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Utility of equilibrium radionuclide angiogram derived measures of dyssynchrony to predict outcomes in heart failure patients undergoing cardiac resynchronization therapy

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Abstract

Objective: We evaluated a novel scintigraphic method employing new parameters of mechanical left ventricular (LV) dyssynchrony and correlated it with clinical outcomes in heart failure patients with reduced ejection fraction (HFrEF) receiving cardiac resynchronization therapy (CRT).

Methods: Sixty-six advanced HF patients referred for CRT with LV ejection fraction (EF) <35% and QRS ≥120 ms were studied. We performed equilibrium radionuclide angiography (ERNA) prior to and six months after CRT. We assessed ventricular dyssynchrony with parameters derived from the first harmonic phase (Ø) analysis of the ERNA time activity curve and evaluated change in these parameters after 6 months of CRT. These parameters include novel indices of synchrony (S), a measure of intraventricular contraction order, and entropy (E), a measure of intraventricular contraction disorder and interventricular synchrony (IVS), a measure of synchronous biventricular function.

Results: Forty-seven (71%) patients improved clinically (responders) at 6 months post CRT while 19 (28.8%) showed no change in NYHA class or worsened (non-responders). The post-CRT changes in QRS duration (p =0.006), echocardiographic (p =0.03) and ERNA LVEF (p =0.0007), LVS (p =0.004), LVE (p =0.006), LVSDØ (p =0.004), and IVS (p =0.05) were significantly different between responders and non-responders. Sixty-two percent of responders had

either LVS <0.84 or IVS ≥18.8° as opposed to only 16% of non-responders (p =0.001). 29 of 32(91%) patients with either of these measures responded to CRT (p < 0.01).

Conclusions: LVS and IVS are novel measures of LV dyssynchrony derived from ERNA planar analysis. Baseline value of LVS <0.84 or IVS ≥18.8° predict a positive response to CRT.

Abbreviations:

BBB = Bundle branch block
ECG = Electrocardiogram
ERNA = Equilibrium radionuclide angiography
EF = Ejection fraction
HF = Heart failure
IVS = Interventricular synchrony: The difference between mean LV and RV S
LV = left ventricle
LVEDVI = LV end diastolic volume index
LVESVI = LV end systolic volume index
MPS = myocardial perfusion scintigraphy
MRI = Magnetic resonance imaging
NYHA = New York Heart Association
RV = Right ventricle
SDLVØ – Standard deviation of LVØ
SDRVØ - Standard deviation of RVØ
SPECT – Single photon emission computed tomography

Introduction

Heart failure (HF) is the most frequent cause of cardiac hospitalization in the USA, effecting 5,000,000 patients with 250,000 deaths yearly (1). Both ventricular systolic function and synchrony have been shown to have significant prognostic impact in HF (2,3). Cardiac resynchronization therapy (CRT) has been proven to reduce both the morbidity and mortality of HF patients who become refractory to medications and present with a wide QRS(2-4). However, improvement of HF with CRT based on clinical and echocardiographic criteria is highly variable with 30% – 40% patients who do not improve or worsen with CRT (2-5).

Scintigraphic methods that image myocardial perfusion and function have been adapted for synchrony analysis(6,7). SPECT myocardial perfusion scintigraphy combines measures of both perfusion and function and extracted parameters have been demonstrated to measure ventricular synchrony and even to predict CRT outcomes(8,9). Equilibrium radionuclide angiography (ERNA) has advantages of higher temporal resolution, greater reproducibility, and volumetric analysis of both ventricles that can be applied for analysis of intra-ventricular and inter-ventricular synchrony (7,10).

Novel, objective measures of regional contraction and global mechanical synchrony based on the first harmonic fit of the ERNA ventricular time versus

radioactivity curve, the synchrony (S) and entropy (E) parameters, have been developed and are generated by in house software. These parameters were demonstrated to be highly reproducible, with both intra- and inter-observer variability in the range of 2 percent (11). Applied in a simulation model, S and E were observed to discriminate better the synchrony profiles among a spectrum of patterns of wall motion than LVEF or the standard deviation of LV phase angle (SDLVØ) measured on the phase histogram which plots Ø on the abscissa versus its frequency on the ordinate within the LV region of interest (ROI) (11). The aim of this study was to correlate these novel parameters of S and E with clinical outcomes in patients with advanced HF undergoing CRT.

Methods

Background: As previously reported from our laboratory (11), with equilibrium radionuclide angiography, phase angle (Ø), and amplitude quantitate regional contraction timing and magnitude and are the basis for novel synchrony (S) and entropy (E) parameters. S is the vector sum of all amplitudes based on the angular distribution of Ø divided by the scalar sum of the length of all vectors. Complete S equals 1, and its absence equals 0. E measures the disorder in the region of interest, is 1 with random contraction and 0 with full synchrony, and differentiates among differing contraction patterns. S and E parameters were highly reproducible and well differentiated among patients with normal wall motion, aneurysm, diffuse dysfunction, and severe regional dysfunction. These novel indices of dyssynchrony

were found superior to SD Ø (SD of ventricular phase) that failed to distinguish these groups of LV dysfunction (11).

Patient Population - All patients signed informed consent approved by the UCSF institutional review board. We evaluated 66 patients with systolic dysfunction, advanced HF, (NYHA Class III or IV), echocardiographic LVEF ≤35%, and QRS duration >120 ms, who were referred for CRT between February 2004 and October 2011. All patients received maximal tolerated medical therapy per their HF specialist (Table 1).

Study Protocol – ERNA was performed one month or less before CRT implantation and after six months of CRT (Table 2) in order to assess serial changes of ventricular volumes, function, and synchrony. As part of the CRT evaluation all patients had serial 2-D echocardiograms within one month before CRT implantation and after 6 months of therapy with calculation of LVEF, LVEDVI and LVESVI. NYHA Class (12) of each patient before and after six months of CRT was determined by consensus of the HF specialist and cardiac electrophysiologist who were blinded to imaging results.

ERNA – Patients were injected with red blood cells labeled with technetium-99m by the "in vivtro" method (13) with an activity of approximately 20mCi/70kg body weight (11MBq/kg). Rest, supine, ECG gated anterior, "best septal" LAO and left lateral planar images were acquired in 16 frames, before and after CRT, using a

Philips Forte camera (Philips Electronics, Inc., Milpitas, CA), processed by commercial software. LVS, LVE, SDLVØ, IVS, RVS, RVE, SDRVØ(see above) were calculated, based on the phase image generated from the first harmonic fit of the ERNA time activity curve displayed by standard laboratory protocols(11,14).

First Harmonic Analysis and Synchrony Measures

In each ERNA pixel, the first harmonic curve fit is characterized by its phase and amplitude, representing surrogates for the timing and magnitude of regional contraction, respectively. For each pixel a harmonic vector can be drawn with direction representing its phase angle (Ø) from 0°, the ECG R wave gating signal, to 360°, and its length representing its amplitude (A). We developed the parameters of Synchrony (S) and Entropy (E), to express LV dyssynchrony, based on pixel Ø and A(11).

Definitions:

Established Parameters: Each calculated from the first harmonic phase histogram in the ventricular ROIs: SDLVØ; SDRVØ; IVS (Difference between mean LVS and RVS); LV Synchrony (S) and LV Entropy (E) are defined mathematically elsewhere (11,14,15).

Synchrony (S) LVS is a measure of contraction efficiency within the ERNA LV ROI, LVS, and is the vector sum of all amplitudes divided by their arithmetic sum.

S ranges from 0 to 1. With complete synchrony, vector numerator and arithmetic sum denominator, are equal and S = 1. S estimates the contraction potential if the ROI were synchronized. The maximum potential functional gain with CRT is 1 - S.

Entropy (E) LVE is a measure of contraction disorder in the same LV ROI. LV S can approach 0 when contraction is random or if the ROI consists of two sub-regions, each 180° delayed with respect to the other. To distinguish these possibilities, and determine the extent of each component, we divided the LV ROI S histogram into 30 adjacent 12° color blocks and formulated E as a measure of the distribution or randomness of Ø across these blocks, from 0, with synchronous motion and a single Ø, to 1 with fully dyssynchronous contraction and Ø distributed in all blocks.

Both RVS and RVE can be calculated for the RV ROI. LVS and LVE calculated on planar ERNA in a group of 30 normal patients studied for clinical indications, were S = 0.99 ± 0.01 and E = 0.45 ± 0.02. Similarly, normal values for RVS and RVE were established (7), as well as that of IVS in those with normal conduction and those with RBBB and LBBB in the absence of HF (9).

The primary endpoint was the clinical CRT response defined as any change in NYHA classification at 6 months post implantation. Secondary analysis included the correlation of the NYHA Class change with changes in synchrony parameters.

Statistics

Continuous variables are expressed as mean ± SD if normally distributed and as median and interquartile range if not normally distributed. The Chi-squared Test compared categorical variables. T-test with welch p-value was used to compare continuous variables given unequal responder and non-responder group size and variance. Statistical significant change in NYHA Class across the three outcomes groups was performed by the Kruskal-Wallis Rank Test. Optimal, statistically significant cut points for baseline variables between groups were made by an apriori value or by receiver operator curve analysis. STATA 10.0(StataCorp, College Station, Texas) was used for all statistical analyses.

Results

We enrolled 66 patients, 51 males (77.3%), mean age 62.9±13.9 years, each in sinus rhythm, 36(55%) with ischemic cardiomyopathy (Table 1). 55 patients were NYHA III and 11 patients were NYHA IV. At 6-months post CRT implantation, 47(71%) patients, improved clinically. The 34 (51.5%) patients who improved by one NYHA class and the 13 (19.7%) who improved by two NYHA Classes were designated as responders, and the 19 (28.8%) who showed no change or worsened

were designated as non-responders. Baseline age, sex, and cardiomyopathy etiology were not related to patient outcomes (Table 1).

Predictive value of pre-CRT measures

Pre-implantation QRS duration, echocardiographic LVEF, LVEDVI, LVSVI, LVEF, and ERNA derived LVE, LVSDØ, RVSDØ, RVS and RVE could not distinguish response to CRT in these patients with class III and IV HF and echocardiographic EF <35%. Baseline LVS and IVS were the only parameters that predicted response to CRT **(**Table 2). CRT responders had lower group mean LVS (0.858 ± 0.12) compared **t**o non-responders (0.915 ± 0.04, P=0.008), and higher IVS (18.3° ± 0.62 vs. 9.76° ± 9.69, P=0.009).

A lower baseline LVS and higher baseline IVS related to a higher rate and magnitude of improvement with CRT. Receiver operator curve (ROC) analysis demonstrated an optimal discrimination LVS threshold of 0.84. Among patients with pre-CRT LVS ≤0.84, 15/16(94%) improved versus 32/50 (64%) with LVS > 0.84, p=0.02.

Mean IVS previously established in patients with LBBB was 18.8°(14). Among patients with baseline IVS ≥18.8°, 21/23(91%) responded to CRT versus 26/43(60%) with IVS <18.8°, p=0.008. Among 32 responders with LVS >0.84, 14(44%) had IVS ≥18.8°. Patients with either LVS <0.84 or IVS ≥18.8°, had a

higher response rate to CRT. Sixty-two percent of responders had either LVS <0.84 or IVS ≥18.8° as opposed to only 16% of non-responders, p =0.001.

Serial changes in post-CRT measures

The post-CRT change in QRS, echocardiographic and ERNA LVEF, LVS, LVE, LVSDØ, and IVS was significantly different between responders and non-responders (Table 3). Responders who improved two NYHA Classes revealed large improvements in these parameters. However, LVEF, LVSDØ, LVS and LVE change but not change in IVS could differentiate the highest responders from the non-responders and modest responders (Table 4). RVSDØ, RVS, and RVE showed no significant change after CRT.

Figure 1 illustrates serial ERNA images in a CRT responder while Figure 2 shows serial images in a non-responder. Figure 3 shows the individual data points of baseline LVS and IVS in responders and non-responders.

Discussion

Main Findings

Although CRT improves ventricular synchrony and symptoms in many HF patients, as in this study, 30–40% do not benefit (2-5). In this study we serially measured established and novel quantitative ERNA parameters of ventricular dyssynchrony, and correlated them with clinical outcomes post-CRT among 66

patients with advanced HF. Given the high failure rate of electrocardiographic and echocardiographic parameters to CRT predict response in patients with advanced HF, an accurate and reproducible method to identify patients who benefit from CRT is needed. In this study pre-CRT IVS and LVS effectively identified CRT responders from non-responders.

Serial ERNA studies showed improvement in LVEF, LVS, LVE, SDLVØ and IVS, differed significantly between responders and non-responders. These characteristics show that both ventricular systolic function and synchrony improve with CRT. We present parameters for dyssynchrony measurement whose improvement correlates well with improved LVEF supporting the belief that improved intraventricular LV synchrony contributes to LVEF improvement post-CRT.

In this initial effort to evaluate the method, we have excluded patients with atrial fibrillation (AF) where the often rapid and irregular ventricular rates would produce artifacts in the data. However, scintigraphic methods could be applied to sample a limited fixed rate window, making the method applicable even in those with AF.

Comparison of Other Imaging Modalities

Imaging methods that capture the extent and sequence of ventricular contraction

could have an important advantage for the measurement of synchrony. A variety of echocardiographic parameters have been used extensively to express LV mechanical dyssynchrony. Although early echocardiography reports seemed promising(16), the relationship of many echocardiographic derived measures of dyssynchrony and the outcomes of CRT are inconsistent and these echocardiographic methods lack reproducibility (17,18). New efforts to assess myocardial deformation by 3D echocardiography and magnetic resonance techniques have been developed (19). However, MRI is costly, not widely available and is not generally recommended or widely applied to patients with implanted devices (19).

Gated Myocardial Perfusion Scintigraphy (MPS) - A novel, commercially available, count-based method, analyzes the curve generated from the variation of myocardial intensity with wall thickening on gated MPS. Repeatability, reproducibility and temporal resolution of histogram derived SDØ, bandwidth, skewness, and kurtosis have been demonstrated. LV synchrony assessed by ECG-gated MPS correlates well with echocardiographic measures (18,19) in limited patient numbers (20,21), and appears to correlate well with HF outcomes (8). Technical limitations of ECG-gated MPS include potential undersampling of conventional 8 frame acquisition protocols, potentially reduced accuracy associated with limited assessment of regional thickening in poorly perfused, heavily scarred, ventricles of CRT patients and potentially complicated by

attenuation artifact of ECG-gated MPS images. Both ERNA and ECG-gated SPECT MPI methods are associated with very low radiation exposure (1 - 10 mSv). The assessment of planar ERNA measurements prior to CRT can potentially identify those most and least likely to benefit from the mechanical pacing therapy and potentially avoid unnecessary instrumentation in those least likely to respond to CRT.

In this study we demonstrate the value of dyssynchrony derived from planar ERNA in predicting clinical outcomes after CRT implantation. Planar ERNA is relatively inexpensive, widely available and widely applied with high accuracy in virtually all patients (22). The sampling rate is sufficient to accurately measure LVEF (23) and temporal resolution is digitally enhanced and objectified by the generation of "parametric" images. The phase image has successfully tracked the sequence of ventricular wall motion in a variety of conduction abnormalities (15,16,20-23). The ability of planar ERNA phase analysis to assess myocardial synchrony is recognized (8,12,20-22). The SDLVØ has demonstrated the influence of synchrony on HF and CRT outcomes and was the only parameter measured in sinus rhythm, which predicted VT intolerance (8, 20-23). ERNA is also the only imaging method that can evaluate adequately both LVS and IVS and their combined contribution to the CRT response in patients with advanced HF.

The potential value of SPECT ERNA was considered and we have now begun to

acquire these studies in both planar and SPECT modes. We are now developing methods to calculate dyssynchrony parameters and others for the SPECT method. SPECT imaging is also highly reproducible, repeatable, and widely available (7). However, unlike planar ERNA, SPECT ERNA may lose accuracy due to under-sampling with 8-frame acquisition, and routine 16-frame acquisition is recommended.

Comparison with ECG

QRS duration and morphology have been shown to be predictors of response to CRT (22-25). The CARE-HF study showed mortality benefit with CRT pacing alone in patients with LBBB morphology and QRS duration >150 ms (22-25). Recent meta-analysis of CRT studies has shown that baseline QRS duration >150ms was one of the best predictors of response to CRT (22-25). Baseline LBBB morphology is associated with significant improvement in HF events, ventricular tachyarrhythmia and death (23-26). We believe planar ERNA measures of mechanical synchrony (LVS and IVS) provide incremental predictive value to CRT response in patients with advanced HF. We have shown pre-CRT LVS and IVS identify high likelihood of clinical improvement of HF with CRT in patients with QRS duration 120-150 ms, and we believe patients with IVCD/RBBB (class II indication as per the new CRT guidelines) will similarly benefit from LVS and IVS where ECG morphology alone is not predictive of CRT response.

Limitations

There is much more that can be done in the effort to measure synchrony and optimize patient selection and clinical outcomes with CRT. The parameters of S and E are not suggested to be the final iteration, but an initial approach to the objective measurement of synchrony. These measures do not consider improvement of function in ventricular segments without amplitude prior to CRT, as can be seen. Further study is needed to identify factors that explain the minority of patients with preserved synchrony who demonstrate clinical improvement of HF with CRT. Neither these parameters, nor this analysis, factor in the presence or location of scar, myocardial viability, the location of the pacing lead, and other yet unknown conditions that likely influence the response to CRT. There remains a need for yet more objective and reproducible methods to measure mechanical dyssynchrony. There is a clinical and economic necessity to identify those who will benefit from CRT and the synchrony imaging software is an effort in this direction (24-27). It would have been desirable to evaluate all the parameters used to assess the functional class of HF patients such as exercise duration and VO2 max (6 minute walk), and others, as we characterize the value of new imaging dyssynchrony parameters. Nonetheless, the NYHA Class is a global clinical measure of HF status, relating to and influenced by all other measures of HF performance. In this initial test of a new and promising imaging measure of synchrony, a blinded evaluation of NYHA Class was sufficient to demonstrate the

proof of concept. A more detailed evaluation of the correlation between HF status and image synchrony parameters is important and will serve to add validity to this preliminary assessment.

Conclusion

We have found novel measures of LV dyssynchrony derived from ERNA planar analysis (LVS and IVS) that predict clinical outcomes in HF patients undergoing CRT. These parameters appear promising in selection of patients most likely to respond to CRT with reduction of advanced heart failure over 6 months. Further study is required to demonstrate the reproducibility and correlation of ERNA derived measures of dyssynchrony on heart failure outcomes, and the cost effectiveness of this approach on patient selection for CRT.

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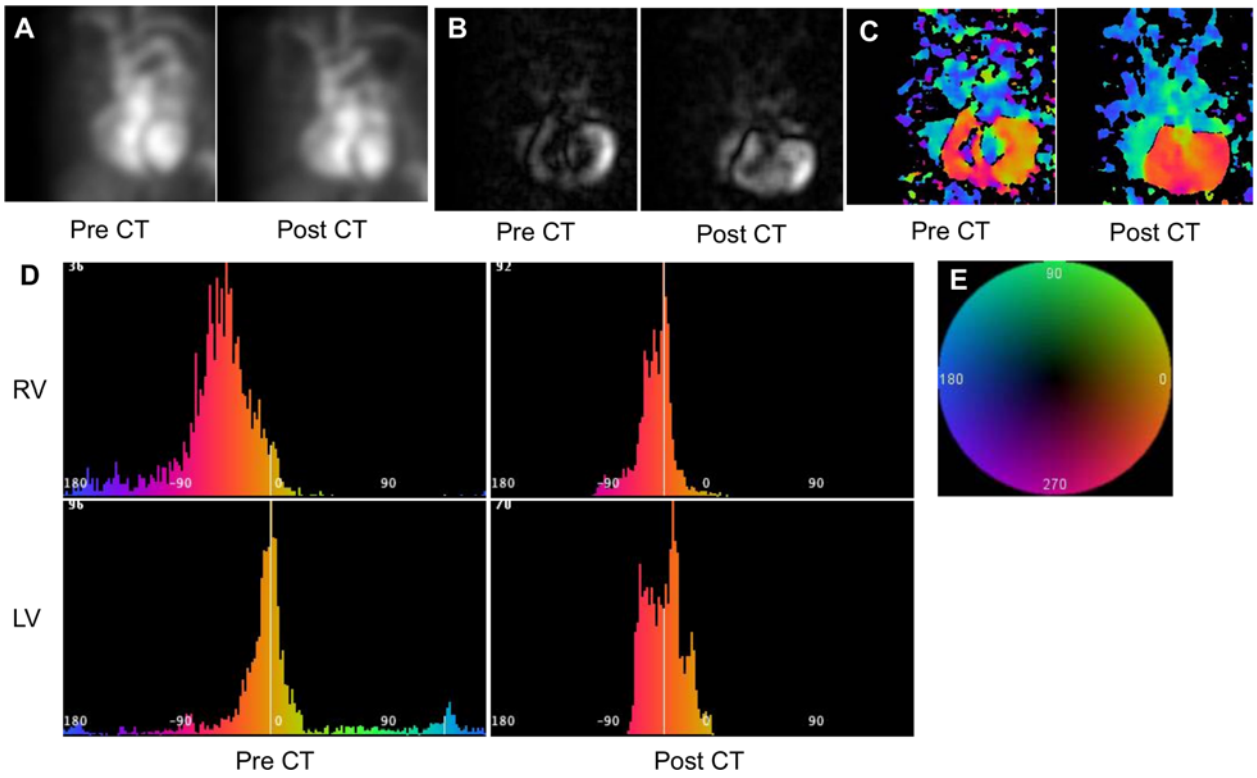
Figure 1: ERNA images of a patient with excellent CRT outcome



A - ERNA Cines – Shown are the "best septal" LAO projections of the gated ERNA acquired in a HF patient with an excellent CRT outcome, pre-CRT, left, and post-CRT, right. NYHA Class fell from III to I as ERNA LVEF increased from 22% to 35%. with CRT.

B - Amplitude Images - Shown are the amplitude images with intensity proportional to amplitude, derived from the cines in **1A**, pre-CRT, left, and post-CRT, right. Note the more complete appearance of the post-CRT image.

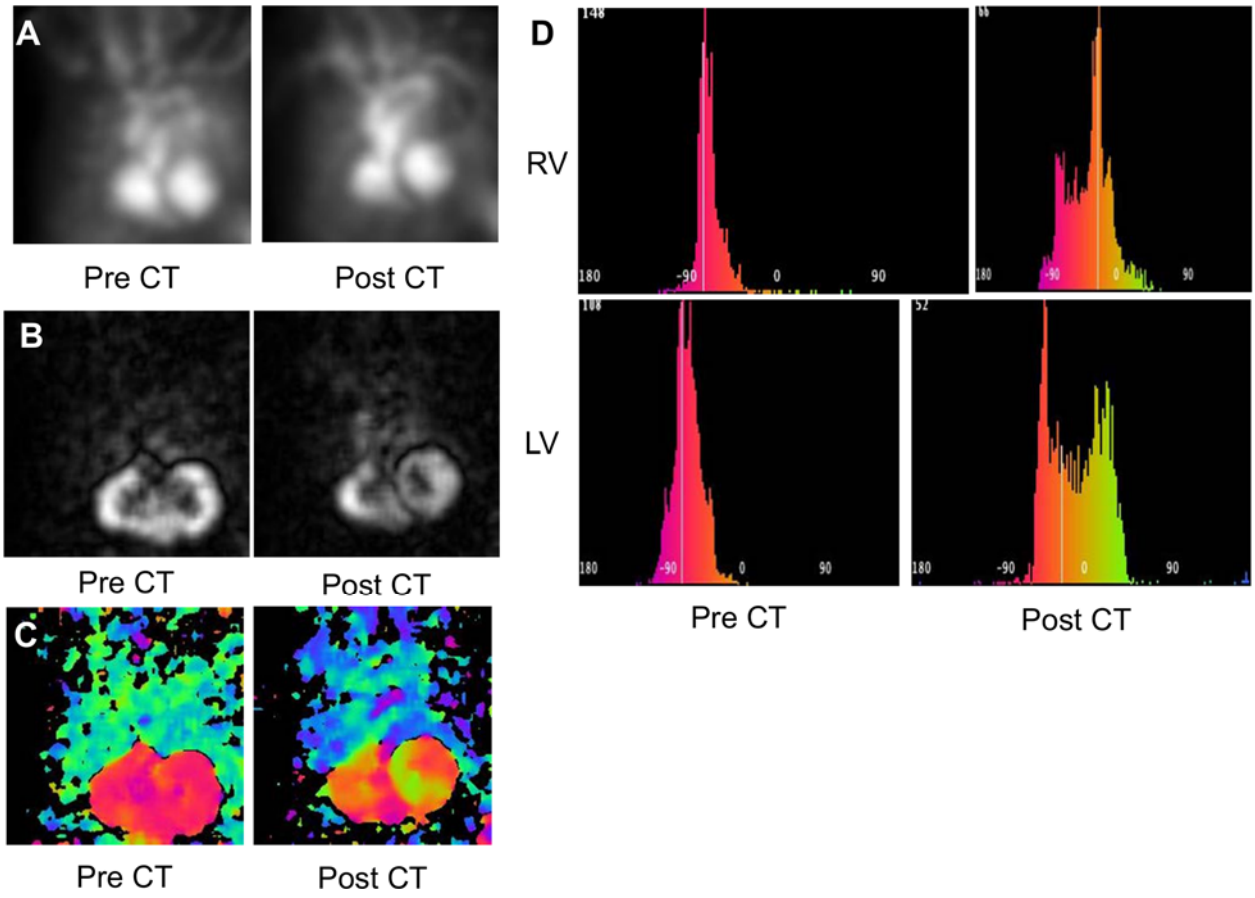
C - Phase Images - Shown are the phase images derived from the cines in **1A**, color coded for phase angle according to the sequence on the color wheel in **1E**,

pre-CRT, left, and post-CRT, right. Note the more homogeneous color distribution across both ventricles post-CRT. Improved intra – and IVS are evident and confirmed on the related histograms, **1D**.

D - Phase Histograms - Shown are the RV phase histograms, above, and the LV phase histograms, below, derived from the phase images shown in **C**, each plotting phase angle on the abscissa and its frequency on the ordinate, within the respective ventricular ROI, color coded for phase angle according to the sequence as in E, pre-CRT left, and post-CRT, right. The reduced width and baseline scatter in both histograms post-CRT supports improved LVS which increased from 0.84 to 0.97, while LVE decreased from 0.69 to 0.50, and LVSDØ decreased from 61.7 to 19.62, with CRT, while the improved vertical alignment of LV and RV histograms post-CRT supports improved IVS which decreased from 41.2 to 6.92.

E - Color Wheel - This is the color code applied to serial phase angles in the images and histograms, above and below, where earliest ventricular phase angle is at approximately 0°.

Figure 2: ERNA images of a patient with poor CRT outcome



A – ERNA Cines - Shown are the "best septal" LAO projections of the gated ERNA acquired in a HF patient with a poor CRT outcome, pre-CRT, left, and post-CRT, right. NYHA Class remained at III as the pre-CRT LVEF of 35% fell to 30% post-CRT.

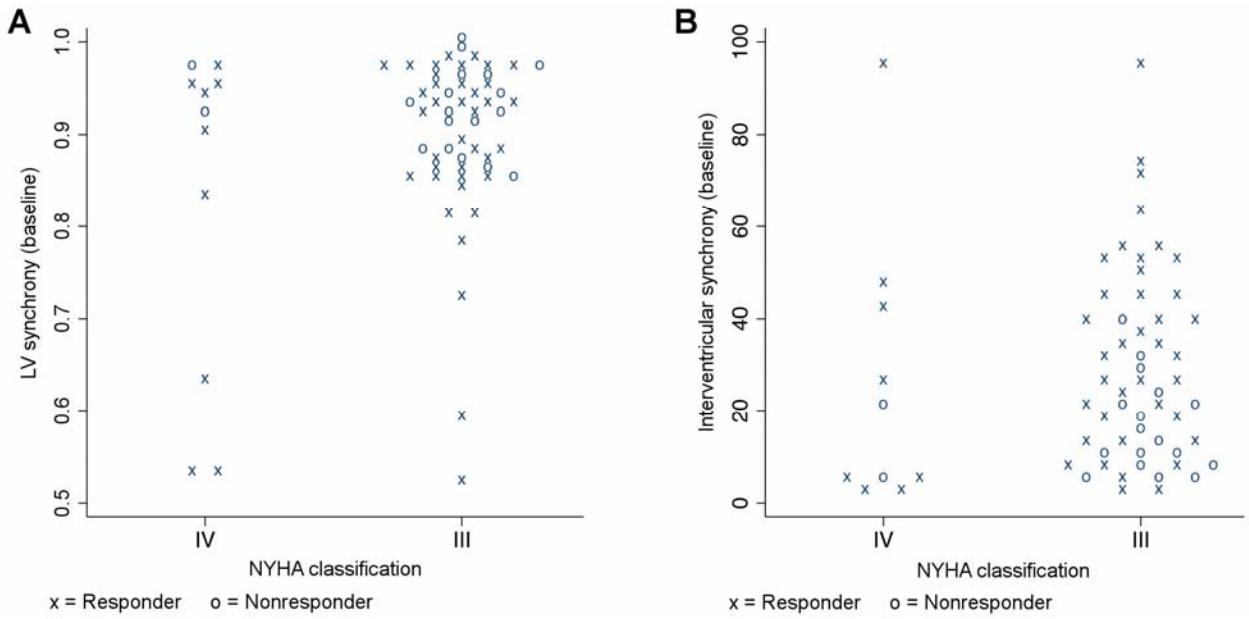
B - Amplitude Images – Shown are the amplitude images derived from the cines in **2A**, above, pre-CRT, left, and post-CRT, right. Note the more heterogeneous appearance of the post-CRT image.

C - Phase Images - Shown are the phase images, pre-CRT, left, and post-CRT,

right, derived from the cines in **2A**, color coded for phase angle according to the sequence on the color wheel in **1E.** Note the more heterogeneous and disparate phase distribution in each ventricle post-CRT compared to the homogeneous biventricular distribution pre-CRT. The color and Ø changes indicate worsening of intra- and interventricular synchrony confirmed on the related histograms, **2D**.

D - LV Phase Histograms - Shown are the RV phase histograms, above, and the LV phase histograms, below, pre-CRT, left, and post-CRT, right, derived from the phase images shown in **2C**. The increased width and spectrum in both histograms post CRT indicates reduced intraventricular synchrony as LVS fell from 0.96 to 0.87, LVE increased 0.36 to 0.66, and LVSDØ increased from 12.29 to 28.34, with CRT while the vertical misalignment of LV and RV histograms, apparent post-CRT, supports the observed increased IVS from 1.97 to 45.19).

Figure 3.



A. Baseline left ventricular synchrony (LVS) plot in patients with NYHA III and IV showing values in responders and non-responders. B. Baseline interventricular synchrony (IVS) plot in patients with NYHA III and IV showing values in responders and non-responders.

Table 1: Baseline Clinical Characteristics

Characteristics	**All (n = 66)**	**Non-Responders* (n = 19)**	**Responders† (n = 47)**	***p* Value**
Male	51 (77%)	13 (68%)	38 (81%)	0.28
Age (in years)	62.9 ± 13.9	58.4 ± 15.7	64.7 ± 12.7	0.09
NYHA Class III	55 (83%)	17	38	0.02
NYHA Class IV	11 (17%)	2	9	0.02
Etiology (Ischemic)	36 (54%)	10 (53%)	26 (55%)	0.84
Hypertension	21 (31.8%)	4 (21%)	17 (36%)	0.23
Diabetes Mellitus	13 (19.7%)	4 (21%)	9 (19%)	0.86

* Negative or 0 change in NYHA classification at 6-month follow-up visit post CRT implant
† Positive 1 or 2 change NYHA classification at 6-month follow-up visit post CRT implant

Table 2: Baseline Parameters Compared to Clinical Outcome

Parameters	Non-Responders* (n =19)	Responders† (n = 47)	*p* Value
QRS Duration	157.68ms ± 25.08	167.47ms ± 28.44	0.2
LVEF (Echo)	34.41% ±10.92	31.19% ± 8.69	0.3
LVEDVI (Echo)	113.64 mL ± 56.97	98.19 mL ± 38.54	0.4
LVESVI (Echo)	82.15 mL ± 46.74	68.79 mL ± 28.05	0.3
LVS	0.915 ± 0.04	0.858 ± 0.12	0.008
LVE	0.618 ± 0.10	0.663 ± 0.10	0.1
LVSDØ	35.8° ± 14.10	43.3° ± 18.20	0.08
LVEF (ERNA)	25.9% ± 8.97	25.7% ± 5.77	0.9
RVS	0.93 ± 0.06	0.93 ± 0.06	0.9
RVE	0.57 ± 0.03	0.58 ± 0.02	0.9
RVSDØ	24.0° ± 10.60	24.7° ± 10.40	0.8
IVS	9.76° ± 9.60	18.3° ± 0.62	0.009

* See text and Table 1

† See text and Table 1

Abbreviations in text above page 3

Table 3: Changes in Parameters Compared to Clinical Outcome

Change in Parameters (Post – Pre)	Non-responders* (n = 19)	Responders† (n = 47)	*p* Value
QRS	9.44ms ± 25.03	-13.46ms ± 34.11	0.006
LVEF (Echo)	1.99% ± 10.61	10.51% ± 13.80	0.03
LVEDVI (Echo)	-5.94ml ± 32.75	-12.54ml ± 31.87	0.6
LVESVI (Echo)	-15.47ml ± 23.81	-15.72ml ± 30.58	0.9
LVS	-0.004 ± 0.04	0.050 ± 0.10	0.004
LVE	0.004 ± 0.08	-0.064 ± 0.10	0.006
LVSDØ	-3.5° ± 11.60	-14.3° ± 16.10	0.004
LVEF (ERNA)	1.13% ± 6.10	8.0% ± 8.80	0.0007
RVSDØ	-0.83° ± 13.60	-1.3° ± 9.10	0.9
RVS	0.006 ± 0.04	0.007 ± 0.05	0.9
RVE	-0.003 ± 0.12	-0.01 ± 0.09	0.8
IVS	2.3° ± 7.60	-3.8° ± 17.50	0.05

* See Text and Table 1

† See Text and table 1

Abbreviations as in text above, page 3

Table 4: NYHA Change in Cardiac Functional Parameters Compared to Improvement in the Number of NYHA Classes Before and After 6 Months of CRT

Change in Parameters (Post – Pre)	**No change in NYHA (n = 19)**	**Improved by 1 NYHA class (n = 34)**	**Improved by 2 NYHA classes (n = 13)**	***p* Value**
QRS	9.44ms ± 25.03	-6.83ms ± 31.13	-28.77ms ± 36.96	0.01
LVEF (Echo)	1.99% ± 10.61	8.71% ± 13.01	13.63% ± 15.20	0.03
LVEDVI	-5.94mL ± 32.75	-6.94mL ± 36.37	-21.25mL ± 22.46	0.5
LVESVI	-15.46mL ± 23.81	-10.75mL ± 35.17	-23.17mL ± 21.61	0.5
LVS	-0.004 ± 0.04	0.024 ± 0.06	0.12 ± 0.15	0.03
LVE	0.004 ± 0.08	-0.04 ± 0.08	-0.12 ± 0.12	0.005
LVSDØ	-3.5° ± 11.60	-11.2° ± 13.00	-22.2° ± 20.90	0.02
LVEF (ERNA)	1.13% ± 6.10	5.2% ± 6.90	15.2% ± 9.20	0.0001
RVSDØ	-0.89° ± 13.30	-1.5° ± 6.80	-0.7° ± 14.10	0.07
RVS	0.006 ± 0.04	0.008 ± 0.04	0.006 ± 0.08	0.8
RVE	-0.004 ± 0.12	-0.011 ± 0.06	-0.13 ± 0.14	0.80
IVS	2.33° ± 7.60	-3.6° ± 16.20	-4.2° ± 21.60	0.3