Three-dimensional echocardiography for left ventricular quantification in heart failure

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Chapter 6

Non-invasive mapping of left ventricular electromechanical synchronicity by three-dimensional echocardiography and semi-automatic contour detection

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Abstract

A system for analyzing left ventricular (LV) electromechanical asynchrony based on transesophageal three-dimensional echocardiography (3DE) and semi-automatic endocardial contour detection is described. Eighteen consecutive patients underwent 3DE. Using TomTec 4DLV software, a three-dimensional endocardial surface was reconstructed throughout the cardiac cycle. Matlab software generated color-coded polar maps, displaying regional LV displacement and its timing. At the segmental level, Bland-Altmann assessment showed intra-observer variability of LV displacement of 0,1 ± 3,0 mm and timing of −5,6 ± 160 ms (bias ± 2 SD) for all segments and −1,6 ± 94 ms for the nonapical segments. The combination of 3DE and semi-automatic contour detection is feasible and provides unique information for assessing regional LV endocardial displacement and electromechanical asynchrony.

The potential improvement of left ventricular (LV) function by the correction of asynchronous LV contraction patterns in patients with left bundle branch block and decreased ejection fractions [1,2] has generated the need to quantify electromechanical LV contraction asynchrony. Regional, detailed, and quantitative measurement of LV contraction and timing is possible only when performed completely in 4 dimensions, that is, if the entire three-dimensional heart can be followed throughout the cardiac cycle with adequate spatial and temporal resolution. The present study describes the feasibility of a system based on transesophageal three-dimensional echocardiography (3DE) in combination with semi-automatic endocardial contour detection that has been developed to assess LV asynchrony.

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In 18 consecutive patients (mean age 64 ± 15 years; 10 men; mean ejection fraction 38 ± 17% [range 15% to 68%], mean QRS duration 134 ± 40 ms [range 76 to 204; measured with 12-lead electrocardiography on the same day of the ultrasound examination]), of whom 4 had left bundle branch block, who underwent transesophageal echocardiography for various clinical reasons, 3DE was performed. A subgroup of 7 patients with biventricular pacemakers was studied twice, with the pacemakers on and off, resulting in a total of 25 acquisitions. All patients gave informed consent after the explanation of the procedure.

The commercially available HP SONOS 5500 (Hewlett-Packard Company, Palo Alto, California) ultrasound machine and multiplane transesophageal echocardiographic probe (Philips Medical Systems, Eindhoven, The Netherlands) were used for 3DE. Three-dimensional echocardiography was performed using a built-in rotational acquisition algorithm that has been previously described [3]. Briefly, multiple long-axis views of the left ventricle with little or no foreshortening were generated. Using electrocardiographic R-wave and respiratory gating, 3DE was performed in 3° or 5° intervals, resulting in either 60 or 36 slices, respectively, at 25 frames/s. Images were stored on magneto-optical discs for subsequent analysis.

A TomTec workstation with TomTec 4DLV analysis software (TomTec GmbH, Munich, Germany) was used for analysis. On the basis of image quality, 8 to 9 approximately

similarly spaced long-axis views, or “slices,” were selected from the data set. After the manual input of locations of the mitral and aortic valve and the apex, in end-diastole and end-systole, the software projected an oval in the LV cavity, the size and shape of which were manually adjusted to an approximate fit. The software detected the endocardial contours automatically throughout the cardiac cycle, with the possibility for manual correction, and extrapolated the three-dimensional endocardial surface. For visual assessment, a cine loop of surface and contours was projected on a screen that could be rotated for viewing at different angles. The TomTec software calculated LV volumes and ejection fractions automatically. End-diastole and end-systole were defined as the frames of mitral and aortic valve closure, respectively.

The endocardial surface was based on a 744-point wire frame, whose numerical coordinates were available in an output format that was read by MatLab software (The MathWorks, Inc., Natick, Massachusetts). By linking the 744 points of the wire frame, 1,440 triangular segments were generated. This could be later converted back to a traditional 16-segment model, in which each segment was composed of approximately 90 of the original 1,440 subsegments. The LV center of gravity was calculated from the end-diastolic frame and fixed over time. Of each endocardial surface point, distance to the LV center of gravity was calculated throughout the cardiac cycle. Displacement was defined as average end-diastolic minus end-systolic distance for every surface point.

Furthermore, the time between the onset of the electrocardiographic R-wave and the moment of maximal endocardial displacement was calculated for each endocardial surface point. The timing of displacement was quantified as the average time from the moment of mitral valve closure to the moment of maximal displacement, and its SD was expressed as dispersion. Because of asynchronous contraction, each endocardial surface point does not show maximal inward displacement exactly at end-systole; dispersion serves as a measure of asynchrony. Thus, 2 temporal variables per left ventricle were obtained, 1 for timing and 1 for dispersion. The parameters were plotted in polar maps. Using this method, dyssynergic regions are displayed in shades of red in a displacement plot, and dispersion can be appreciated by the heterogeneity of the colors in a timing plot (figure 1).

Displacement and timing were calculated per segment, using the American Society of Echocardiography's 16-segment model [4]. Dispersion was calculated per left ventricle. To

assess reproducibility, all measurements were performed twice by an experienced observer at a 1-month interval.

In 5 of 25 acquisitions, 3DE analysis was not possible because of motion artifacts (n = 1), mitral valve calcifications partly concealing the endocardial contour (n = 3), and the development of bigeminy during acquisition (n = 1), yielding 20 left ventricles with 16 segments each. A total of 362 frames were analyzed. The acquisition time was approximately 3 minutes per left ventricle. After a training period, the analysis time was approximately 30 minutes per left ventricle.

Examples of displacement and timing polar maps are shown in figure 1. Bland-Altman plots of the reproducibility of timing are shown in figure 2. Patient data are listed in table 1. Table 2 lists average values and reproducibility per segment of displacement, timing, and dispersion, based on a 16-segment model, and of LV volumes and ejection fractions. Because of the averaging effect, the reproducibility per segment of timing and dispersion was better for each segment of the 16-segment model than for the 1,440-segment model (data not shown). The reproducibility of the timing of nonapical (vs apical) segments was significantly better (−1,6 ± 94 ms [bias ± 2 SD] vs 0,7 ± 200 ms; p = 0,0001, respectively). In the subgroup of patients who underwent 3DE before and during biventricular pacing, the average timing (i.e., the average duration of time to maximal displacement) remained stable (406 ± 82 to 431 ± 75 ms, p = NS), whereas dispersion decreased significantly (117 ± 29 to 78 ± 23 ms, p = 0,01). QRS duration increased nonsignificantly from 151 ± 26 to 179 ± 15 ms (p = 0,06).

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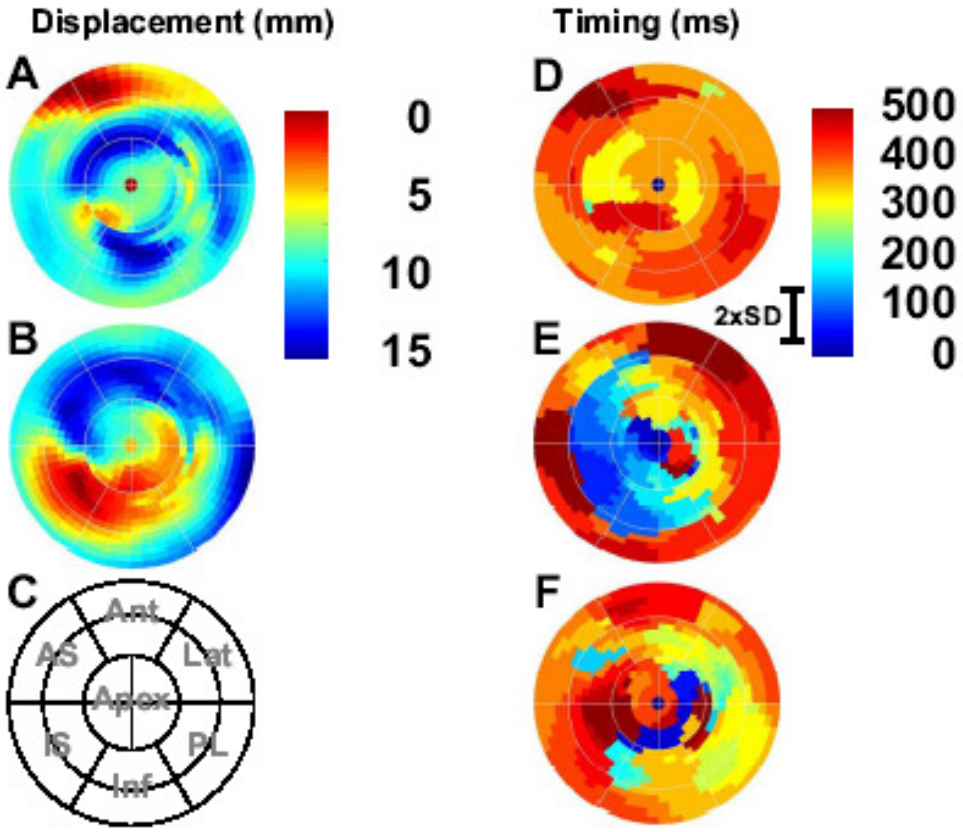
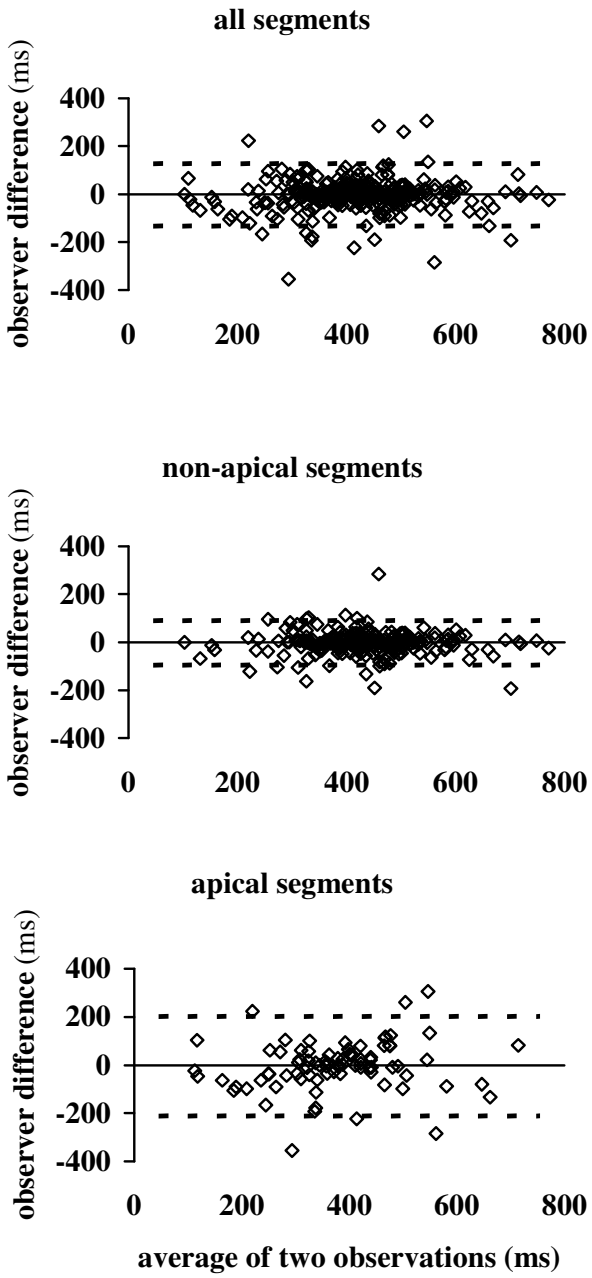
Figure 1.



Examples of polar maps depicting the extent of maximal regional LV endocardial displacement (left panel), and timing (right panel). The displacement scale indicates endocardial displacement (from blue to red as wall motion worsens) in millimetres from end-diastole to end-systole. In the timing plots, the time scale (0 to 500 ms; blue - early, red - late) indicates the moment of maximal endocardial displacement in milliseconds from the onset of the R wave to the moment of maximal inward displacement. The 95% confidence interval of reproducibility (of nonapical segments) is indicated along the color bar for comparison. In the displacement plots, 2 examples are shown: (A) normal; absence of inward displacement in the left ventricular outflow tract; and (B) inferoseptal infarction; dyssynergy in the inferoseptum. (C) Schematic showing the location of each segment. In the timing plots, 3 examples are shown: (D) Narrow QRS complex, normal ejection fraction. The entire endocardial wall reaches maximal inward displacement at approximately the same moment, resulting in a homogeneous color of the polar map. (E) Ischemic cardiomyopathy, left bundle branch block, low ejection fraction. The early activation of the septum results in early maximal inward displacement in that region (blue), whereas the delayed activation of the basal anterolateral wall causes late maximal inward displacement (red). (F) The same patient as in (B), during biventricular pacing. The posterolateral wall is activated early by the pacemaker, as is evident from the blue to yellow "spot" (in the 4 o'clock position). The septum takes longer to reach maximal inward displacement. A marked reduction of asynchrony is clear from the more homogeneous color of the polar map. Ant, anterior; AS, anteroseptal; Lat, lateral; PL, posterolateral; Inf, inferior; IS, inferoseptal.

Figure 2.



Bland-Altman plots of the reproducibility of timing. The horizontal axis is the average of 2 measurements and the vertical axis the difference between the first and second measurements of 1 observer (in milliseconds). Dashed lines, the 95% confidence interval. (top) The reproducibility of all segments, (center) the reproducibility of non-apical segments, and (bottom) the reproducibility of apical segments. The reproducibility of nonapical (vs apical) segments was significantly better.

Table 1. Patient Data

Patient No.	Ischemic CMP	NYHA Class	Pacemaker	QRS Duration (ms)	BBB	Displacement (mm)	Average Duration to Maximal Inward Displacement (ms)	Dispersion (ms)	Ejection Fraction (%)
1	–	1	0	120	right				50
2	+	3	0	110	-	2,0 ± 2,5	451	128	17
3	–	?	0						25
4	–	3	0	94	-	7,0 ± 2,3	399	52	56
5	+	3	0	133	right	4,2 ± 3,6	294	109	43
6	+	2	0	96	left	3,4 ± 2,2	467	91	36
7	–	1	0	80	-	5,8 ± 2,9	420	113	63
8	–	1	0	90	-	6,8 ± 3,5	390	86	60
9	–	1	0	108	-	6,0 ± 1,5	488	62	46
10	–	1	0	82	-	5,8 ± 3,4	426	144	58
11	–	1	0	76	-	7,9 ± 1,8	345	42	56
12	+	4	Off	158	left	2,4 ± 3,9	320	149	19
			On	172		2,8 ± 2,1	422	117	23
13	+	3	Off	158	left	3,0 ± 2,5	375	117	28
			On	190		2,3 ± 3,1	391	99	38
14	+	3	Off	136	left	1,7 ± 1,9	515	145	16
			On	163		2,4 ± 1,9	542	83	21
15	+	2	Off	190	left	1,5 ± 1,9	351	145	20
			On	172		3,4 ± 1,9	360	135	15
17	+	3	Off	150	-				
			On	204		3,6 ± 3,6	566	127	28
18	–	2	Off	112	-	2,7 ± 2,2	462	77	26
			On	172		3,4 ± 1,9	436	36	26

BBB = bundle branch block; CMP = cardiomyopathy; NYHA = New York Heart Association.

Table 2. Reproducibility

Variable	Value (average ± SD)	Reproducibility (bias ± 2 SD)
Displacement (mm)	3,9 ± 2,0	0,1 ± 3,0
Timing (ms)		
All segments	422 ± 73	- 5,6 ± 160 ms
Nonapical segments		- 1,6 ± 94 ms
Apical segments		0,7 ± 200 ms
Dispersion (ms)	92 ± 30	21 ± 50
End-diastolic volume (ml)	145 ± 54	- 1,2 ± 11,9
End-systolic volume (ml)	98 ± 57	- 0,3 ± 11,8
Ejection fraction (%)	38 ± 18	- 0,3 ± 4,2

The visual assessment of myocardial asynchrony is difficult; differences < 70 to 90 ms cannot be measured in a reproducible fashion by the naked eye [5]. Color kinesia [6] and Fourier analysis [7] are at present based on 2-dimensional echocardiography and are far from ideal. Tissue Doppler [8] provides good temporal resolution, but inward displacement and its timing is obtained in only 1 dimension and dependent on the insonification angle [9]. Magnetic resonance imaging is not yet compatible with pacemakers, prohibiting its use. A recently innovated nonfluoroscopic system for electromechanical mapping uses a catheter tip, which is in contact with the endocardium [10]. It provides continuous spatial localization based on magnetic field technology. Although it is three-dimensional, has good spatial and temporal resolution, and might be adapted for use in asynchrony measurement, its invasive nature precludes widespread use. Moreover, its primary use is in electrical activation mapping, whereas in asynchronous contraction, mechanical rather than electrical asynchrony appears to be more relevant [11]. This is demonstrated by the increased QRS duration observed during pacing, despite a decrease in dispersion. We hypothesize that this phenomenon may be due to the relatively large proportion of patients with diffuse intraventricular conduction delay, who may have relatively late free-wall electrical activation times and/or delayed electromechanical coupling [12].

The present method is based on 4-dimensional endocardial contour mapping, allowing very accurate spatial and reasonably accurate temporal quantification of LV wall motion patterns in nonapical segments, obviating semiquantitative scoring [4]. The apical segments heavily affect overall reproducibility, which is not surprising, considering the

apex is a problematic area for transesophageal echocardiography. The reproducibility of the nonapical segments is reasonable, if one takes into account that the average duration of the time to maximal endocardial displacement of the study population ranged from about 300 to 600 ms. The size of the measurement error is shown on the timing polar map of figure 1 on the color bar (in milliseconds; y axis). The overall information of the electromechanical timing plot (early vs late activation) is not affected by this reproducibility. Further improvements in the algorithm, toward full automation, will further improve reproducibility.

Acquisition by transthoracic real-time 3DE may have obvious practical as well as theoretical advantages (better imaging of apical segments), although 3DE may allow the better evaluation of mitral valve regurgitation, which is an important and often ignored variable in the context of resynchronization therapy. Image quality, however, is usually poorer with real-time 3DE, and therefore, the diagnostic yield in unselected patients will be much less, with a negative effect on reproducibility. Because endocardial definition is paramount, currently, the 4-dimensional analysis system was tested only in 3DE data sets. Ultrasound contrast is therefore indicated if real-time 3DE is to be used. The semi-automatic endocardial contour detection system is not yet suited for use with contrast-enhanced, real-time 3DE. With a new 4-dimensional analysis algorithm, contrast LV opacification in conjunction with real-time 3DE may overcome this problem and may allow the practically instantaneous acquisition of a three-dimensional data set.

The level of temporal and spatial resolution that is needed to detect clinically relevant asynchrony is not yet known but may be in the 40- to 80-ms range [13]. Our hypothesis is that the relatively low frame rate of 3DE, in comparison with tissue Doppler techniques, may be compensated by its accurate assessment of regional displacement, because both are important in resynchronization therapy. In the subgroup of 7 patients with biventricular pacemakers, dispersion decreased significantly during pacing. This could be readily observed on the polar map, which might indicate that temporal resolution may be good enough.

Our study is a feasibility study for asynchrony assessment by 3DE, in which tissue Doppler measurements were not made. In future studies, it would be interesting to compare the current method with velocity- and strain (rate)-based tissue Doppler methods for the

assessment of asynchrony and to study the ability of the 2 techniques in predicting the optimal stimulation site and hemodynamic response after resynchronization.

The combination of 3DE with semi-automatic contour detection is a feasible, new technique for the assessment of asynchrony, both spatially and temporally. It enables the reconstruction of the LV endocardial surface in 4 dimensions, with good spatial resolution and reasonable temporal resolution. Technologic advances not far from the horizon may improve temporal resolution. Asynchrony can be displayed on electromechanical polar maps of timing in a readily understandable way, which might aid in the identification of candidates for resynchronization therapy and improve lead site selection. Three-dimensional echocardiography with semi-automatic contour detection may emerge as a unique technique, combining the assessment of timing, displacement, and the severity of mitral regurgitation.

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