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**Myocardial Contractile Function in the Region of the
Left Ventricular Pacing Lead Predicts the Response to
Cardiac Resynchronization Therapy Assessed by
Two-Dimensional Speckle Tracking Echocardiography**

左室ペーシングリード留置部位の心筋収縮能は心臓再同期療法
への反応性を予測する
—2D スペックルトラッキング心エコー図法を用いた検討—

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Key words: Cardiac resynchronization therapy, Heart failure, Dyssynchrony,
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ABSTRACT

Objective: The aim of this study was to test the impact of the posterolateral myocardial systolic function on response to cardiac resynchronization therapy (CRT).

Methods: Forty patients were studied before and 4 ± 2 months after CRT.

Dyssynchrony was defined as anteroseptal wall-to-posterior wall delay (≥ 130 ms) caused by speckle-tracking radial strain. The average longitudinal strain in 4 posterior and lateral segments (ϵ -pl) in which the left ventricular pacing lead was positioned was calculated by automated functional imaging. Response to CRT was defined as a $\geq 15\%$ decrease in end-systolic volume.

Results: The negative value of ϵ -pl in responders was significantly higher than that in non-responders at baseline ($-7.8 \pm 6.9\%$ vs $-2.1 \pm 4.9\%$, $P < 0.01$). Combining dyssynchrony with ϵ -pl $< -7.8\%$ was more effective for predicting response to CRT than dyssynchrony parameters alone (92% vs 75%).

Conclusion: The addition of posterolateral myocardial systolic function to the measurement of dyssynchrony appears to be of value for predicting response to CRT.

Cardiac resynchronization therapy (CRT) is an established therapeutic option for patients with advanced heart failure (HF). Previous studies have demonstrated that CRT reduces HF symptoms and improves acute and chronic hemodynamics, exercise capacity, the quality of life, survival, and left ventricular (LV) systolic function.¹⁻⁷ Randomized clinical trials have demonstrated, however, that up to one third of patients with HF do not favorably respond to CRT with standard clinical selection criteria, including electrocardiographic QRS width.^{1, 3, 4, 7} Accordingly, the quantification of LV mechanical dyssynchrony by echocardiography has emerged as an important option for predicting response to CRT. Although LV mechanical dyssynchrony has been associated with response to CRT, some patients with LV mechanical dyssynchrony assessed by echocardiography do not respond to CRT. Other factors, such as LV lead position or scar burden, may also influence response to CRT, regardless of the presence of dyssynchrony. Previous investigators have reported that myocardial viability or scar tissue is an important marker for response to CRT.⁸⁻¹⁰ However, the impact of regional myocardial systolic function assessed by echocardiography in the posterolateral wall, where the LV pacing lead is positioned for response to CRT, is not known. Automated function imaging (AFI), based on 2-dimensional speckle tracking imaging, can be used for the assessment of regional longitudinal strain of the 17-segment left ventricle as a bull's-eye map.^{11, 12}

Our objective was thus to test the impact of posterolateral myocardial systolic function assessed by AFI on the response to CRT. Furthermore, we evaluated the hypothesis that the addition of posterolateral myocardial systolic function to LV dyssynchrony assessed by echocardiography would further improve the ability to

predict response to CRT.

METHODS

Study Population

We studied 47 consecutive patients with HF who underwent CRT. The selection criteria for CRT included chronic severe HF (New York Heart Association functional class III or IV), LV ejection fraction (EF) $\leq 35\%$, and QRS duration ≥ 120 ms. Seven patients were excluded from subsequent analysis because their echocardiographic images were technically unsatisfactory. Accordingly, the patient study group consisted of 40 patients with HF, 28 (70%) in New York Heart Association functional class III and 12 (30%) in class IV at the initial evaluation. The group's mean age was 67 ± 12 years, 10 (25 %) were women, the mean EF was $25 \pm 8\%$, the mean QRS duration was 163 ± 25 ms, and 9 patients (23%) had ischemic cardiomyopathy (Table 1). Twenty-four patients were diagnosed with sinus rhythm and 6 with atrial fibrillation, while 10 had previously undergone the implantation of permanent right ventricular pacemakers ≥ 1 year before enrollment, and they were predominantly right ventricular paced, which was defined as $\geq 90\%$ paced when the device was interrogated at the time of enrollment. All patients were on optimal pharmacological therapy, if tolerated. Written informed consent to participate in the study was obtained from all patients.

Echocardiography

All echocardiographic studies were performed with a commercially available echocardiography system (Vivid 7; GE Vingmed Ultrasound AS, Horton, Norway).

Patients were studied before and 4 ± 2 months after CRT. Echocardiographic images were obtained in the left lateral decubitus position with a 3.5-MHz transducer. The mean frame rate was 65 ± 15 frames/s for grayscale imaging used for speckle-tracking analysis. Sector width was optimized for complete myocardial visualization while maximizing the frame rate. Gain settings were adjusted for routine grayscale 2-dimensional imaging to optimize endocardial definition. Pulsed-wave Doppler of the LV outflow tract was obtained to determine LV ejection phase. The end-diastolic wall thickness of the posterior wall was measured using routine grayscale 2-dimensional imaging. LV end-diastolic volume, LV end-systolic volume (ESV), and EF were calculated from the apical 2-chamber and 4-chamber images using the biplane Simpson's technique.¹³ For patients with atrial fibrillation, measurements of standard echocardiographic and speckle-tracking parameters were obtained as the averages of ≥ 3 consecutive cardiac cycles. Response to CRT was defined as reverse remodeling detected by a relative decrease in end-systolic volume $\geq 15\%$ from baseline.^{14, 15} Patients were defined as nonresponders if they did not show the above prespecified echocardiographic changes. Mitral regurgitation was visually assessed on the basis of the ratio of regurgitant jet area to left atrial area as none (grade 0), mild (grade 1), moderate (grade 2), severe (grade 3).

LV Dyssynchrony Analysis

Speckle tracking of routine grayscale mid-LV short-axis images was performed as previously described to assess LV dyssynchrony.¹⁶⁻¹⁸ The measurements were performed offline using dedicated software (EchoPAC version BTO6; GE-Vingmed Ultrasound AS). Briefly, an end-systolic circular region of

interest was traced on the endocardial cavity using a point-and-click approach, with special care taken to adjust tracking of all endocardial segments. A second and larger concentric circle was then automatically generated and manually adjusted near the epicardium. Speckle tracking automatically analyzed frame-by-frame movement of the stable patterns of natural acoustic markers, or speckles, over the cardiac cycle. Significant LV dyssynchrony was defined as a time difference > 130 ms between the anteroseptal and posterior wall peak strain¹⁶⁻¹⁸ (Figure 1).

Regional Myocardial Functional Analysis

Regional myocardial function was quantified using AFI. The measurements were performed offline using dedicated software (EchoPAC version BTO6). This technique was based on 2-dimensional speckle-tracking imaging that can be used for the assessment of regional longitudinal strain of the left ventricle and was performed as previously described in detail.^{11, 12, 19} Briefly, the mitral annulus and LV apex with 3 index points in the standard 3 apical views were defined at end-systole. The LV end-systolic frame was defined in the apical long-axis view, and the closure of the aortic valve was marked. The time interval between the R wave and aortic valve closure was used as a reference for the 4-chamber and 2-chamber view loops.¹⁹ The software then automatically detected the endocardium and tracked myocardial motion during the entire cardiac cycle. The left ventricle was automatically divided into 6 segments for each apical view and the peak systolic longitudinal strain was displayed for each plane, after which the results for all 3 images were combined into a single bull's-eye summary using a 17-segment model (Figure 2), which was automatically translated from the 18-segment model (Figure 3A). Myocardial

lengthening (positive value) is color-coded red and shortening (negative value) blue (Figure 2). Inadequately tracked segments determined by a tracking score obtained with the speckle-tracking algorithm were automatically excluded from analysis. If the tracking by AFI was poor, the region of interest was manually fine-tuned using visual assessment during the cine loop play to ensure that all segmental wall motions were included throughout the cardiac cycle. In this study, two different types of regional myocardial functional indices were determined by AFI: ϵ -global was calculated as the average of all 17 segments and ϵ -pl as the average of 4 posterior and lateral segments in which the LV pacing lead was positioned (Figure 3B). In normal subjects, longitudinal strain values are generally negative, with a larger negative value indicating greater longitudinal strain. The peak longitudinal strain was used for regional myocardial functional analysis by AFI. In cases of segments with positive or biphasic strain curves, a peak-positive or a larger peak strain was used, respectively.

Pacemaker Implantation and LV Pacing Lead Position

The LV pacing lead was inserted transvenously via the subclavian route in 38 patients, and the epicardial surgical approach was used for remaining 2 patients. The LV pacing lead was positioned in the lateral or posterolateral vein, corresponding to segments 1 to 4 in the 17-segment LV model (Figure 3B). Device implantation was successful in all patients, without major complications. After implantation, the atrio-ventricular interval was optimized for maximal diastolic filling using Doppler echocardiography.²⁰

Statistical Analysis

All parametric data are expressed as mean $\pm$ SD. Group comparisons

between before and after CRT were performed using the paired t test and group comparisons between responders and nonresponders using the unpaired t test. Proportional differences were evaluated using Fisher's exact test or the χ^2 test as appropriate. Correlation analysis was performed using linear regression, and results are expressed as Pearson's correlation coefficient. Analysis of the receiver operating characteristic curve was used to assess the optimal cutoff values to predict response to CRT. For all tests, P values < 0.05 were considered statistically significant.

RESULTS

Patient Characteristics

Thirty patients (75%) were considered responders 4 $\pm$ 2 months after CRT according to the predefined criteria, and the remaining 10 patients (25%) were classified as nonresponders. Baseline echocardiographic characteristics of responders and nonresponders were similar (Table 1). Compared with nonresponders, responders tended to have smaller LV volumes and larger dyssynchrony, although the difference was not statistically significant (Table 1). Of the 6 patients with atrial fibrillation, 2 underwent atrioventricular junction ablation at the same time as CRT, and 2 were defibrillated first, and their atrial fibrillation disappeared after CRT. All 6 patients with atrial fibrillation received digoxin, β -blockers, and amiodarone for rate control before CRT. The LV lead position was assessed from a chest x-ray using the frontal and lateral views.²¹ The LV pacing lead was positioned mid lateral (n=21), basal lateral (n=2), mid posterior (n=13), and basal posterior (n=4). These lead positions corresponded to segments 1, 2, 3, and 4, respectively, in Figure 3B. Overall, speckle-

tracking analysis by AFI was possible for 97% of the 1,360 segments from 40 subjects (baseline and follow-up), with technically adequate images subjected to the analysis, so that only 3% had to be excluded. Interobserver and intraobserver variability were 8.4% and 4.9% for ϵ -global, 5.4% and 6.9% for ϵ -pl, and 4.2% and 1.8% for LV dyssynchrony, respectively.

Impact of Regional Myocardial Function on Response to CRT

Values of ϵ -global in both responders and non-responders were similar ($-6.7 \pm 3.0\%$ vs. $-5.1 \pm 2.4\%$, $P=NS$), but the negative value of ϵ -pl in responders was significantly higher than that in nonresponders at baseline ($-7.8 \pm 6.9\%$ vs $-2.1 \pm 4.9\%$, $P < 0.01$; Figure 4). After CRT, the negative value of ϵ -global increased significantly in responders from $-6.7 \pm 3.0\%$ to $-11.4 \pm 3.8\%$ ($P < 0.01$ vs baseline) but remained virtually unchanged in nonresponders from $-5.1 \pm 2.4\%$ to $-6.6 \pm 1.6\%$ (Figure 5). Figure 6 shows representative images of the bull's-eye map produced by AFI for responders and nonresponders before and after CRT. Receiver operating characteristic curve analysis was performed to obtain the optimal cutoff value of ϵ -pl for predicting response to CRT. A ϵ -pl of -7.8% had 90% sensitivity and 60% specificity for the prediction of response to CRT. Twenty-eight patients (70%) showed evidence of LV dyssynchrony at baseline, defined as a time difference > 130 ms between the anteroseptal and posterior wall peak strain. The response rate after CRT for patients with dyssynchrony was 75%. Furthermore, patients with both significant dyssynchrony and ϵ -pl $< -7.8\%$ determined by receiver operating characteristic curve analysis were associated with a high incidence of LV functional improvement, with a response rate of 92%.

Relationship Between LV EF and LV Longitudinal Strain

At baseline, ϵ -global correlated significantly with EF ($r = -0.34$, $P < 0.05$; Figure 7A). Furthermore, an even closer correlation was found between ϵ -global and EF after CRT ($r = -0.84$, $P < 0.0001$; Figure 7B).

Changes in LV Dyssynchrony After CRT

After CRT, LV dyssynchrony improved in responders from 272 ± 154 to 53 ± 39 ms ($P < 0.001$) but remained virtually unchanged in nonresponders, from 216 ± 151 to 168 ± 66 ms (Table 1). The improvement in LV dyssynchrony correlated with a relative increase in EF after CRT (Figure 8).

DISCUSSION

This study demonstrates that regional myocardial systolic function in the posterolateral wall, where the LV pacing lead was positioned, was associated with response to CRT. Importantly, combining LV mechanical dyssynchrony with posterolateral myocardial systolic function assessed by AFI was more useful for predicting response to CRT than dyssynchrony parameters alone.

CRT is an established therapeutic option for patients with advanced HF. Previous studies have demonstrated that CRT reduces HF symptoms and improves acute and chronic hemodynamics, exercise capacity, the quality of life, survival, and LV systolic function.^{1-7, 22} Randomized clinical trials have shown that up to one third of patients with HF do not favorably respond to CRT when standard clinical selection criteria are used, including the electrocardiographic QRS width.^{1, 3, 4, 7} Accordingly, the quantification of LV mechanical dyssynchrony by echocardiography has emerged

as an important options for predicting response to CRT.

Assessment of LV Dyssynchrony

This study focused on radial thickening resulting from speckle tracking of radial strain to assess LV dyssynchrony. The largest body of published studies on LV dyssynchrony and prediction of response to CRT report their results in terms of LV longitudinal shortening velocities using tissue Doppler imaging from the apical views^{14, 23-25}. However, the recent Predictors of Responders to CRT (PROSPECT) study used several echocardiographic dyssynchrony indices, including tissue Doppler imaging and suggested that dyssynchrony indices based on tissue Doppler velocity could not replace routine selection criteria for CRT.²⁶ Speckle-tracking echocardiography, on the other hand, may be applied to routine grayscale images and is not limited by the Doppler angle of incidence. As a result, speckle-tracking radial strain analysis allows for an accurate quantification of regional wall thickening. Suffoletto et al¹⁸ demonstrated that baseline speckle-tracking radial dyssynchrony, defined as a time difference ≥ 130 ms between the anteroseptal and posterior wall peak strain, predicted chronic EF response to CRT (8 ± 5 months after CRT) with 89% sensitivity and 83% specificity. Furthermore, several investigators have also demonstrated the utility of speckle-tracking radial strain for predicting response to CRT.^{16, 17, 27}

Impact of Myocardial Function on Response to CRT

Although LV mechanical dyssynchrony has been associated with response to CRT, some patients with LV mechanical dyssynchrony identified by echocardiography do not respond to CRT. Other factors, such as LV lead position or

scar burden, may influence response to CRT, regardless of LV dyssynchrony. Previous investigators have reported that myocardial viability or scar tissue is an important marker for the response to CRT.⁸⁻¹⁰ In this study, we showed that the posterolateral systolic function where the LV pacing lead was positioned in responders was significantly higher than that in nonresponders ($-7.8 \pm 6.9\%$ vs $-2.1 \pm 4.9\%$). This was recently corroborated by Bleeker et al,⁸ who demonstrated that patients with transmural scar in the posterolateral region assessed by contrast-enhanced magnetic resonance imaging did not respond to CRT, whereas 81% of the patients without posterolateral scar responded well to CRT. In addition, Hummel et al,⁹ using contrast echocardiography to identify myocardial viability, reported similar findings for 21 patients with ischemic cardiomyopathy; viability in the posterior and lateral regions correlated with improvement in LV EF after 6 months of CRT. Furthermore, Ypenburg et al,¹⁰ using single photon-emission computed tomography with ^{99m}Tc tetrofosmin to identify posterolateral myocardial viability, reported similar findings for 51 patients with ischemic cardiomyopathy. In addition, we observed that combining speckle-tracking radial dyssynchrony ≥ 130 ms with posterolateral myocardial systolic function assessed by AFI $< -7.8\%$ was more useful for predicting response to CRT than speckle-tracking radial dyssynchrony parameters alone (92% vs 75%). With this method, we observed significant differences between responders and nonresponders in myocardial systolic function assessed by AFI in the LV pacing target region. These data provide further support for the need for assessment of myocardial systolic function in the region of the LV pacing lead in addition to LV dyssynchrony only when selecting patients for CRT.

Impact of LV Lead Location

Although the LV lead is routinely positioned in a posterior or lateral epicardial vein through the coronary sinus, previous investigators have inferred that LV lead position affects patient response to CRT. Ansalone et al²⁸ demonstrated that LV lead placement at the most delayed segment resulted in the greatest immediate improvements after CRT. They also showed that the LV segment with the greatest delay in activation was most commonly the posterior or lateral wall. Becker et al, using 2-dimensional speckle-tracking circumferential strain²⁹ or real-time 3-dimensional echocardiography,³⁰ found that patients who had the LV lead tip position concordant with the site of the latest mechanical activation had greater degrees of EF increase after CRT than patients with discordant LV lead positioning.

AFI

AFI is based on 2-dimensional speckle-tracking imaging, which is applied to routine grayscale images and is not limited by the Doppler angle of incidence.^{11, 12, 19} Therefore, speckle-tracking strain analysis allows for accurate quantification of regional myocardial function. Because AFI can assess regional longitudinal strain from 17 LV segments as a bull's-eye map, this technique facilitates a rapid visual assessment of regional myocardial systolic function.

Relationship Between Two Indices of Global LV Systolic Function

Several authors have demonstrated the relationship between regional and global systolic function.^{19, 27, 31} Delgado et al¹⁹ reported that regional systolic function assessed by AFI was linearly related to biplane EF. We previously reported regional myocardial systolic function assessed by tissue Doppler strain rate imaging

was closely correlated with biplane EF in patients with coronary artery disease.²⁷ In this study, ϵ -global was found to correlate with EF at baseline, and an even closer correlation was observed after CRT. Time to peak systolic strain of each of the segments was dispersed at baseline in the presence of LV dyssynchrony, so that correlation of EF and ϵ -global may not be so close before CRT. Our results suggest that ϵ -global correlated closely with EF if no substantial LV dyssynchrony was present.

Study Limitations

This study included a small number of patients, and future larger studies are needed to further elucidate the role of regional myocardial systolic function for predicting response to CRT. Another limitation is that only 23% of the study population consisted of patients with ischemic cardiomyopathy, so that the beneficial response to CRT is somewhat higher than in previous studies. Although the exact reason remains unknown, one possible reason might be the difference of the etiology between patients with chronic severe HF in Japan and other areas, especially the United States and Europe. Osada et al³² reported 80% of patients with chronic severe HF among 284 applicants for heart transplantation in Japan were diagnosed with idiopathic dilated cardiomyopathy.

This study population was not homogeneous, because patients in sinus rhythm (n = 24), atrial fibrillation (n = 6), and previous implantations of permanent right ventricular pacemakers (n=10) were included. This heterogeneity may have affected the baseline data or response to CRT. Although current criteria for consideration of CRT do not include patients with HF with previous implantations of

permanent right ventricular pacemakers, upgrading of right ventricular pacing systems to CRT devices has become routine in many centers. Moreover, several investigators have reported that such upgrading was associated with long-term effects on mortality and morbidity similar to those for HF patients undergoing de novo CRT.³³⁻³⁵

Because this was a 2-dimensional study, it was not possible to simultaneously acquire 3 different apical views for the assessment of regional myocardial function by AFI. However, the R-R interval was similar (variation < 10%), and the frame rate was the same for each of the 3 different apical views in all patients. A newly developed 3-dimensional speckle-tracking system appears to be a possible solution for this problem.

Although several authors have suggested that scar burden or scar location might affect the response to CRT,^{8-10, 36} in this study we could not quantify myocardial scar burden or scar location by means of magnetic resonance imaging or myocardial perfusion imaging.

CONCLUSIONS

The reduced myocardial systolic function assessed by AFI in the region of the LV pacing lead was associated with inadequate LV resynchronization and resulted in nonresponse to CRT. The addition of posterolateral myocardial systolic function to measurement of dyssynchrony appears to be of value for predicting response to CRT and has potential clinical applications.

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FIGURE LEGENDS

Figure 1 An example of a 2-dimensional midventricular short-axis image demonstrating radial time strain curves in a patients with heart failure with left bundle branch block. Dyssynchrony is shown as the time difference (arrow) between the peak strain in the anterior septum (yellow curve) and in the posterior wall (purple curve).

Figure 2 An example of a bull's-eye map generated by AFI from 3 standard apical views. Myocardial lengthening is color-coded red and shortening blue.

Figure 3 A) Method for translation from the 18-segment model to the 17-segment model showing apical LV short-axis images. (GE Healthcare) B) The LV pacing lead was positioned in the lateral or posterolateral vein, corresponding to segments 1 to 4 in the LV 17-segment model.

Figure 4 Bar graphs of mean ϵ -global and ϵ -pl values for responders and nonresponders at baseline. Values of ϵ -global for both responders and nonresponders were similar, but the negative value of ϵ -pl was significantly higher for responders than that for nonresponders.

Figure 5 Bar graphs of mean ϵ -global values for responders and nonresponders at baseline and after CRT. The negative value of ϵ -global increased significantly in responders but did not increase in nonresponders.

Figure 6 LV 17-segment bull's-eye map presentation of regional strain before and after CRT in representative cases of a responder (A) and a nonresponder (B). ANT, Anterior; ANT_SEPT, anteroseptal; INF, inferior; LAT, lateral; POST, posterior; SEPT, septal.

Figure 7 (A) Scatterplot showing the correlations between ϵ -global and EF before CRT, demonstrating significant correlation. (B) Scatterplot showing the correlations between ϵ -global and EF after CRT, demonstrating closer correlation than before CRT.

Figure 8 Scatterplot showing the correlation between change in LV dyssynchrony and relative increase LV EF, demonstrating a significant correlation.

TABLE

Table 1. Baseline characteristics of patients and their responses to CRT

	All patients (n=40)	Responders (n=30)	Nonresponders (n=10)
Age (y)	67±12	68±12	66±10
Men/women	30/10	22/8	8/2
NYHA class (III/IV)	28/12	22/8	6/4
QRS duration (ms)	163±25	164±25	161±26
Left bundle branch block	22 (55%)	19 (63%)	3 (30%)
Rhythm (SR/AF/Paced)	24/6/10	19/3/8	5/3/2
HR (beats/min)	73±13	73±13	74±11
PR duration (ms)	188±29	187±28	191±35
Posterior wall thickness (mm)	10±2	10±2	10±2
Mitral regurgitation grade (0/1/2/3)	27/12/1/0	21/9/0/0	6/3/1/0
Etiology (ischemic/nonischemic)	9/31	6/24	3/7
Medication			
Diuretics	34 (85%)	24 (80%)	10 (100%)
ACE inhibitors/ARBs	37 (93%)	28 (93%)	9 (90%)
β-blockers	33 (83%)	25 (83%)	8 (80%)
Ejection fraction (%)			
Baseline	25±8	25±9	26±6
Follow-up	35±14	39±14*	24±5
End-diastolic volume (mL)			
Baseline	170±77	154±56	217±109
Follow-up	139±80	113±51*	216±104
End-systolic volume (mL)			
Baseline	131±67	119±53	166±95
Follow-up	95±69	72±44*	165±82
LV dyssynchrony (ms)			
Baseline	258±154	272±154	216±151
Follow-up	81±68	53±39*	168±66

ACE, Angiotensin-converting enzyme; AF, atrial fibrillation; ARB, angiotensin type1 receptor blocker; NYHA, New York Heart Association; SR, sinus rhythm.

Data are presented as means ± SD or as number.

* P < 0.05 vs baseline.

Figure 1

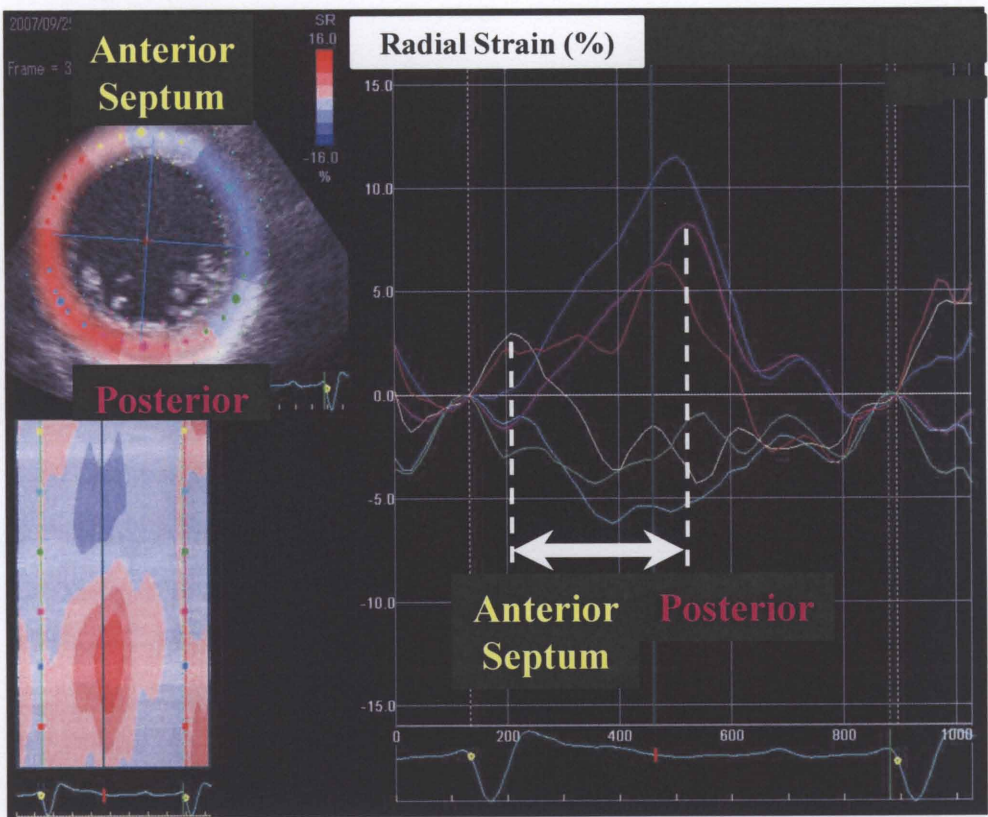


Figure 2

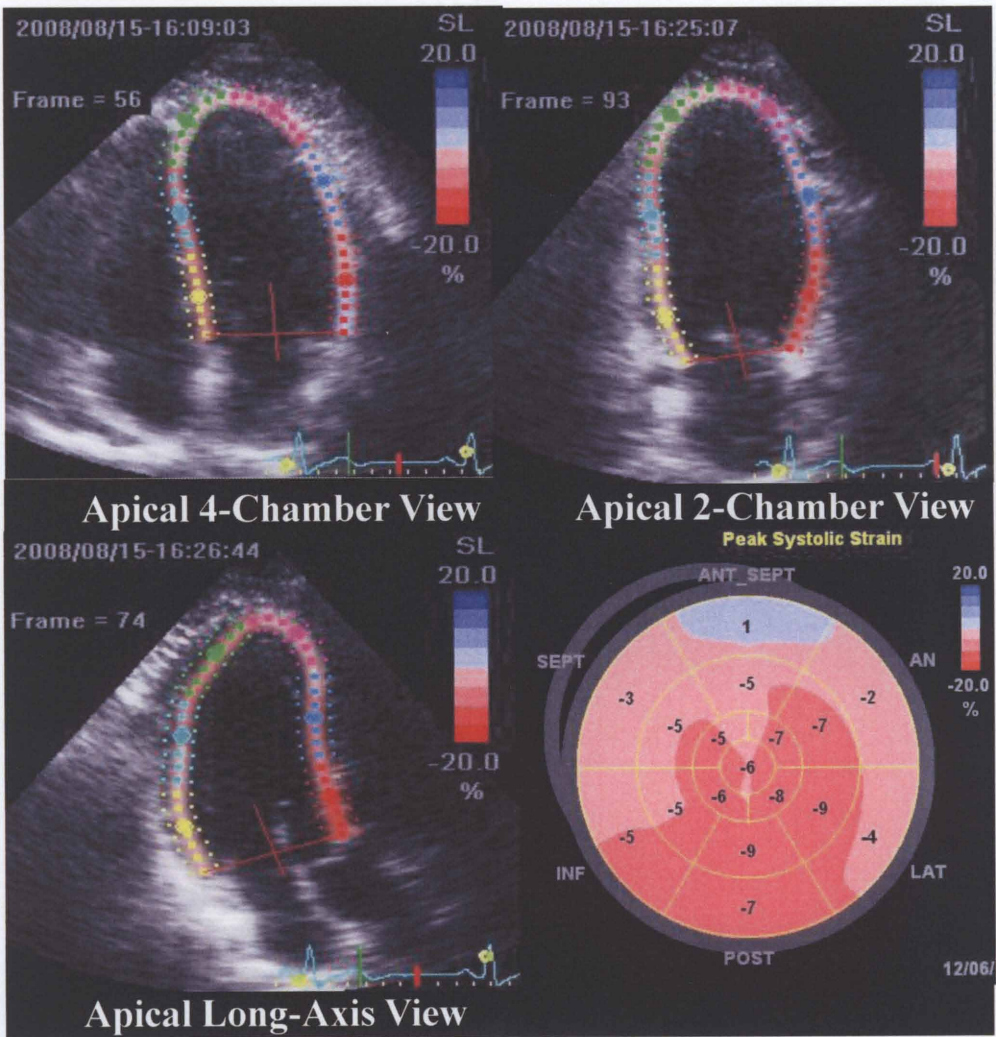
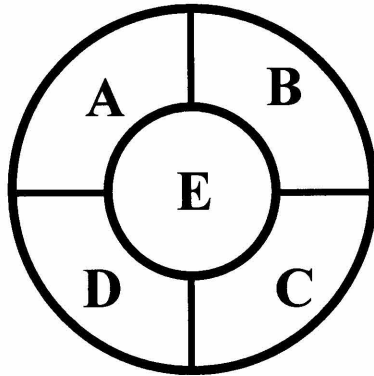


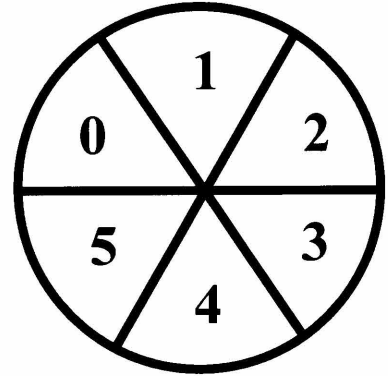
Figure 3

A)

17-segment model



18-segment model



$$\text{Value (A)} = \frac{2}{3} * [\text{Value (0)} + 0.5 * \text{Value (1)}]$$

$$\text{Value (B)} = \frac{2}{3} * [\text{Value (2)} + 0.5 * \text{Value (1)}]$$

$$\text{Value (C)} = \frac{2}{3} * [\text{Value (3)} + 0.5 * \text{Value (4)}]$$

$$\text{Value (D)} = \frac{2}{3} * [\text{Value (5)} + 0.5 * \text{Value (4)}]$$

$$\text{Value (E)} = \frac{1}{6} * [\text{Value (0)} + \text{Value (1)} + \text{Value (2)} + \text{Value (3)} + \text{Value (4)} + \text{Value (5)}]$$

B)

Anterior Septum

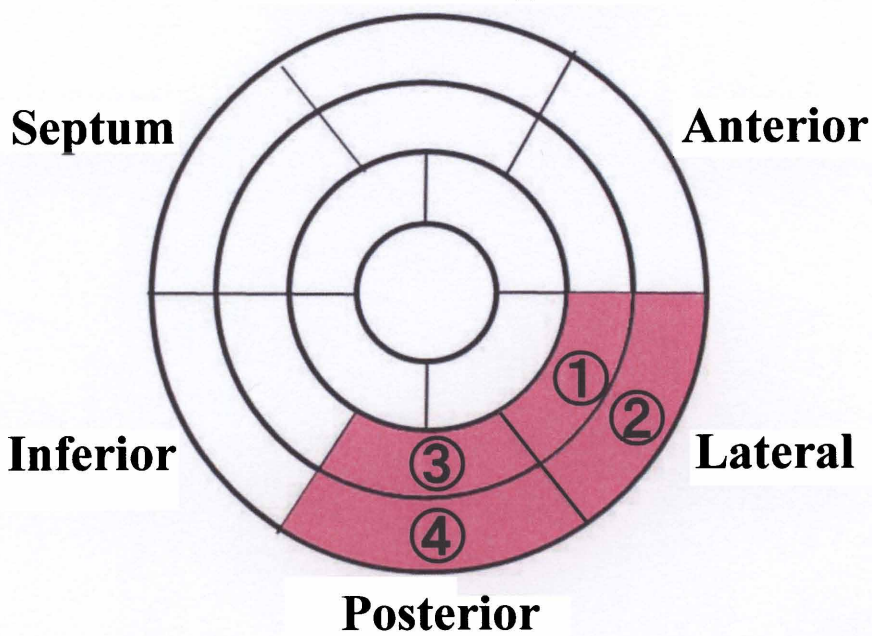


Figure 4

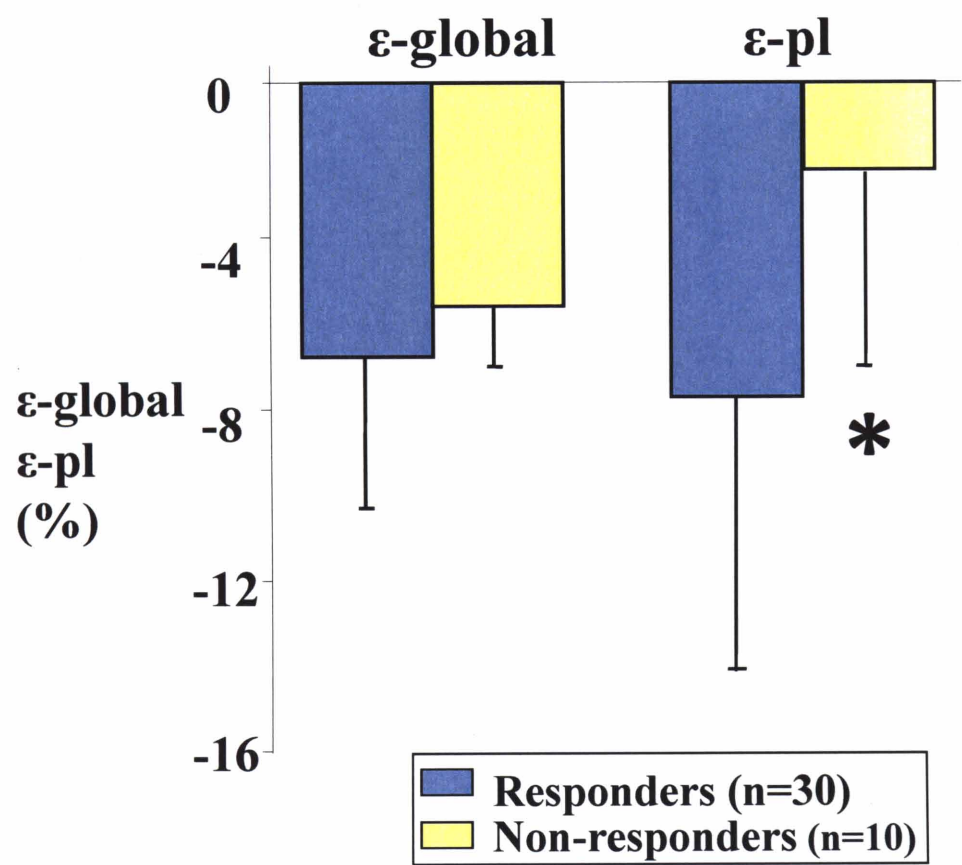


Figure 5

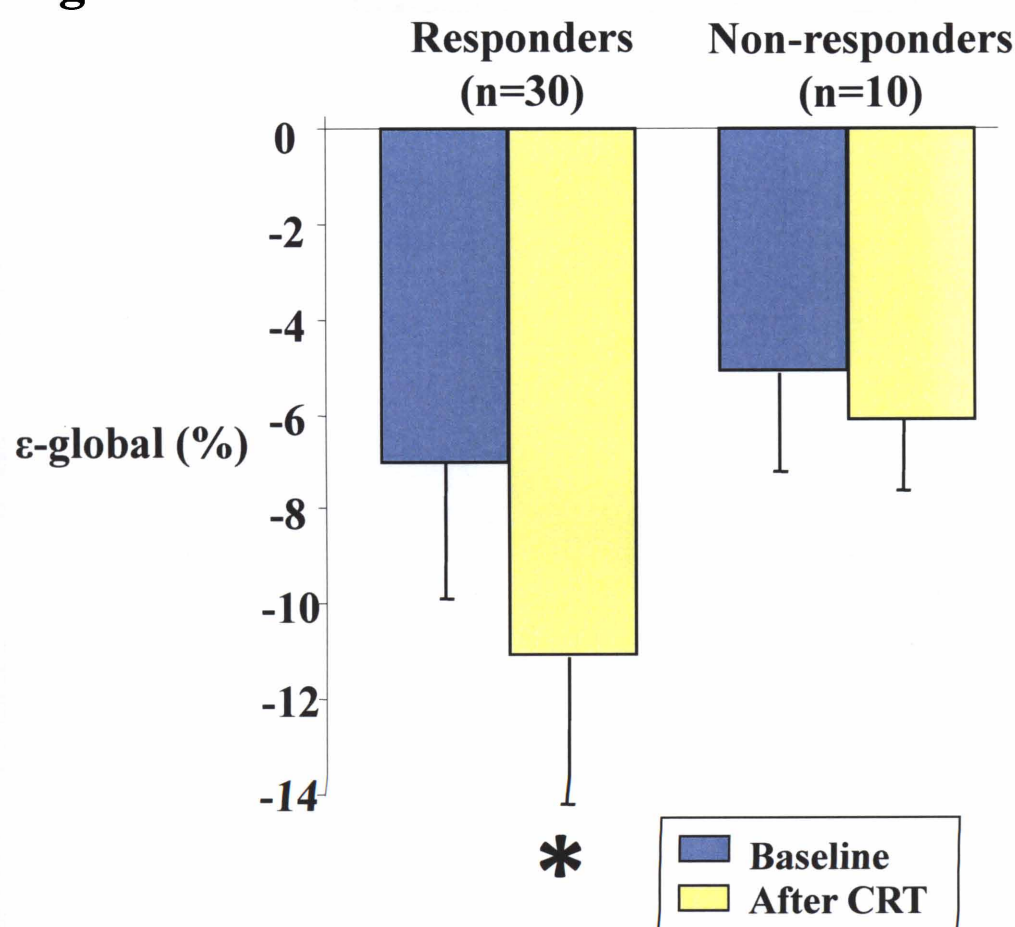
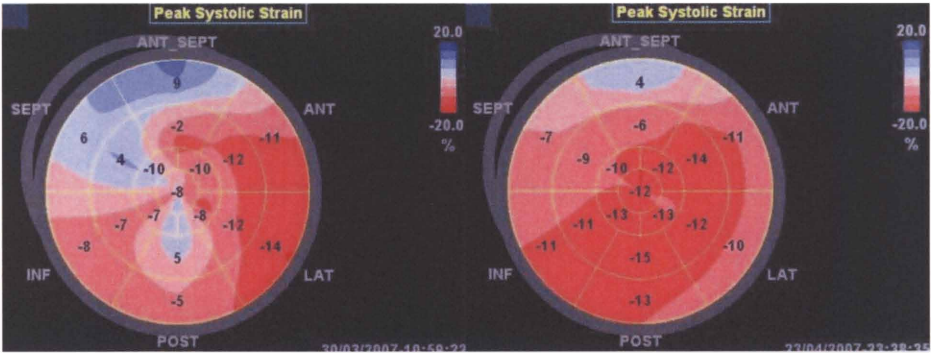


Figure 6

A) Responder

Before CRT

After CRT



B) Non-responder

Before CRT

After CRT

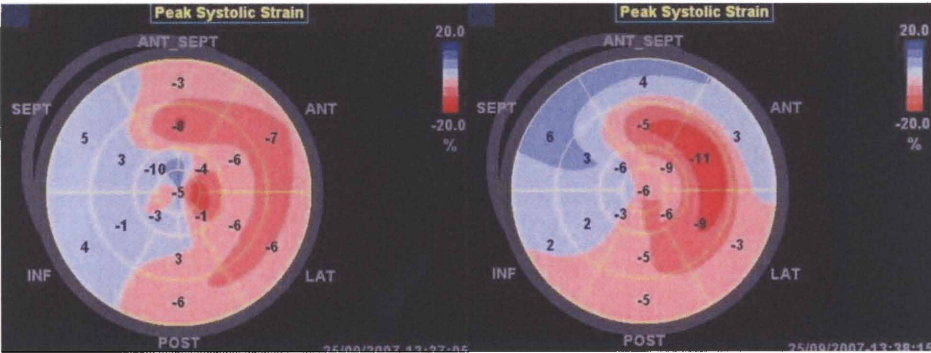


Figure 7

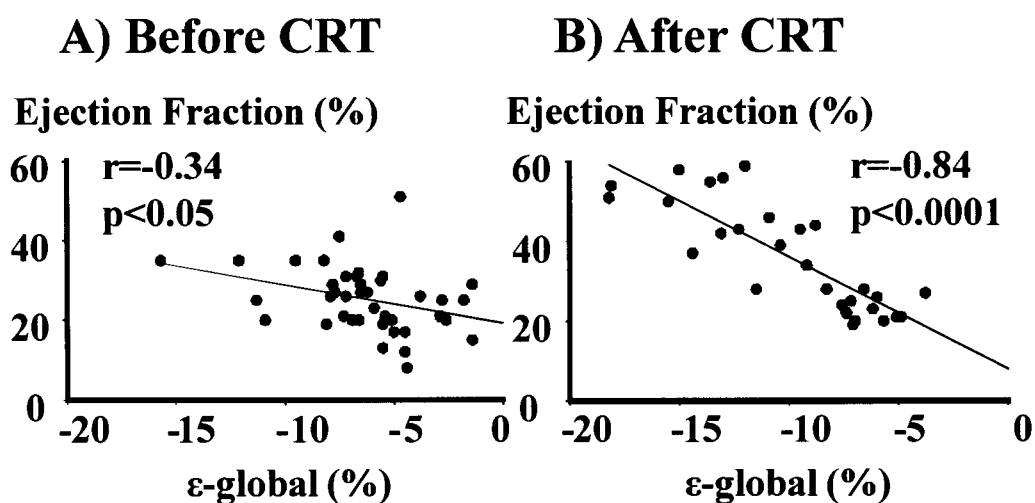


Figure 8

