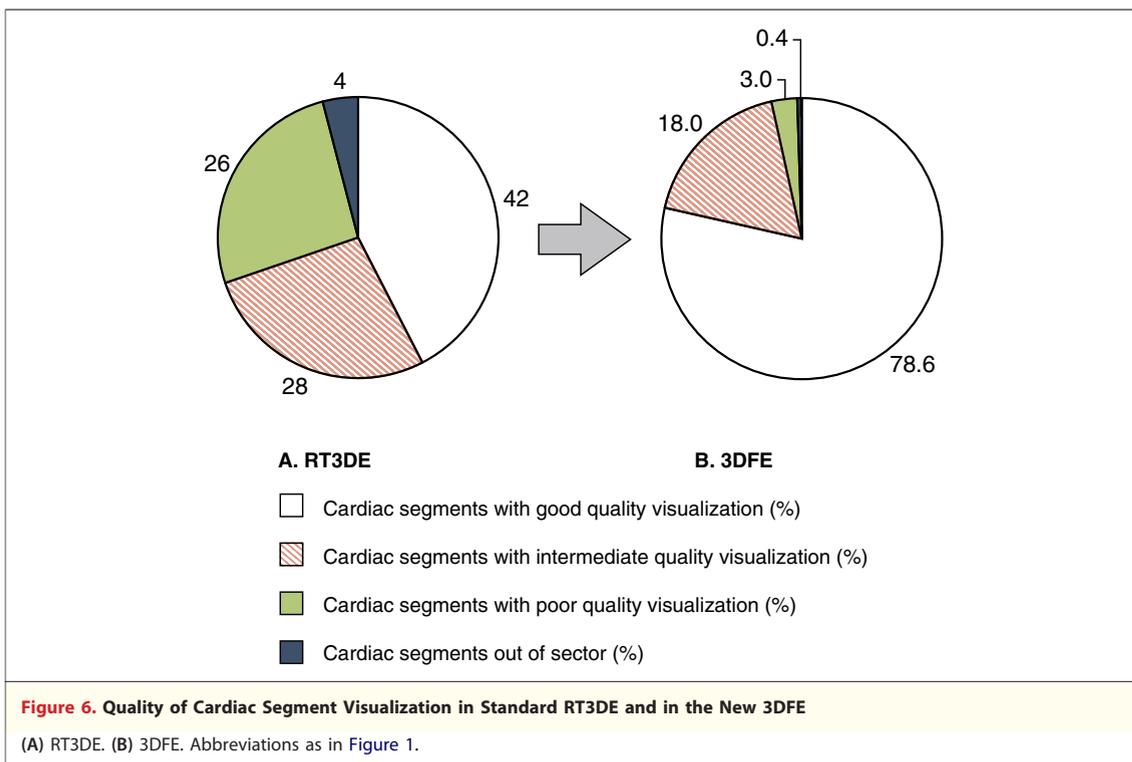


Figure 6. Quality of Cardiac Segment Visualization in Standard RT3DE and in the New 3DFE

(A) RT3DE. (B) 3DFE. Abbreviations as in Figure 1.

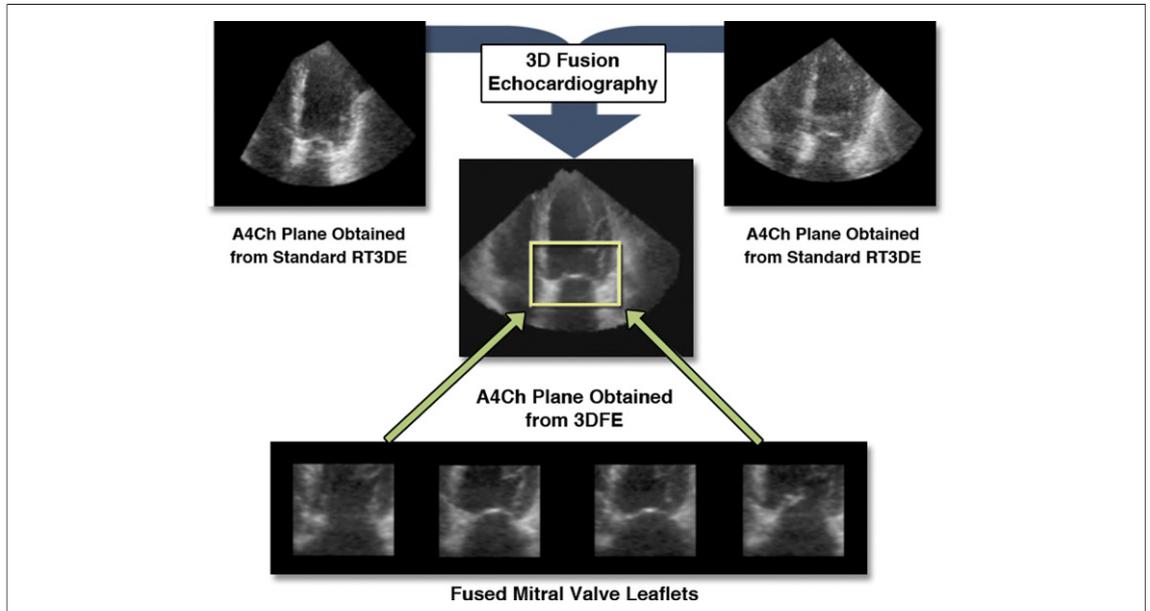


Figure 7. Example of Improvement in Image Quality Observed With the Fusion Technique
See Online Videos 1, 2, 3, and 4.

all patients, the endocardial border was impossible to delineate with RT3DE in at least 2 segments, and 4 or more segments could not be delineated in 75% of the patients. The proportion of participants

with general image quality graded as good or intermediate quality rose from 70% with standard RT3DE to 96.6% with 3DFE. This difference should translate into improved diagnostic potential

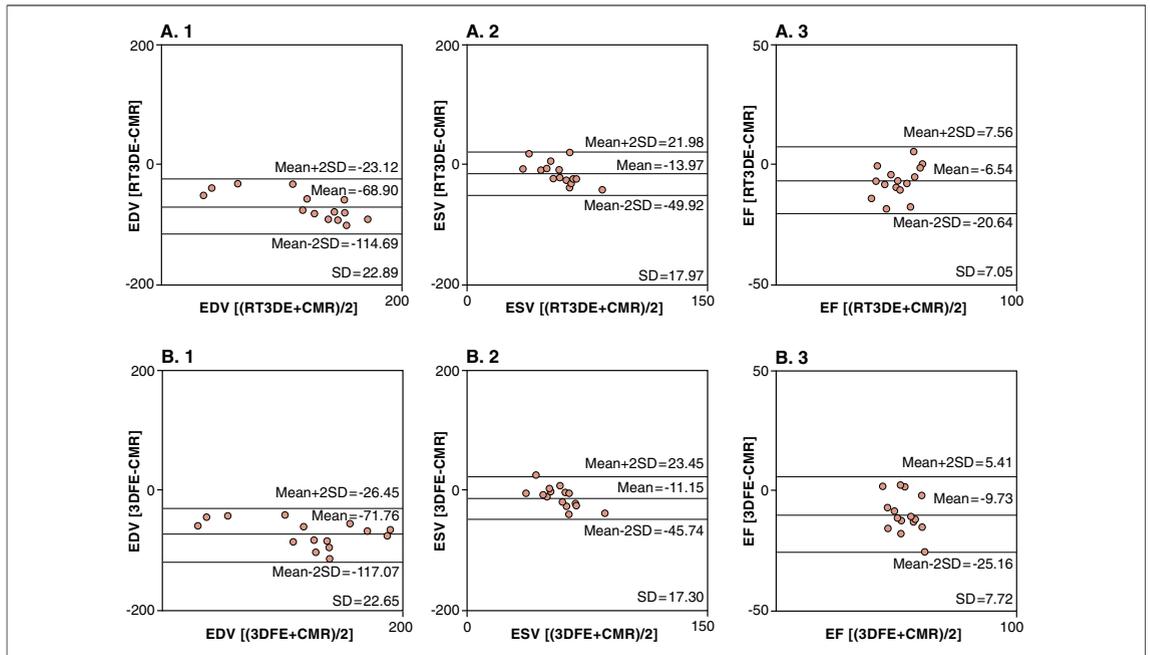


Figure 8. Results of Bland-Altman Analysis for Agreement in Volumetric Measurements Between Nonfused (RT3DE) and Fused (3DFE) Datasets and CMR
(A1) EDV RT3DE. (A2) ESV RT3DE. (A3) EF RT3DE. (B1) EDV 3DFE. (B2) ESV 3DFE. (B3) EF 3DFE. 3DFE = 3-dimensional fusion echocardiography; CMR = cardiac magnetic resonance; EDV = end-diastolic volume; EF = ejection fraction; ESV = end-systolic volume; other abbreviations as in Figure 1.

for even small areas of wall motion abnormality. Additionally, the technique could improve the sensitivity and reproducibility of measurements in patients with large ventricles, which are often not completely visualized in standard RT3DE volumes. At this stage, we have not included patients with dilated cardiomyopathy. However, there were several athletes from the University of Oxford rowing squad, with LV EDVs reaching up to 247 ml. In these participants, the entire heart did not fit into a single pyramidal full volume. After fusion of several datasets (pyramidal volumes), however, the entire LV volume could be displayed.

The anterior wall of the LV had the worst visibility on standard RT3DE, in common with the literature (16). Difficulties with placing the large RT3DE probe in the intercostal space may account for this. Fusion of full volumes from different apical acoustic windows appears to be a unique approach to overcome this problem, and our 3D fusion technology can be applied without the external position sensor, which makes 3DFE different than older compound techniques.

The 3DFE technique relies on a sophisticated algorithm, which fuses 3D datasets based on voxel similarity across the 3D datasets. One dataset "floats" through the other dataset in a multiresolution framework until maximal similarity is reached.

In principle, fusion can be performed with datasets obtained from any view. However, in this study, we used datasets from apical views because the fusion process is accelerated if the datasets are not too different. There are also options for fusion of apical and parasternal long-axis views, as described previously by the authors (5,17). However, at present, they require much higher computer power and take much longer to process.

The new 3DFE yielded similar volumes to standard RT3DE in both patients and in a cardiac phantom, suggesting the fusion method did not result in distortion of volume measurements.

Study limitations. The 3DFE technique is still a time-consuming, offline technique, and in this pilot

study, the number of patients was small. However, at this early stage of development, we focused on the feasibility of this new approach for 3D echocardiography. Moreover, with further progress in the software, automated acquisition, and registration technique, a substantial decrease in processing time should soon be possible. Further clinical validation of 3DFE, on larger numbers of subjects with more diverse LV morphologies, is necessary. These patients have not been selected for a specific cardiovascular pathology, and it will be important to assess the technique for the severely diseased heart.

Fusion can be performed with full-volume datasets, composed from several consecutive heartbeats and from datasets with 1 heartbeat acquisition. The so-called flash 3D datasets obtained in 1 beat have the advantage of not having stitching artifacts. That should further improve the fusion process. Fusion can be also used for different imaging modalities, like CMR. These new applications are currently being investigated in our unit.

CONCLUSIONS

Fusion of 3D datasets from different echocardiographic windows resulted in improvement in the endocardial borders, image quality, and completeness of the 3D datasets, without altering volumes. Although these results are encouraging, further studies are needed in larger groups of patients. Fusion may facilitate more widespread usage of 3D echocardiography in the future.

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Key Words: echocardiography ■
ultrasonics ■ imaging.

APPENDIX

For accompanying videos, please see the online version of this article.