

Impact of left ventricular lead position in cardiac resynchronization therapy on left ventricular remodelling. A circumferential strain analysis based on 2D echocardiography

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KEYWORDS

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Aims To assess if myocardial deformation imaging allows definition of an optimal left ventricular (LV) lead position with improved effectiveness of cardiac resynchronization therapy (CRT) on LV reverse remodelling.

Methods Circumferential strain imaging based on tracking of acoustic markers within 2D echo images (GE Ultrasound) was performed in 47 heart failure patients (59 ± 9 years, 28 men) at baseline, one day postoperatively, 3 and 10 months after initiation of CRT. Myocardial deformation imaging was used to determine¹ the segment with latest peak negative systolic circumferential strain prior to CRT, and² the segment with maximal temporal difference of peak strain before-to-on CRT as the segment with greatest benefit of CRT and assumed LV lead position. Anatomic LV lead position was determined by fluoroscopy. Optimal LV lead position was defined as concordance or immediate neighbouring of the segment with latest systolic strain prior to CRT and segment with assumed LV lead position.

Results Agreement of assumed LV lead position based on strain analysis and LV lead position defined by fluoroscopy were high ($\kappa = 0.847$). At 10 month follow-up, there was greater increase of EF (12 ± 3 vs. $7 \pm 4\%$, $P < 0.001$), greater decrease of left ventricular end-diastolic volume (LVEDV) (23 ± 8 vs. 13 ± 7 mL, $P < 0.001$) and left ventricular end-systolic volume (LVESV) (42 ± 10 vs. 27 ± 8 mL, $P < 0.001$), and greater increase of VO_2max (2.8 ± 0.8 vs. 1.9 ± 1.0 mL/kg/min, $P = 0.035$) in the optimal ($n = 28$ patients) compared to the non-optimal LV lead position group ($n = 19$ patients). The distance between segment with latest systolic strain prior to CRT and segment with assumed LV lead position was the only independent predictor of ΔLVEDV and ΔLVESV at 10 month follow-up ($R^2 = 0.2175$, $P = 0.0197$) and ($R^2 = 0.3774$, $P = 0.0054$), respectively.

Conclusion Detailed analysis of the myocardial contraction sequence using circumferential strain imaging allows determination of the LV lead position in CRT. Optimal LV lead position in CRT defined by circumferential strain analysis results in greater improvement in LV function and more LV reverse remodelling than non-optimal LV lead position.

Introduction

The introduction of cardiac resynchronization therapy (CRT) in patients with severe treatment refractory heart failure (HF) and bundle branch block has resulted in improvements in clinical symptoms, left ventricular (LV) function, and reverse remodelling even during long-term follow-up.^{1–6} Several clinical trials have demonstrated that a significant

part of patients do not respond favourable to CRT using standard clinical selection criteria.^{1–3,7} The severity of LV dyssynchrony defined by echocardiography has been noted to have a significant impact on the patients response to CRT.^{8–14} Echocardiography has therefore gained substantial importance in patient selection prior to CRT. However, the success of CRT is not only dependent on the degree of dyssynchrony but also on technical factors such as programming of the CRT system and optimized LV lead placement. The LV lead should be placed best in the area of greatest delay in

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electrical activation and mechanical contraction to achieve the optimal resynchronization effect.¹⁵ Still, identification of the optimal LV lead position has found less attention so far. This relates to difficulties in defining the LV segment with the greatest mechanical delay as well as defining the LV lead position and their spatial concordance.

A recently introduced myocardial deformation imaging based on tracking of acoustic markers from frame-to-frame in 2D echocardiographic images allows detailed analysis of myocardial deformation parameters including circumferential strain analysis.^{16,17} It may allow advanced assessment of LV dyssynchrony and effects of CRT.

This study sought to¹ identify the LV segment with latest mechanical contraction (defined by its deformation properties) prior to CRT based on circumferential strain analysis,² evaluate if circumferential strain analysis allows determination of the LV lead position based on a detailed analysis of the myocardial contraction sequence,³ determine the CRT effectiveness on LV function and reverse remodelling as well as improvement in cardiovascular capacity during a 10 month follow-up period in relation to the LV lead position defined by detailed circumferential strain analysis. Fluoroscopy was performed to define the anatomical LV lead position and used for assessment of the LV lead position determined by circumferential strain analysis.

Methods

Patients

Between June 2004 and December 2005, 63 patients with end-stage HF, scheduled for implantation of a biventricular pacemaker were screened for this study. Criteria for CRT implantation were New York Heart Association (NYHA) functional class III or IV despite optimal pharmacologic therapy, ejection fraction <35%, and a QRS-width >120 ms. Nine patients with atrial fibrillation or an implanted pacemaker and three patients with a poor echocardiographic window were excluded. Within the 51 patients, four patients refused participation in the current study and 47 patients [mean age 59 ± 9 years, 28 men, NYHA III ($n = 32$) and NYHA IV ($n = 15$)] gave written informed consent. This study was approved by the local ethical committee.

Biventricular device implantation

All patients received a biventricular cardioverter-defibrillator (Attain-System with InSync Marquis, Medtronic, $n = 32$ or Aesula-System with Epic HF V-339, St Jude Medical, $n = 15$).

The right atrial and ventricular leads were positioned conventionally. The LV pacing lead was inserted by a transvenous approach through the coronary sinus into a cardiac vein of the free wall. The physician who implanted the LV lead tried to achieve an optimal LV lead position intraoperatively by sampling different cardiac veins (mean 2.2 ± 0.3 veins). The aim was a preferably short width of the QRS complex and a preferably high increase in arterial systolic pressure with biventricular pacing.

Postoperatively, the atrioventricular delay was optimized using Doppler echocardiography by searching maximal transmitral diastolic filling without premature termination of atrial filling. Forty-six patients had an optimal AV time between 100 and 150 ms (mean time 128 ± 16 ms). In one patient, it was necessary to program a shorter AV time (70 ms). The VV timing was set to zero in all patients. There was another control of the device at 10 (± 3) months follow-up to ensure that no LV lead dislocation or change of the CRT programming had occurred. The AV interval was fixed during exercise testing.

On the basis of previous studies,^{17,18} patients with a reduction in LVESV $\geq 15\%$ were classified as adequate clinical responders.

Echocardiography

All studies were performed before CRT, one day postoperatively and at 3 month and 10 month (± 3) follow-up using a Vivid Seven digital ultrasound scanner (General Electrics, Horton, Norway). LV ejection fraction (EF), LV end-systolic volume and LV end-diastolic volume were determined by manual tracing of end-systolic and end-diastolic endocardial borders using apical 4-chamber and 2-chamber views, employing biplane Simpson's Method. Endsystole was marked as aortic valve closure in apical long axis views.

Four parasternal short axis views (mitral valve level, papillary muscle level, apical level, and an additional apical level which allowed just visualization of the LV cavity) were acquired using 2D tissue harmonic imaging. The focus was adjusted to the centre of the LV cavity to optimize myocardial tissue characterization of all segments of the short axis views. The frame rate was between 56 and 92 frames/s. Analysis of the parasternal short axis 2D echocardiographic images was performed offline on a personal computer with the aid of a customized software package (EchoPAC BT 05.2, General Electrics) using two consecutive cardiac cycles of acquired loops. This system follows acoustic markers accurately within the myocardium during several consecutive frames.^{19,20} It is assumed that the natural acoustic markers change their position from frame to frame in accordance with the surrounding tissue motion.²⁰ The system calculates mean strain values for whole predefined LV segments. Regarding the width between endocardial and pericardial trace, a tracking setting was selected which included as much myocardium as possible but prevented inclusion of tissue outside the myocardium.

The software facilitates an automatic grading of each segment regarding the tracking quality on a scale ranging from 1.0 for optimal to 3.0 for unacceptable. Segments with suboptimal tracking quality (grading >2.0) were systematically dismissed from the analysis. Visual control of tracking quality was performed to ensure accurate automatic tracking. Echocardiographic image quality was found to be adequate to allow strain analysis in 662 of all 752 analysed segments (88%). The location of the non-evaluable segments was mainly apical anterior and anteroseptal and therefore not relevant for the LV lead position.

Analysis of myocardial deformation

For analysis of LV myocardial deformation, the 17 segment model was applied on the parasternal short axis views. For the parasternal short axis views on the basal and papillary muscle level six segments were analysed, for the short axis view on the apical level four segments were analysed, and for the most apical level only one segment was analysed. For each segment with adequate tracking quality, circumferential strain was calculated as a mean over the whole segment. Circumferential strain relates to circumferential deformation along the curvature of the left ventricle in the parasternal short axis.

The circumferential strain values over time for each segment were given as strain-time curves (*Figure 1*). For each point on these curves, the exact time after the QRS complex and the strain value are displayed on demand. The segment with latest peak negative circumferential strain before CRT in relation to the QRS complex was determined (*Figure 1*). Strain-time curves before CRT during intrinsic conduction (heart rate 65 ± 12 /min) and on active CRT one day after implantation (heart rate 68 ± 16 , $P = 0.093$) were compared to determine the segment with the maximal temporal difference in peak negative circumferential strain (*Figure 2*). This segment was assumed to be the location of the LV lead.

For time-to-peak negative circumferential strain intraobserver and interobserver variability were 5.5 ± 2.8 and $9.0 \pm 3.2\%$, respectively.

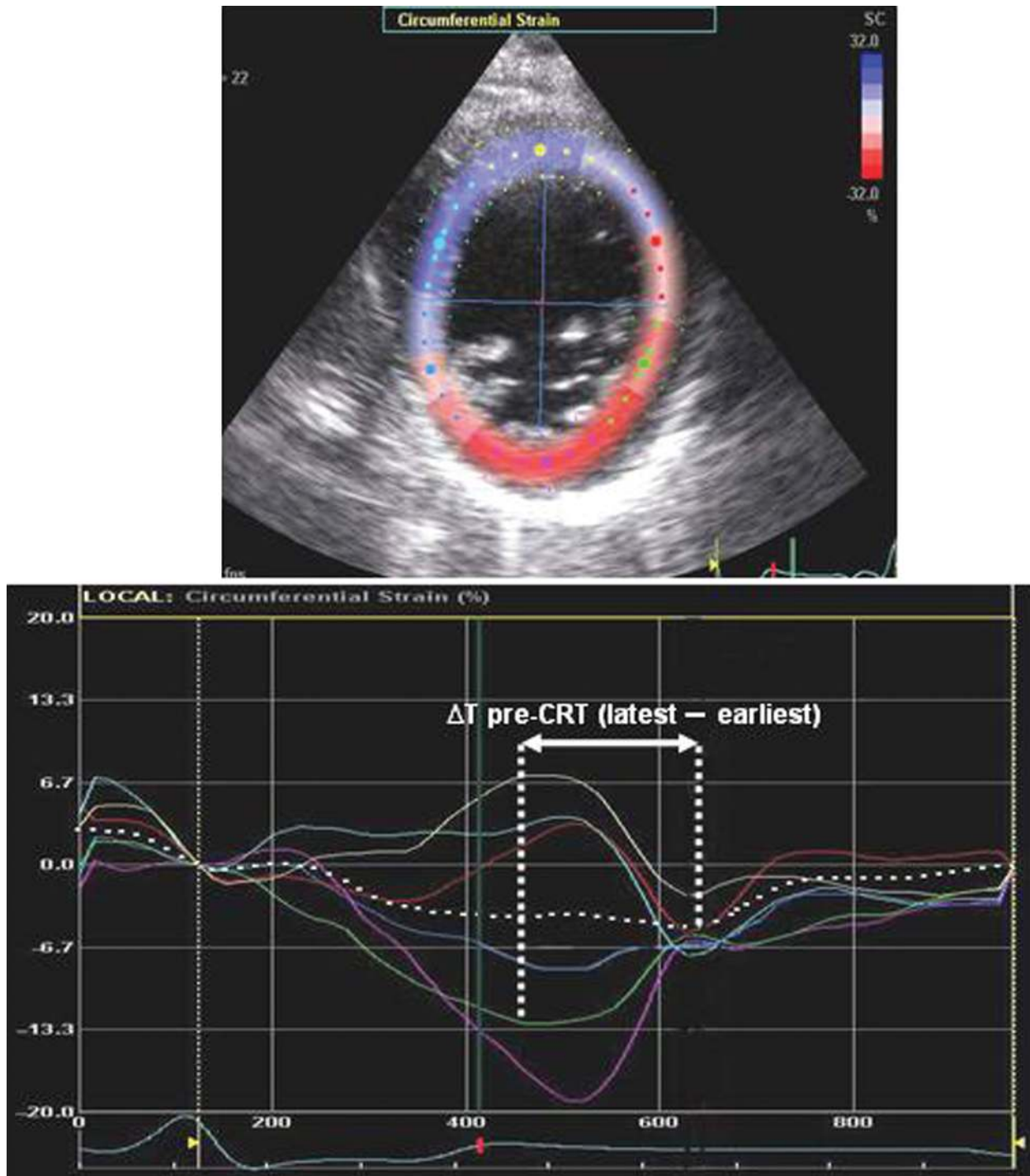


Figure 1 Upper panel: short axis view with circumferential strain display prior to cardiac resynchronization therapy at end-systole with inhomogeneous colour distribution due to dyssynchronous contraction. Lower panel: there are six circumferential strain tracings for the six evaluated segments within the circumference. The dotted white line indicates the mean circumferential strain of all six segments. The time difference between segment with earliest and latest peak strain is marked.

The distance between the assumed LV lead position and the segment with maximal baseline dyssynchrony was counted in number of segments referring to the four apico-basal levels and up to six segments within one circumference. One distance step was related either to the apico-basal level or to the circumferential level. Optimal position of the LV lead was defined as concurrence of segments or immediate neighbouring (≤ 1 distance step) of the segment with maximal dyssynchrony and the segment with assumed location of the LV lead. Non-optimal position of the LV lead was defined as a greater distance (≥ 2 distance steps)

between segment with maximal dyssynchrony and segment with assumed LV lead position.

The physician performing the echocardiographic analysis and classification of LV lead position as optimal or non-optimal were blinded to possible difficulties during LV lead placement, anatomic limitations, or substrate disparities.

Fluoroscopy

After CRT implantation, biplane fluoroscopy in orthogonal views (LAO 60° and RAO 30°) was performed. These loops were analysed

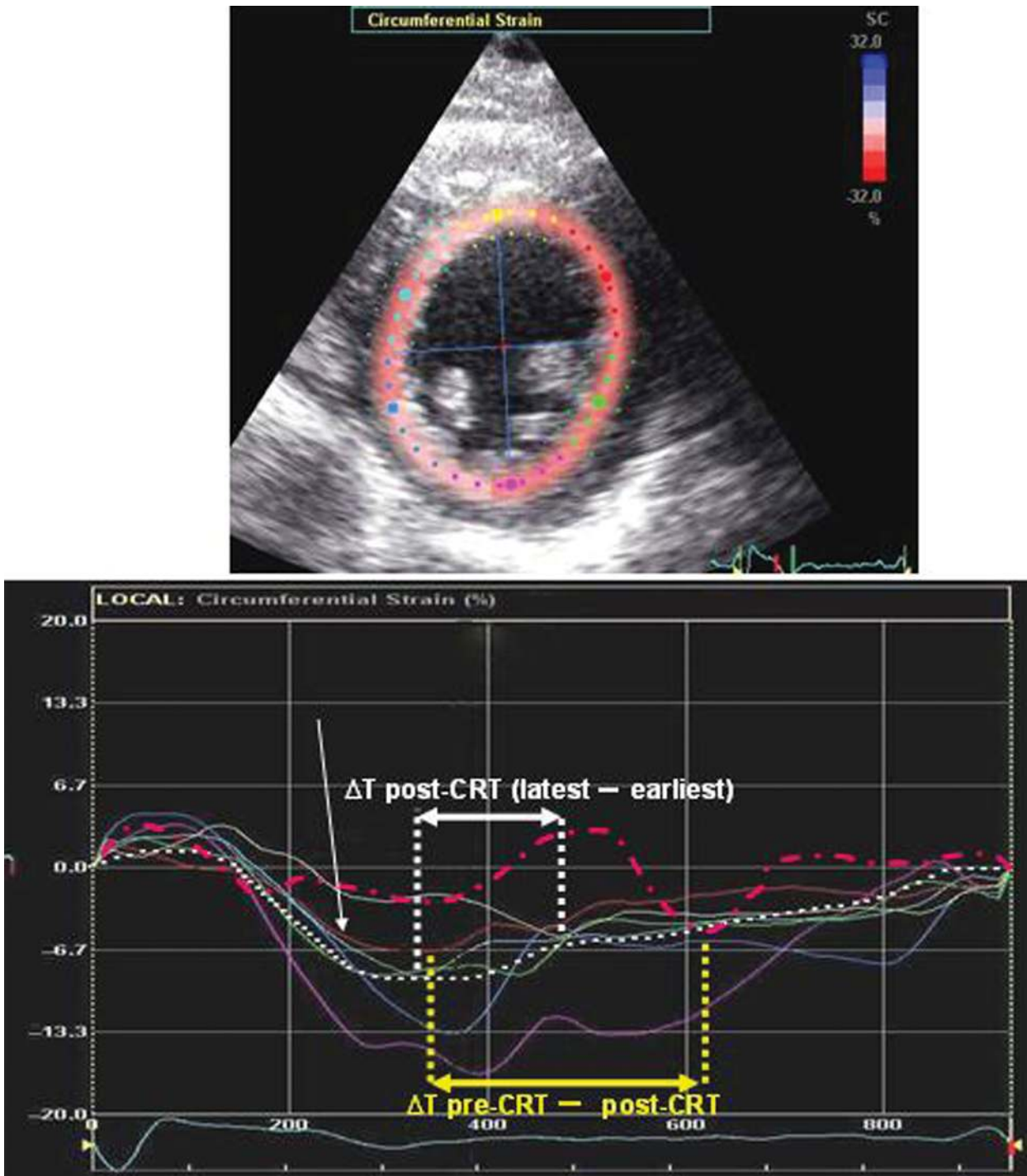


Figure 2 Upper panel: short axis view with circumferential strain display during cardiac resynchronization therapy at end-systole with homogenous colour distribution due to synchronous contraction. Lower panel: circumferential strain tracings from the six evaluated segments within the circumference. The time difference between segment with earliest and latest peak strain during cardiac resynchronization therapy is given in white. The tracing obtained prior to cardiac resynchronization therapy from the segment with latest peak strain is added as interrupted purple line. The tracing of the segment during resynchronization therapy is marked with a white arrow. The reduction in contraction delay with cardiac resynchronization therapy compared to prior to therapy for this segment is marked as yellow distance. It was greatest among all 17 left ventricular-segments of this patient indicating the left ventricular lead position.

by two blinded readers to determine the anatomical location of the LV lead tip. The RAO view was used to define the baso-apical location of the lead tip. The LV was divided into four levels: basal, medial, apical, and apex (*Figure 3*, left panel). The LAO view was subsequently used to determine the location within the circumference of that level. For this purpose, the 17 segment

scheme introduced by Cerqueira *et al.*²¹ was projected into the LAO view (*Figure 3*, right panel).

Peak oxygen consumption

Patients underwent bicycle cardiopulmonary exercise testing (10 W per min increments) at baseline and after 10 ± 3 months

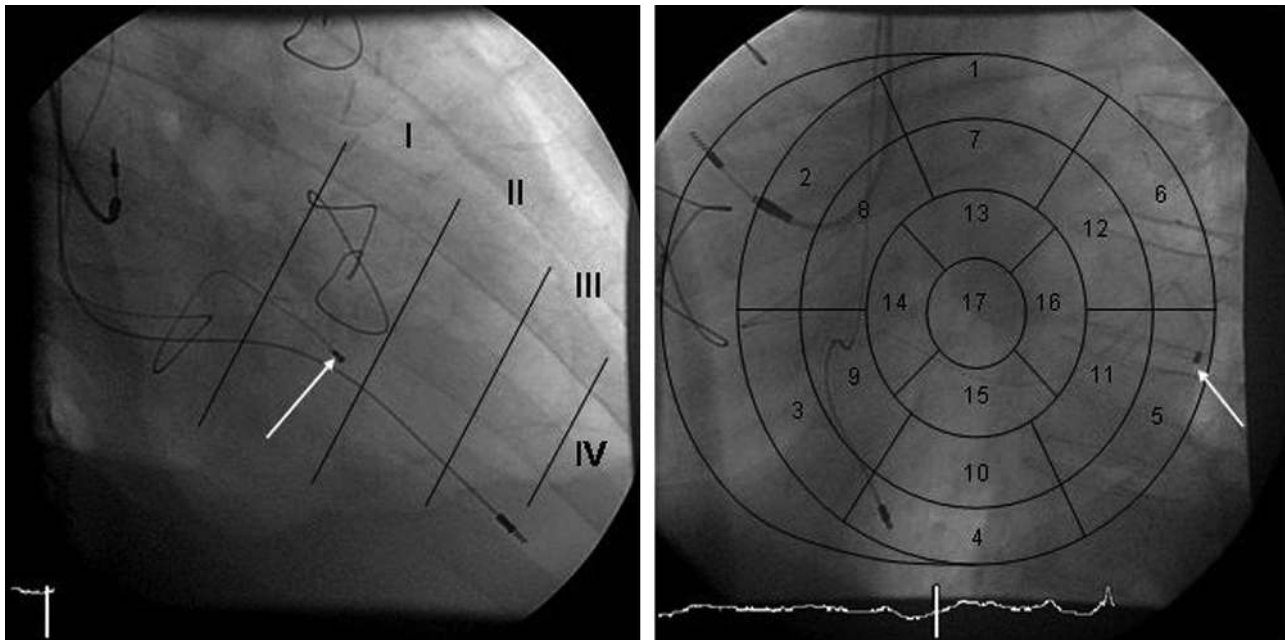


Figure 3 Orthogonal fluoroscopy views (RAO 30° and LAO 60°) acquired after cardiac resynchronization therapy implantation to determine the anatomical left ventricular lead position. The RAO view (left panel) was used to define the left ventricular lead position in the baso-apical direction (I: basal level, II: midventricular level, III: apical level, IV: apex). The basal border of the basal level was defined as 1 cm apical to the left ventricular lead course within the great cardiac vein. The LAO view (right panel) was subsequently used to define the position within the circumference of that level. For this purpose, the 17 segment scheme was projected onto the LAO view. The images show the tip of the left ventricular lead (arrows) to be in segment 5.

of CRT. VO_{2max} at peak exercise was defined as the highest oxygen consumption measured during the symptom-limited exercise test and expressed as mL/kg/min.

Statistics

Outcomes were measured at baseline and at 3 months and 10 months after CRT implantation. The primary outcome was change in LVEDV from baseline to 10 months. Secondary outcomes included change in LVEF, LVESV, VO_{2max} , and extent of LV dyssynchrony. Continuous variables are presented as mean \pm standard deviation. Categorical data are presented by frequencies and percentages. The sample size calculation was based on change in LVEDV at 10 month after implantation of the CRT device. A mean reduction in LVEDV of 22 mL with a standard deviation of 10 was assumed for the optimal group. Furthermore, a difference of 40% for the primary endpoint at 10 month follow-up was assumed. To detect this difference between the two groups of LV lead position with a 5% two-sided significance and 80% power, 23 patients in each group needed to be enrolled. For the analysis of the primary outcome 'change in LVEDV', a repeated measures ANOVA was performed including the values at baseline, 3 months and 10 months as dependent variables and the fixed effect of time, LV lead group, and time by group interaction as independent variables. Model assumptions were checked graphically by qq-plots. We analysed all secondary endpoints except extent of LV dyssynchrony with the same approach. For the extent of LV dyssynchrony, we assessed the maximal temporal difference between segments with earliest and latest peak systolic negative circumferential strain between the two groups of LV lead position with unpaired Student *t*-test, before and on CRT with paired Student *t*-test.

Linear regression analysis to identify predictors of reduction in LVEDV and LVESV at 10 months follow-up was performed including width of the QRS complex prior to CRT, location of latest systolic contraction prior to CRT, assumed LV lead position based on deformation imaging, fluoroscopic LV lead position, and distance in number of LV segments between segment with latest systolic contraction prior to CRT and segment with assumed LV lead position.

Model assumptions were checked graphically by qq-plots and by plots of predicted vs. residuals. We calculated Cohen's kappa coefficient with 95% confidence intervals to evaluate the agreement between anatomical LV lead position determined by fluoroscopy and assumed LV lead position determined by detailed circumferential strain analysis.²² All tests were two-sided and assessed at the 5% significance level. Because of the exploratory nature of the secondary endpoints, no adjustment was made to the significance level to account for multiple testing. All analyses were performed with SAS version 9.1.3.

Results

Baseline clinical characteristics prior to CRT are given in *Table 1*. Considering a reduction of LVESV $\geq 15\%$, 41 patients were classified as adequate responders (27 patients in the optimal and 14 patients in the non-optimal LV position group) and six patients as inadequate clinical responders (one patient in the optimal and five patients in the non-optimal LV position group).

Location of latest systolic contraction prior to cardiac resynchronization therapy

The location of the segment with latest maximal systolic strain prior to CRT was as follows: 12 anterior (seven basal, five medial), 21 lateral (14 basal, five medial, two apical), seven posterior (three basal, four medial), three inferior (one basal, two apical), and four at the apex. There was no difference in the distribution of the location of latest contraction prior to CRT between patients found to have optimal LV lead position and those found to have non-optimal LV lead position.

Table 1 Baseline clinical characteristics prior to cardiac resynchronization therapy

	Optimal LV lead position (n = 28)	Non-optimal LV lead position (n = 19)	P
Age (years)	59 ± 10	58 ± 9	0.673
Males/females	16/12	12/7	0.512
Ischaemic cardiomyopathy	22 (77%)	15 (76%)	0.138
QRS duration (ms)	160 ± 19	156 ± 15	0.375
NYHA classification	3.1 ± 0.6	3.3 ± 0.7	0.414
Concomitant therapy			
ACE inhibitors	20 (73%)	14 (74%)	0.672
ARB's	6 (23%)	4 (21%)	0.470
Beta-blockers	26 (92%)	17 (89%)	0.087
Digitalis	14 (50%)	10 (53%)	0.822
Diuretics	10 (34%)	6 (32%)	0.787
Aldosterone antagonists	18 (65%)	12 (63%)	0.651

ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blockers.

Location of the assumed left ventricular lead position based on strain analysis

In 28 patients, the assumed position of the LV lead based on peak negative circumferential strain analysis was in agreement or immediately neighbouring the location of latest contraction prior to CRT (optimal LV lead position). The LV lead position in these patients was assumed to be in the following segments: seven anterior (five basal, two medial), 16 lateral (11 basal, five medial), four posterior (two basal, two medial), and one at the apex.

In 19 patients, the assumed position of the LV lead was not in agreement or immediately neighbouring the location of latest contraction prior to CRT (non-optimal LV lead position). The LV lead position in these patients was assumed to be in the following segments: six anterior (four basal, two medial), nine lateral (four basal, four medial, one apical), and four posterior (two basal, two medial).

Anatomical location of the left ventricular lead position

Based on fluoroscopy, the LV lead position was as follows: 11 anterior (seven basal, three medial, one apical), 26 lateral (14 basal, nine medial, three apical), 10 posterior (six basal, four medial). There was a complete agreement between anatomical location of the LV lead position defined by fluoroscopy and assumed LV lead position determined by MDI in 41 patients. In six patients, the LV lead position by fluoroscopy was found to be different than the LV lead position determined by circumferential strain analysis (Figure 4). Thus, the agreement on LV lead position was 0.847 (95% CI 0.719–0.963) as determined by kappa analysis. There was a distance of 0.16 ± 0.35 (range 0–2) segments between the position defined by fluoroscopy and the position determined by circumferential strain analysis. Three patients in the non-optimal LV lead position group would have been classified as having optimal LV lead position

Anatomical and assumed LV-lead position

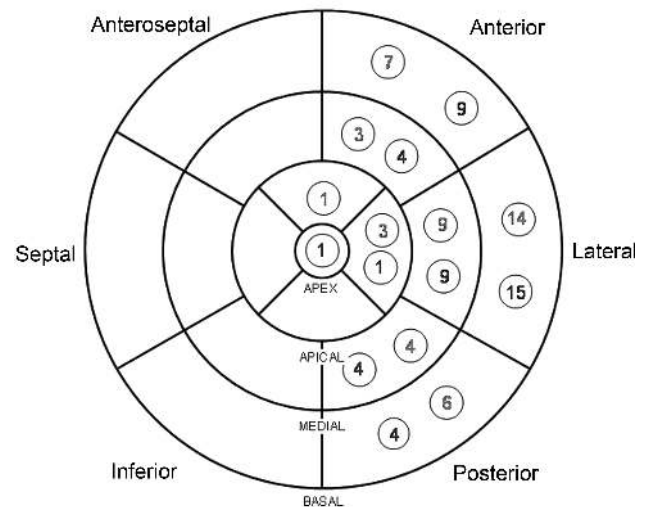


Figure 4 Position of the left ventricular lead for all 47 patients in the 17 segment left ventricular model as defined by fluoroscopy (anatomical lead position, shown in red) and as defined by circumferential strain analysis (assumed lead position, shown in blue).

using the location determined by fluoroscopy. In the other three patients classification would not have been different.

Extent of left ventricular dyssynchrony

The maximal temporal difference between the segment with earliest and latest peak negative circumferential strain before CRT was 161 ± 32 ms in the optimal LV-lead position group and 159 ± 35 ms in the non-optimal LV-lead position group ($P = 0.841$). Additionally, the segments with second and third latest peak systolic strain were determined. Eighty-one percent of segments with second latest peak negative circumferential strain and 72% of segments with third latest peak systolic strain were within a two segment distance to the segment with latest peak systolic strain. The temporal delay in the segment with second and third latest peak systolic strain was 9 ± 4 and 13 ± 3 ms less than in the segment with latest peak systolic strain.

With active CRT, the maximal temporal difference between segments with earliest and latest contraction was significantly reduced in both groups ($P < 0.001$). It was 110 ± 18 ms in the optimal and 118 ± 22 ms in the non-optimal LV lead group. The reduction in the maximal temporal difference was 24% higher in the optimal LV lead position group than in the non-optimal lead position group (51 ± 16 ms vs. 41 ± 15 ms, $P = 0.0365$).

Left ventricular function and remodelling related to left ventricular lead position

Prior to CRT, there were no differences in clinical characteristics between patients found to have optimal or non-optimal LV lead position (Table 1). Similarly EF, LV end-systolic volume, LV end-diastolic volume, and VO_2 max were similar between the two patient groups prior to CRT (Table 2).

At 3 month follow-up after initiation of CRT, reduction of LV volumes was greater in the optimal LV lead group compared to the non-optimal LV lead group and EF was higher (Tables 2 and 3).

Table 2 Left ventricular function, left ventricular volumes, and cardiopulmonary capacity at baseline, 3 and 10 months following initiation of resynchronization therapy

	Optimal LV lead position (n = 28)	Non-optimal LV lead position (n = 19)	P
baseline:	31 ± 5	29 ± 7	0.244
LVEF (%)			
LVESV (mL)	214 ± 68	216 ± 61	0.967
LVEDV (mL)	312 ± 97	306 ± 89	0.917
VO ₂ max (mL/kg/min)	13.7 ± 2.1	14.0 ± 2.2	0.430
3 months FU:	39 ± 7	33 ± 6	0.001
LVEF (%)			
LVESV (mL)	185 ± 62	197 ± 56	0.503
LVEDV (mL)	294 ± 78	296 ± 82	0.972
10 months FU:	43 ± 7	36 ± 7	<0.001
LVEF (%)			
LVESV (mL)	172 ± 60	189 ± 59	0.310
LVEDV (mL)	289 ± 81	293 ± 86	0.829
VO ₂ max (mL/kg/min)	16.5 ± 1.9	15.9 ± 1.8	0.456

FU, follow-up, VO₂max, peak oxygen consumption.

At 10 month follow-up, there was even greater difference in the improvement of LV EF and LV reverse remodelling between the optimal and non-optimal LV lead position groups (Table 3). VO₂max and the increase of VO₂max at 10 month follow-up on CRT was greater in the optimal compared to the non-optimal LV lead group. More detailed analysis on the impact of the distance between the segment with latest peak systolic strain prior to CRT to the segment with assumed LV lead position demonstrated a declining effectiveness of CRT on EF and LV reverse remodelling with increasing distance (Figure 5).

The distance between segment with latest systolic strain prior to CRT and segment with assumed LV lead position was the only independent predictor of Δ LVEDV ($R^2 = 0.2175$, $P = 0.0197$) and of Δ LVESV ($R^2 = 0.3774$, $P = 0.0054$) at 10 month follow-up (see complete results of the linear regression model in the appendix).

If the LV lead position determined by fluoroscopy would have been used instead of the assumed LV lead position based on myocardial deformation imaging analysis results for the optimal and non-optimal LV lead position group would not have been significantly different.

Discussion

The major findings of this study are the following: (i) circumferential strain analysis based on tracking of acoustic markers in parasternal 2D echocardiographic images can be used in CRT to describe the temporal course of LV contraction, (ii) myocardial deformation imaging analysis allows an accurate assumption on the LV lead position in CRT based on a detailed analysis of the myocardial contraction sequence, (iii) concurrence or neighbourhood of the segment with assumed LV lead position based on circumferential strain analysis with the LV

Table 3 Change in LV function, LV volumes, and cardiopulmonary capacity compared to baseline at 3 and 10 months following initiation of resynchronization therapy

	Optimal LV lead position (n = 28)	Non-optimal LV lead position (n = 19)	P
Δ LVEF (%) at 3 month FU	8 ± 3	4 ± 2	<0.001
Δ LVESV (mL) at 3 month FU	29 ± 6	19 ± 4	<0.001
Δ LVEDV (mL) at 3 month FU	18 ± 5	10 ± 6	<0.001
Δ LVEF (%) at 10 month FU	12 ± 4	7 ± 3	<0.001
Δ LVESV (mL) at 10 month FU	42 ± 10	27 ± 8	<0.001
Δ LVEDV (mL) at 10 month FU	23 ± 8	13 ± 7	<0.001
Δ VO ₂ max (mL/kg/min) at 10 month FU	2.8 ± 0.8	1.9 ± 1.0	0.035

segment demonstrating latest peak systolic strain prior to CRT results in significantly greater improvement in LV function and more reverse remodelling at 10 month follow-up on CRT.

Circumferential strain analysis of left ventricular contraction

Multiple Doppler echocardiographic studies have been performed to describe the temporal course of LV contraction.²³⁻²⁵ The applied techniques focused on determination of the degree of dyssynchrony in LV contraction. Based on the severity of dyssynchrony determined by the tissue Doppler imaging techniques the effectiveness of CRT on symptoms, LV function and reverse remodelling were predicted. However, Echo-Doppler methods rely on longitudinal LV motion. Helm *et al.* demonstrated that longitudinal motion analysis may be less sensitive to dyssynchrony, because it follows different time courses than circumferential deformation and may therefore not adequately demonstrate CRT benefit depending on pacing mode.²⁴ The applied tissue pixel tracking technique allows determination of circumferential deformation parameters from parasternal 2D echocardiographic views.^{16,17} It has already been used to quantify dyssynchrony and predict response to CRT.²⁶ The present study is the first to evaluate dyssynchrony prior to CRT and the effect of CRT on LV dyssynchrony using a circumferential strain analysis. Circumferential strain analysis demonstrated significant temporal differences in the contraction sequence prior to CRT. Furthermore, a significant reduction of dyssynchrony as determined by the maximal temporal difference between the segment with earliest and latest peak strain could be demonstrated with CRT irrespective of optimal or non-optimal LV lead position.

Optimal left ventricular lead position in cardiac resynchronization therapy

Most studies which evaluated predictors of CRT success aimed at identification of patients with a higher degree of

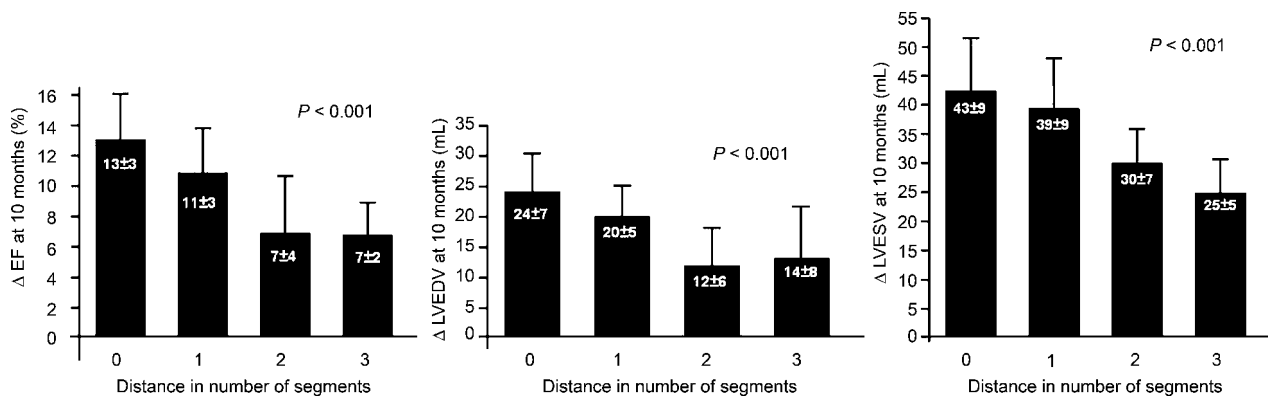


Figure 5 Improvement in ejection fraction (left panel), reduction of left ventricular end-diastolic (middle panel), and end-systolic volumes (right panel) at 10 month follow-up on cardiac resynchronization therapy related to distance (counted in segments in the 17 segment model) from segment with latest peak systolic strain prior to cardiac resynchronization therapy to segment with assumed left ventricular lead position.

asynchrony. However, the success of CRT is not only dependent on the degree of asynchrony but also on technical factors, in particular the correct LV lead position.²⁷ Based on experimental electrophysiological studies,²⁵ a LV lead position in the area of the latest contraction prior to CRT should result in the best resynchronization effect. Still, tailoring of the LV lead position to the area of maximal mechanical delay has found less attention. The current study demonstrates a relatively simple approach to determine the LV lead position based on a detailed analysis of the myocardial contraction sequence before and on CRT. The LV lead position determined by circumferential strain analysis was found to be in high agreement with the anatomical LV lead position defined by fluoroscopy.

A great reduction of QRS duration has been demonstrated to be an electrical marker of optimal CRT pacing.²⁸ This study evaluated concordance of the segment with greatest temporal reduction in time to peak strain with CRT and the segment with latest peak strain before CRT as mechanical marker for optimal CRT. There was a significant relationship between the distance of the assumed LV lead position defined by a detailed myocardial deformation imaging analysis to the segment with greatest need for pacing and the improvement in LV function. Agreement of the assumed LV position and segment with latest contraction prior to CRT resulted in greatest functional response.

It has to be acknowledged that there are several technical factors which have an impact on LV lead placement and may limit the ability for optimal LV lead placement considering the commonly used transvenous implantation techniques.²⁹ A distant anatomical run of the cardiac veins in relationship to the latest LV contraction, impossibilities to reach a desired vein, insufficient anchoring of the LV lead in the desired place, or scar formation not allowing sufficient electrical response in the desired lead position are the most frequent technical problems. Although there might be technical difficulties to reach the optimal LV lead site, this study indicates also that even a neighbourhood to the optimal LV lead site results in greater improvement of functional performance.

At this centre several efforts were taken to improve the effect of CRT. This included careful patient selection and intraoperative methods to optimize the immediate haemodynamic and electric effects. A mean of 2.2 LV lead positions was evaluated in order to optimize the effect of CRT. The

careful intraoperative optimization of the CRT effect is likely to have increased the clinical responder rate.

Limitations

Using myocardial deformation imaging, the location of the LV lead was determined based on the assumption that the segment with greatest reduction in contraction delay on CRT is the location of the LV lead. This hypothesis reflects pathophysiologic considerations: the electric current of the LV lead will affect the nearest segment first and strongest and therefore result in greatest effect of CRT in this segment. This assumption has not been proven by experimental studies but the excellent concordance of the LV lead position defined on this assumption and the LV lead position determined by fluoroscopy in orthogonal views support this approach. Biplane fluoroscopy allows only an approximate definition of the LV lead position considering the three-dimensional structure of the LV. The precise position of the LV lead will be determined only by an imaging modality with 3D capacity, such as computer tomography. The apical segment within the 17-segment model was analysed from a parasternal short axis view. This approach may have resulted in a rather basal analysis of this apical segment. However, this had to be done to allow application of circumferential strain analysis.

Tracking of acoustic markers in 2D echocardiographic images was not possible in all segments, therefore the segment with latest systolic contraction or the segment with optimal LV lead position may be missed in some patients. However, this should not have affected the principle findings of this study.

The definition of the optimal LV lead position as concurrence or immediate neighbourhood of the segment with maximal temporal difference in peak negative circumferential strain before and with CRT to the segment with latest peak negative strain prior to CRT is arbitrary. A different definition of optimal lead position considering a greater distance of the lead segment from the segment with latest contraction prior to CRT would have resulted in a higher number of patients with optimal lead position. The precise definition of the optimal LV lead position in relation to the segment with latest contraction prior to CRT resulting in functional and clinical improvements should be determined in future

studies. However, there was a continuous reduction of LV reverse remodelling on CRT with increasing distance between LV lead position and segment with latest contraction prior to CRT.

The described echocardiographic analysis is still time-consuming. In the future, semi-automatic analysis software may facilitate this approach for application during LV lead implantation.

Conclusion

Detailed analysis of the myocardial deformation sequence prior and on CRT allows determination of the LV lead position.

Concurrence of the LV lead position and the LV segment with latest contraction prior to CRT results in significantly better effectiveness of CRT on LV function and reverse remodelling during a 10 months follow-up.

Conflict of interest: R.H. has received financial research support at the end of the year 2006 for the first time from General Electrics, Horton, Norway. The other authors have no conflicts of interest.

Appendix

Multiple regression model of Δ LVEDV and Δ LVESV at 10 month follow-up:

Multiple regression model Δ LVEDV

Variable	Parameter estimate	P-value	95% Confidence limits	
Intercept	35.04710	<.0001	28.53493	41.55928
Location of latest systolic contraction prior to CRT	0.03032	0.9260	-0.62853	0.68918
Fluoroscopic LV lead position	-0.41940	0.3637	-1.34571	0.50691
Distance between segment with latest systolic contraction prior to CRT and segment with assumed LV lead position	-4.22778	0.0197	-7.73634	-0.71921

Multiple regression model Δ LVESV

Variable	Parameter estimate	P-value	95% confidence limits	
Intercept	31.33229	<0.001	25.23842	37.87235
Location of latest systolic contraction prior to CRT	-0.13737	0.5372	-0.58600	0.31126
Assumed LV lead position based on deformation imaging	-0.70798	0.2067	-1.82679	0.41083
Fluoroscopic LV lead position	0.16407	0.7545	-0.89571	1.22384
Distance between segment with latest systolic contraction prior to CRT and segment with assumed LV lead position	-3.10360	0.0054	-5.22070	-0.98650

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