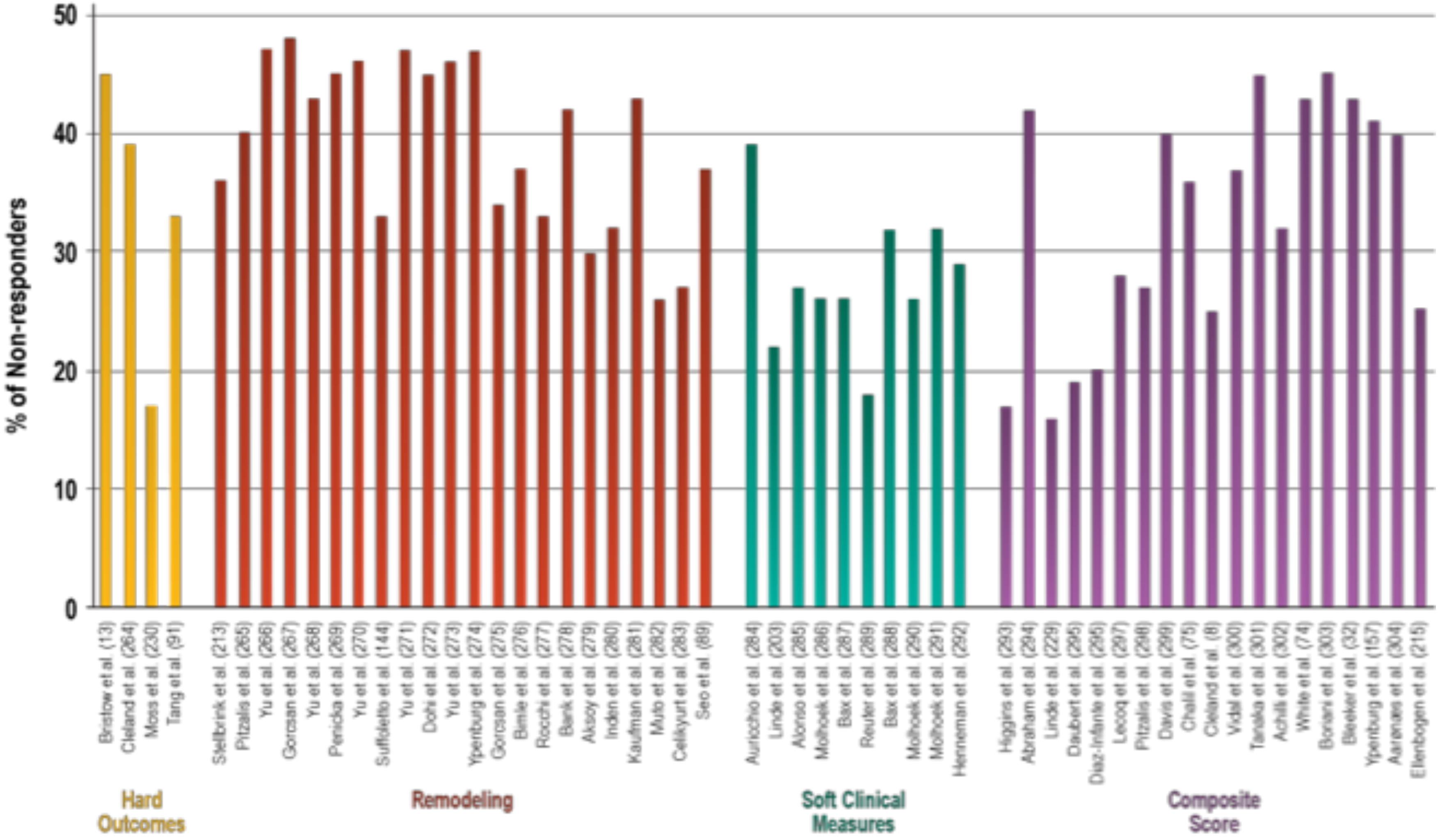
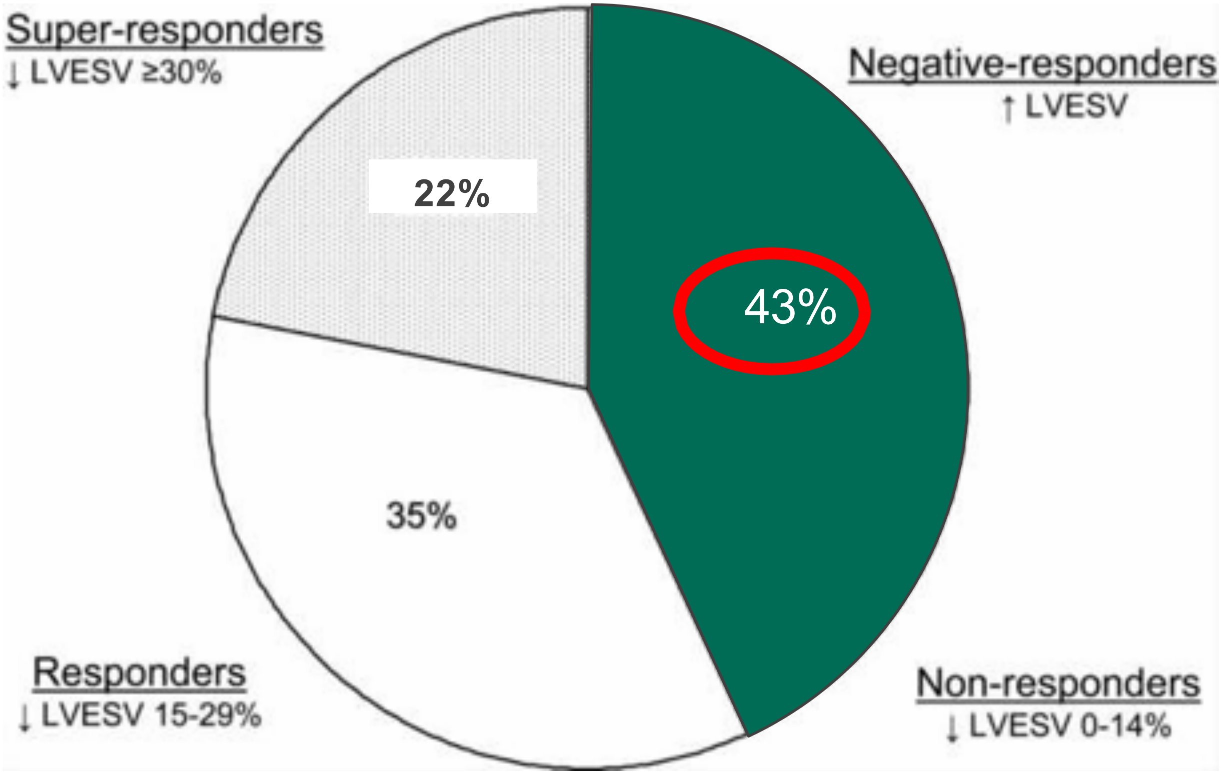
CRT Response: Inadequate and unpredictable



Daubert, J.C., et al. Europace, 2012

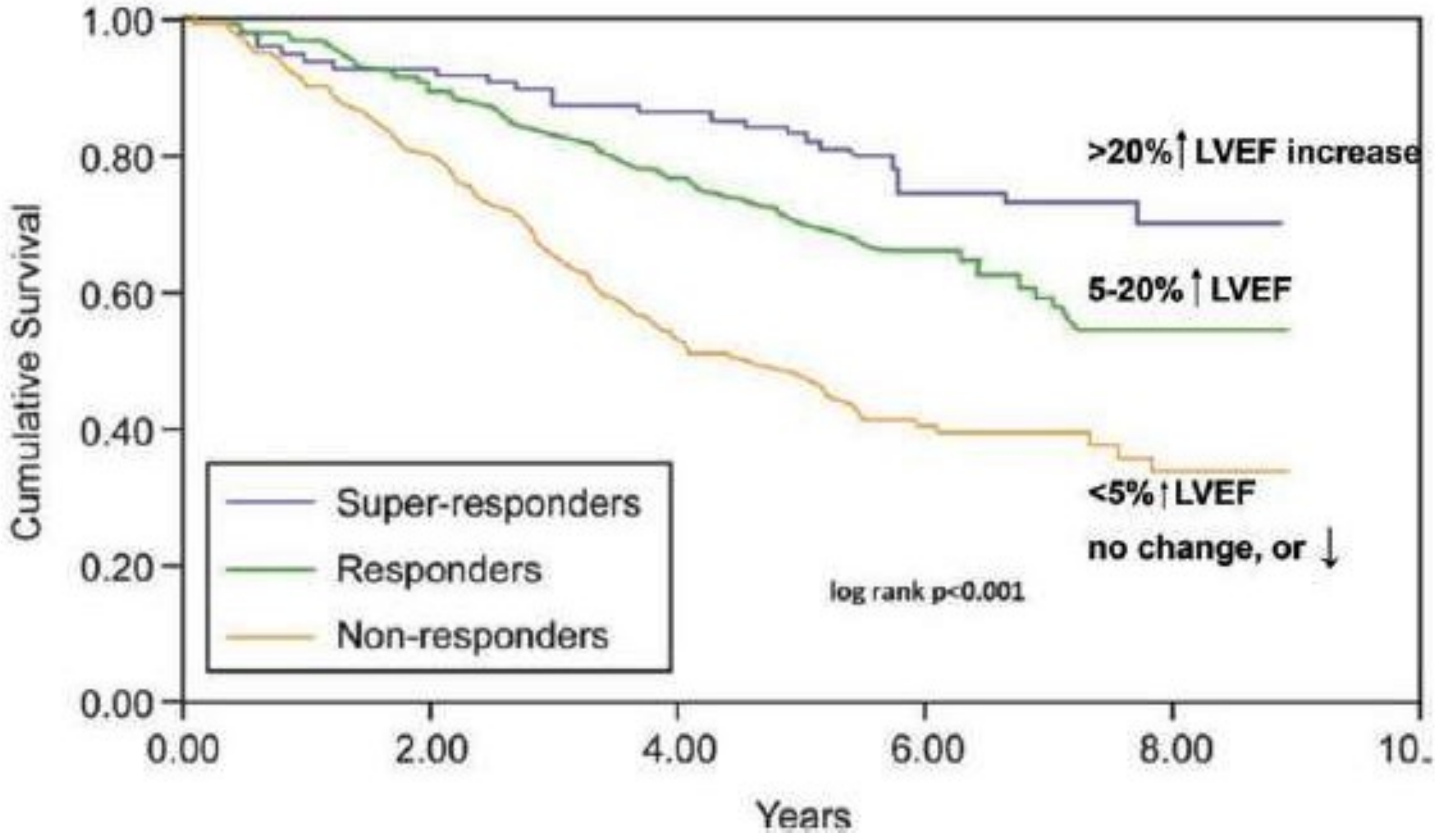
CRT Challenge



43% of CRT patients classified as negative or non-responders after 6 months

Ypenburg, C., et al. Journal of the American College of Cardiology 2009

Survival Effect of CRT of Super-Responders, Responders, an
Non-Responders



Rickard et al. Heart Rhythm 2014

CRT Response
Current Issues

Multiple different factors between individual pts can affect response:

Genetic & gender differences Stage &

CHF etiology

LV lead location

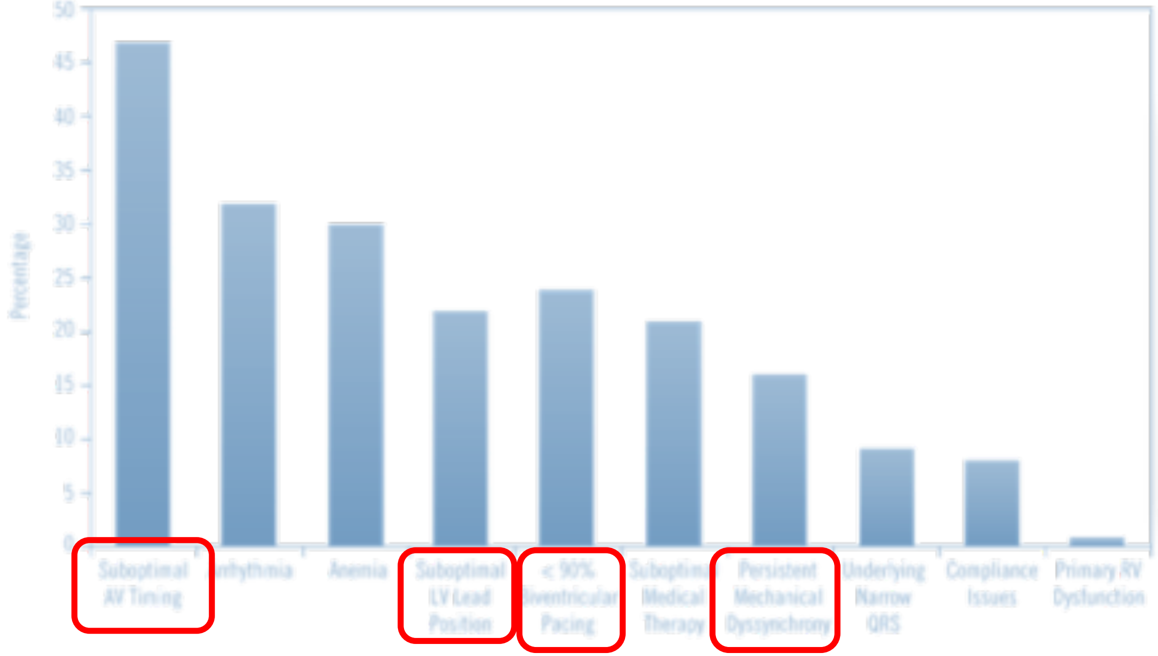
QRS morphology & width

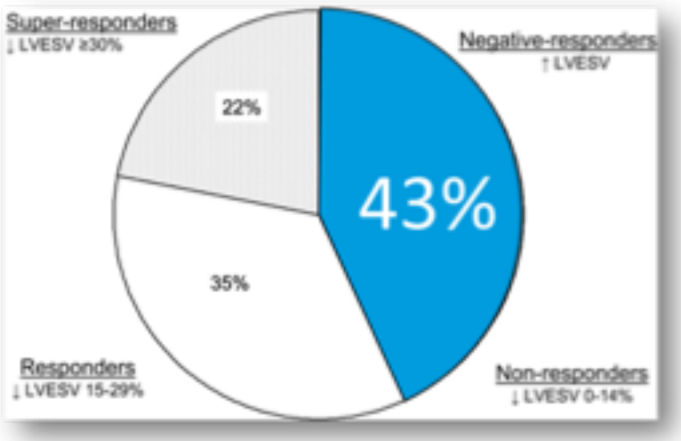
Presence of co-morbidities, LV scar, & AF/PVC’s

Coronary sinus valves/stenosis/limited target vessels Device

management: AV & VV optimization, ensuring BiV pacing

Identificare le Cause del problema per cercare una soluzione





Mullens W, et al. JACC. 2009;53:765-773
McAlister FA et al. JAMA. 2007;297:2502–14

- RITARDO AV NON OTTIMIZZATO
- POSIZIONE NON OTTIMALE DEL LEAD VSX
- STIMOLAZIONE BIVENTRICOLARE< 90%
- PERSISTENZA DELLA DISSINCRONIA MECCANICA

Definition of success in CRT recipients

Table 1. Seventeen Different Response Criteria Identified From the 26 Relevant Publications

Response criteria

Echocardiographic

1. ↑ LVEF ≥5% (absolute)[1,2]
2. ↑ LVEF ≥15%[3,4]
3. ↓ LVESV ≥10% and did not die of progressive HF within 6 months[20,27]
4. ↓ LVESV >15%[2,5–10]
5. LVESV <115% of baseline[26]
6. ↓ LVESVI >15%[25]
7. ↓ LVEDV >15%[2]
8. ↑ Stroke volume ≥15%[4,21,22]

Clinical

9. ↓ NYHA ≥1[2,12–14]
10. ↓ NYHA ≥1 and did not die of progressive HF within 6 months[23]
11. ↓ NYHA ≥1 and ↑ 6MWD ≥25%[15]
12. ↓ NYHA ≥1 and ↑ 6MWD ≥25% and did not die of progressive HF within 6 months[16,17]
13. ↑ 6MWD >10%, no heart transplant, did not die of progressive HF within 6 months[11]
14. (↓ NYHA ≥1 or ↑ $\dot{V}O_2$max >10% or ↑ 6MWD >10%) and alive, no hospitalization for decompensated HF[24]
15. Two of 3:[5]
    - ↓ NYHA ≥1
    - ↑ 6MWD ≥50 m
    - ↓ QOL ≥15
16. Clinical composite score improved[10]

Combined

17. (↑ LVEF ≥5% [absolute] or ↑ 6MWD ≥30 m) and (↓ NYHA ≥1 or ↓ QOL ≥10)[18]

Table 4. Response Rates for the Different Criteria

Response Criteria	Response Rate, %	No. Evaluable (% of Total)
Echocardiographic		
↑ LVEF >5 units	51	286 (67)
↑ LVEF >15% (relative)	54	286 (67)
↓ LVESV ≥10%, no HF death	62	291 (68)
↓ LVESV >15%	56	286 (67)
LVESV <115% of baseline	91	286 (67)
↓ LVEDV >15%	49	286 (67)
↑ Stroke volume ≥15%	34	286 (67)
Clinical		
↓ NYHA ≥1	71	385 (90)
↓ NYHA ≥1, no HF death	70	390 (92)
↓ NYHA ≥1 and ↑ 6MWD ≥25%	33	348 (82)
↓ NYHA ≥1 and ↑ 6MWD ≥25%, no HF death	32	353 (83)
↑ 6MWD ≥10%, no HF death, no transplant	61	353 (83)
Two of the following 3: ↓ NYHA ≥1, ↑ 6MWD ≥50 m, ↓ QOL ≥15	63	339 (80)
Clinical composite score improved	69	426 (100)
Combined		
↑ LVEF >5 units or ↑ 6MWD ≥50 m and ↓ NYHA ≥1 or ↓ QOL ≥10	71	250 (59)

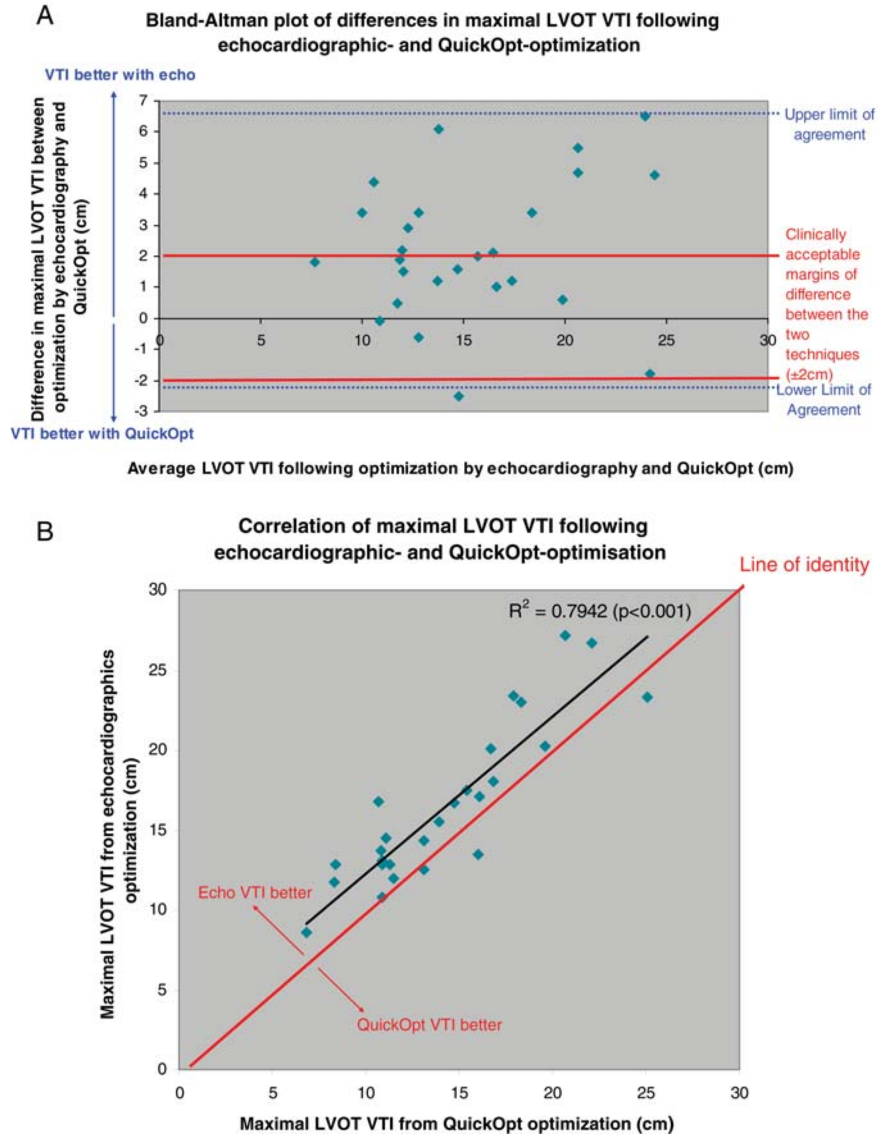
A prospective comparison of echocardiography and device algorithms for atrioventricular and interventricular interval optimization in cardiac resynchronization therapy

Ravindu Kamdar, Evelyn Frain, Fiona Warburton, Laura Richmond, Victoria Mullan, Thomas Berriman, Glyn Thomas, Joanna Tenkorang, Mehul Dhinoja, Mark Earley, Simon Sporton, and Richard Schilling*

Aims Echocardiographic optimization of atrioventricular (AV) and interventricular (VV) intervals in cardiac resynchronization therapy (CRT) is costly, time-consuming, and requires skill and expertise so is usually undertaken only in 'non-responder' patients. An algorithm in St Jude Medical CRT devices (QuickOpt™) claims to optimize these settings automatically. The aim of this study was to compare the two optimization techniques.

Methods and results Optimization of AV and VV intervals was performed a month after CRT device implantation in 26 patients with heart failure, first by echocardiography then by QuickOpt. The left ventricular outflow tract (LVOT) velocity–time integral (VTI) was measured after optimization by each method. Agreement between the optimization methods was assessed by the Bland–Altman analysis and correlation by Pearson's correlation coefficient. There was good correlation between the LVOT VTI following optimization by both methods ($R^2 = 0.77$, $P < 0.001$). However, agreement between the two methods was poor, with 15 of 26 and 10 of 26 patients having a >20 ms difference in the optimal AV and VV interval values, respectively. Left ventricular outflow tract VTI was significantly better (22 of 26 patients; $P < 0.001$) in patients optimized by echocardiography than by QuickOpt.

Conclusion There is a poor agreement in optimal AV and VV intervals determined by echocardiography and QuickOpt, with echocardiographic optimization giving a superior haemodynamic outcome.



FREEDOM trial (Frequent Optimization Study Using the QuickOpt Method)

Kamdar R et al. Europace 2010;12: 84–91

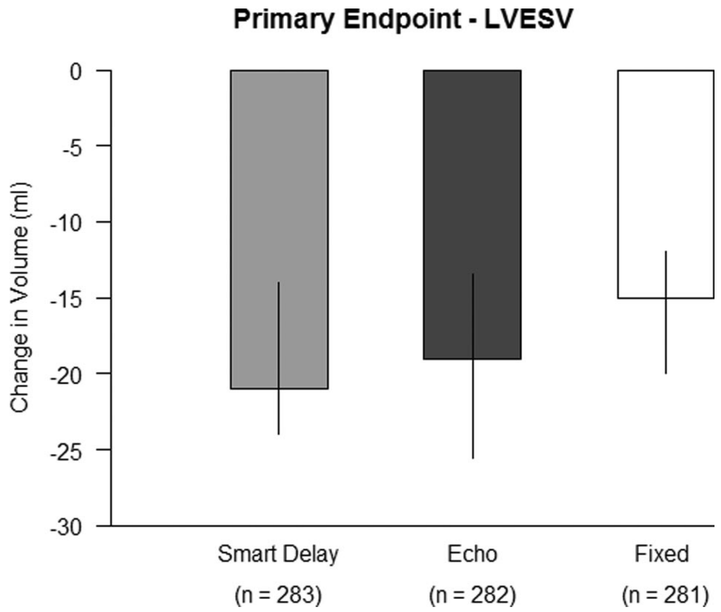
Primary Results From the SmartDelay Determined AV Optimization: A Comparison to Other AV Delay Methods Used in Cardiac Resynchronization Therapy (SMART-AV) Trial

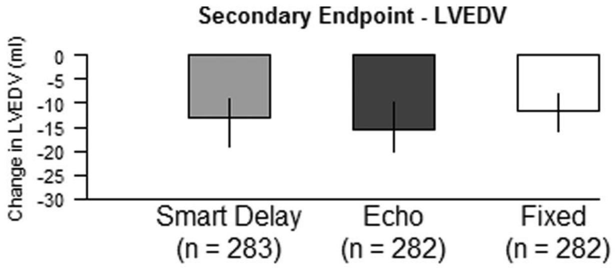
A Randomized Trial Comparing Empirical, Echocardiography-Guided, and Algorithmic Atrioventricular Delay Programming in Cardiac Resynchronization Therapy

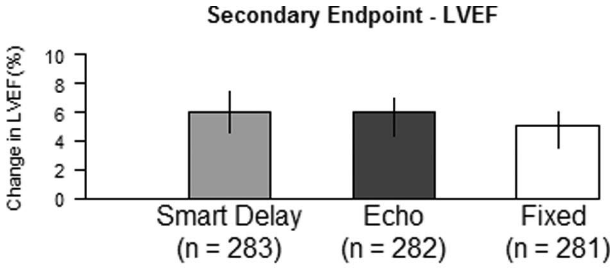
Background—One variable that may influence cardiac resynchronization therapy response is the programmed atrioventricular (AV) delay. The SmartDelay Determined AV Optimization: A Comparison to Other AV Delay Methods Used in Cardiac Resynchronization Therapy (SMART-AV) Trial prospectively randomized patients to a fixed empirical AV delay (120 milliseconds), echocardiographically optimized AV delay, or AV delay optimized with SmartDelay, an electrogram-based algorithm.

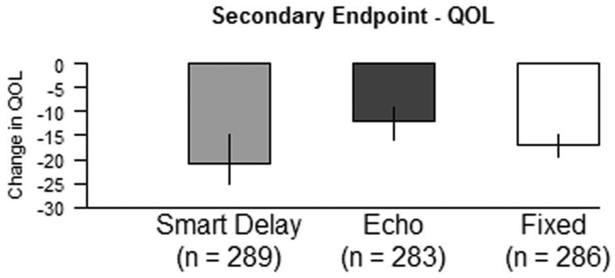
Methods and Results—A total of 1014 patients (68% men; mean age, 66±11 years; mean left ventricular ejection fraction, 25±7%) who met enrollment criteria received a cardiac resynchronization therapy defibrillator, and 980 patients were randomized in a 1:1:1 ratio. All patients were programmed (DDD-60 or DDDR-60) and evaluated after implantation and 3 and 6 months later. The primary end point was left ventricular end-systolic volume. Secondary end points included New York Heart Association class, quality-of-life score, 6-minute walk distance, left ventricular end-diastolic volume, and left ventricular ejection fraction. The medians (quartiles 1 and 3) for change in left ventricular end-systolic volume at 6 months for the SmartDelay, echocardiography, and fixed arms were −21 mL (−45 and 6 mL), −19 mL (−45 and 6 mL), and −15 mL (−41 and 6 mL), respectively. No difference in improvement in left ventricular end-systolic volume at 6 months was observed between the SmartDelay and echocardiography arms (*P*=0.52) or the SmartDelay and fixed arms (*P*=0.66). Secondary end points, including structural (left ventricular end-diastolic volume and left ventricular ejection fraction) and functional (6-minute walk, quality of life, and New York Heart Association classification) measures, were not significantly different between arms.

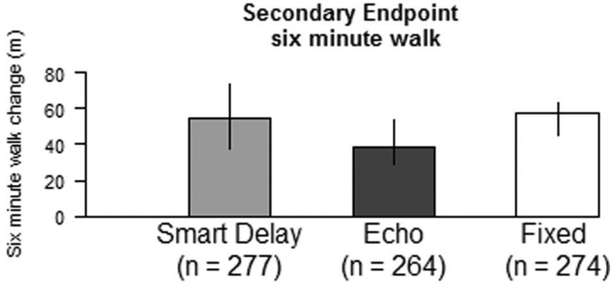
Conclusions—Neither SmartDelay nor echocardiography was superior to a fixed AV delay of 120 milliseconds. The routine use of AV optimization techniques assessed in this trial is not warranted. However, these data do not exclude possible utility in selected patients who do not respond to cardiac resynchronization therapy.

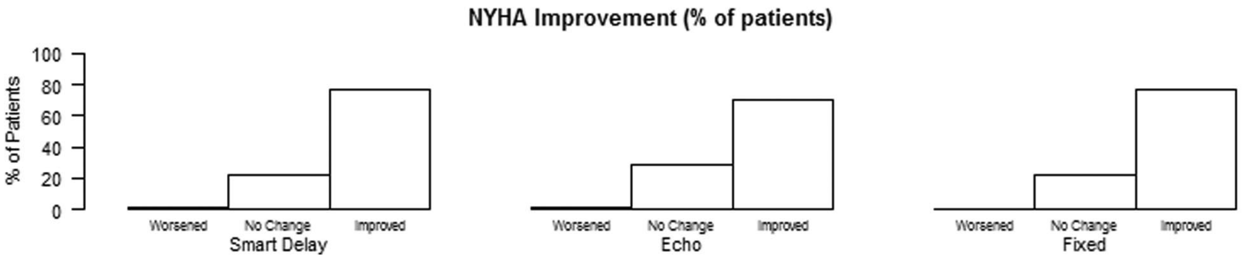












Ellenbogen KA et al. Circulation. 2010;122:2660-2668

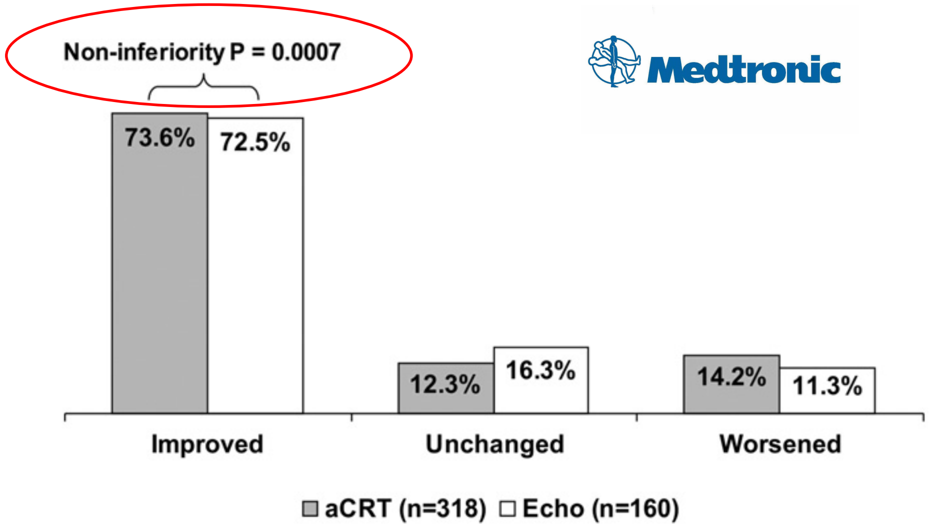
Investigation of a novel algorithm for synchronized left-ventricular pacing and ambulatory optimization of cardiac resynchronization therapy: Results of the adaptive CRT trial

David O. Martin, MD, MPH,* Bernd Lemke, MD,† David Birnie, MD, MB, ChB,‡
Henry Krum, MBBS, PhD,§ Kathy Lai-Fun Lee, MD,‖ Kazutaka Aonuma, MD, PhD,¶
Maurizio Gasparini, MD,# Randall C. Starling, MD, MPH,* Goran Milasinovic, MD,**
Tyson Rogers, MS,†† Alex Sambelashvili, PhD,†† John Gorcsan III, MD,§§
Mahmoud Houmsse, MD, FHRS,‡‡ Adaptive CRT Study Investigators

BACKGROUND In patients with sinus rhythm and normal atrioventricular conduction, pacing only the left ventricle with appropriate atrioventricular delays can result in superior left ventricular and right ventricular function compared with standard biventricular (BiV) pacing.

OBJECTIVE To evaluate a novel adaptive cardiac resynchronization therapy ((aCRT) algorithm for CRT pacing that provides automatic ambulatory selection between synchronized left ventricular or BiV pacing with dynamic optimization of atrioventricular and interventricular delays.

	aCRT (n = 318)		Echo (n = 160)			
	n	Mean ± SD	n	Mean ± SD	Difference (95% CI)	P* (margin)
LVESVi (mL/m²)						
Baseline	291	71.7 ± 28.3	140	74.0 ± 30.9		
6-mo postrandomization	268	63.5 ± 31.9	137	64.7 ± 32.7		
Paired difference at 6 mo	250	~8.3 ± 23.3	123	~10.5 ± 24.2	2.3 ~(2.8 to 7.4)	<.0001 (15)
LVEF (%)						
Baseline	291	29.6 ± 9.2	140	30.3 ± 8.4		
6-mo postrandomization	268	33.6 ± 10.4	137	32.9 ± 10.1		
Paired difference at 6 mo	250	3.9 ± 10.0	123	2.9 ± 9.8	1.0 ~(1.2 to 3.1)	0.0009 ~(2.5)
NYHA						
Baseline	318	3.0 ± 0.2	160	3.0 ± 0.3		
6-mo postrandomization	296	2.0 ± 0.8	153	2.2 ± 0.8		
Paired difference at 6 mo	296	~1.0 ± 0.8	153	~0.8 ± 0.8	~0.15 (0.3 to 0.0)	<.0001 (0.3)
6-min walk distance (m)						
Baseline	312	276.8 ± 127.5	156	277.7 ± 137.8		
6-mo postrandomization	288	325.5 ± 130.4	146	311.4 ± 152.0		
Paired difference at 6 mo	284	42.4 ± 103.3	142	29.0 ± 123.0	13.4 ~(8.9 to 35.7)	0.0002 ~(30)
MLWHF QOL						
Baseline	286	48.5 ± 24.1	142	46.3 ± 23.6		
6-mo postrandomization	263	28.2 ± 22.0	139	28.4 ± 23.0		
Paired difference at 6 mo	261	~19.3 ± 20.7	135	~17.6 ± 23.8	~1.7 ~(6.3 to 2.8)	0.002 (5.1)



METHODS Patients (n = 522) indicated for a CRT-defibrillator were randomized to aCRT vs echo-optimized BiV pacing (Echo) in a 2:1 ratio and followed at 1-, 3-, and 6-month postrandomization.

RESULTS The study met all 3 noninferiority primary objectives: (1) the percentage of aCRT patients who improved in their clinical composite score at 6 months was at least as high in the aCRT arm as in the Echo arm (73.6% vs 72.5%, with a noninferiority margin of 12%; P = .0007); (2) aCRT and echo-optimized settings resulted in similar cardiac performance, as demonstrated by a high concordance correlation coefficient between aortic velocity time integrals at aCRT and Echo settings at randomization (concordance correlation coefficient = 0.93; 95% confidence interval 0.91–0.94) and at 6-month postrandomization (concordance correlation coefficient = 0.90; 95% confidence interval 0.87–0.92); and (3) aCRT did not result in inappropriate device settings. There were no significant differences between the arms with respect to heart failure events or ventricular arrhythmia episodes. Secondary end points showed similar benefit, and right-ventricular pacing was reduced by 44% in the aCRT arm.

CONCLUSIONS The aCRT algorithm is safe and at least as effective as BiV pacing with comprehensive echocardiographic optimization.

Martin DO et al. Heart Rhythm 2012;9:1807–1814

Contractility sensor-guided optimization of cardiac resynchronization therapy: results from the RESPOND-CRT trial

LivaNova
Health innovation that matters

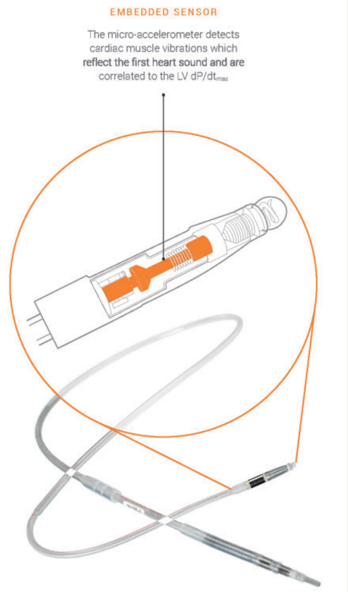
Josep Brugada[1]*, Peter Paul Delnoy[2], Johannes Brachmann[3], Dwight Reynolds[4], Luigi Padeletti[5], Georg Noelker[6], Charan Kantipudi[7], José Manuel Rubin Lopez[8], Wolfgang Dichtl[9], Alberto Borri-Brunetto[10], Luc Verhees[11], Philippe Ritter[12], and Jagmeet P. Singh[13], for the RESPOND CRT Investigators†

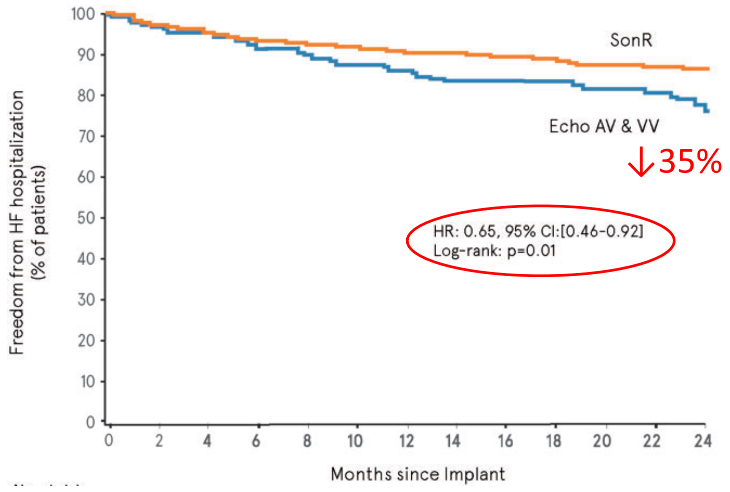
Aims Although cardiac resynchronization therapy (CRT) is effective in patients with systolic heart failure (HF) and a wide QRS interval, a substantial proportion of patients remain non-responsive. The SonR contractility sensor embedded in the right atrial lead enables individualized automatic optimization of the atrioventricular (AV) and interventricular (VV) timings. The RESPOND-CRT study investigated the safety and efficacy of the contractility sensor system in HF patients undergoing CRT.

Methods and results RESPOND-CRT was a prospective, randomized, double-blinded, multicentre, non-inferiority trial. Patients were randomized (2:1, respectively) to receive weekly, automatic CRT optimization with SonR vs. an Echo-guided optimization of AV and VV timings. The primary efficacy endpoint was the rate of clinical responders (patients alive, without adjudicated HF-related events, with improvement in New York Heart Association class or quality of life), at 12 months. The study randomized 998 patients. Responder rates were 75.0% in the SonR arm and 70.4% in the Echo arm (mean difference, 4.6%; 95% CI, −1.4% to 10.6%; P < 0.001 for non-inferiority margin −10.0%) (Table 2). At an overall mean follow-up of 548 ± 190 days SonR was associated with a 35% risk reduction in HF hospitalization (hazard ratio, 0.65; 95% CI, 0.46–0.92; log-rank $P = 0.01$).

Conclusion Automatic AV and VV optimization using the contractility sensor was safe and as effective as Echo-guided AV and VV optimization in increasing response to CRT.

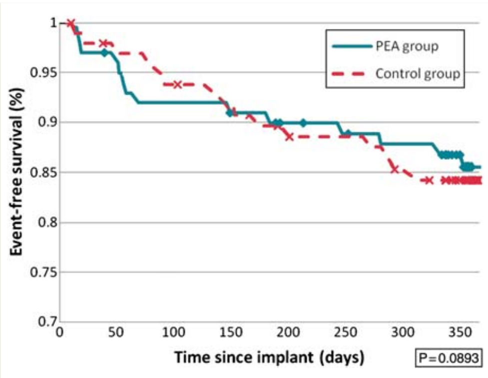
Outcome	SonR (*N*=649) % (*n*)	Echo (*N*=318)	Mean % difference (95% CI)	*P*-value: Non-inferiority	*P*-value: Superiority
Clinical responders[a]	75.0 (487)	70.4 (224)	4.6 (−1.4, 10.6)	<0.001	0.13
NYHA improved	65.6 (426)	61.9 (197)			
Stable NYHA, improved quality of life	9.4 (61)	8.5 (27)			
Clinical non-responders[b]	25.0 (162)	29.6 (94)			
Clinically stable	4.0 (26)	4.4 (14)			
Clinically worsened: secondary endpoint	21.0 (136)	25.2 (80)	4.2 (−1.5, 9.9)	<0.001	0.15
Death from any cause	5.5 (36)	6.0 (19)			
If no death, HF-related event	10.2 (66)	12.9 (41)			
Worsened NYHA class	0.9 (6)	0.3 (1)			
Worsened quality of life; stable NYHA stable	4.3 (28)	6.0 (19)			
Death or HF hospitalization	14.2 (92)	17.6 (56)	3.4 (−1.5, 8.4)	<0.001	0.18





A randomized pilot study of optimization of cardiac resynchronization therapy in sinus rhythm patients using a peak endocardial acceleration sensor vs. standard methods

Philippe Ritter[1]*, Peter Paul HM Delnoy[2], Luigi Padeletti[3], Maurizio Lunati[4], Herbert Naegele[5], Alberto Borri-Brunetto[6], and Jorge Silvestre[7]



Brugada J et al. Eur Heart J 2017;38:730–738

LV Pacing and Location: ***Anatomical Specific*** LV Lead placement

LBBB

- Conventional: LV Site of electrical & mechanical delay = lateral and PL wall
- Target Lateral or PL branch of the CS

Issues

- 30-40% Non-responder rate
- 8-10% of eligible pts do not receive CRT due to anatomical constraints

Issue: QRS Duration & LBBB

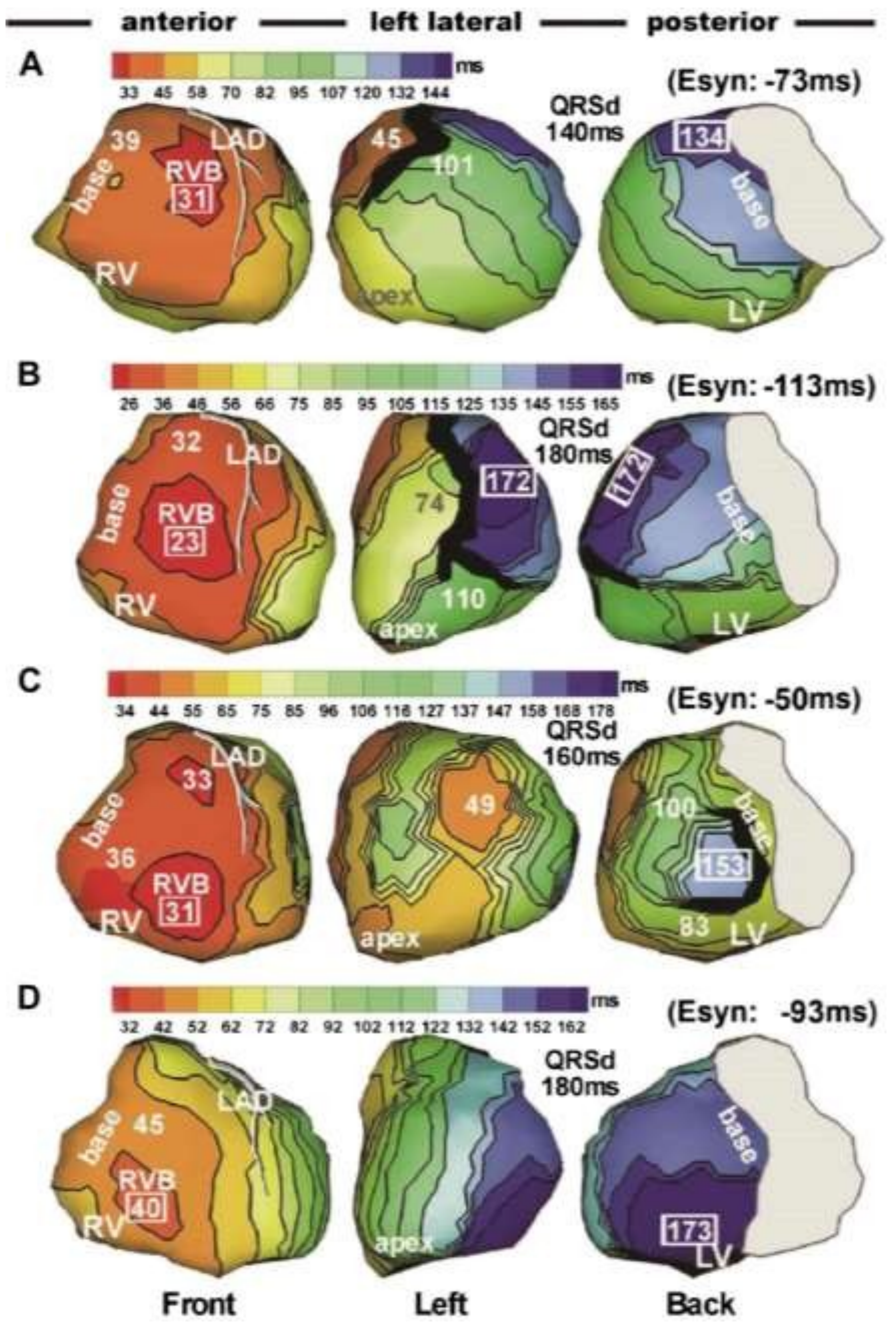
12 lead surface QRS duration limited information

Reflection of total duration of ventricular activation but not a reliable marker of LV activation

Significant variations of LV activation with typical LBBB can be be seen

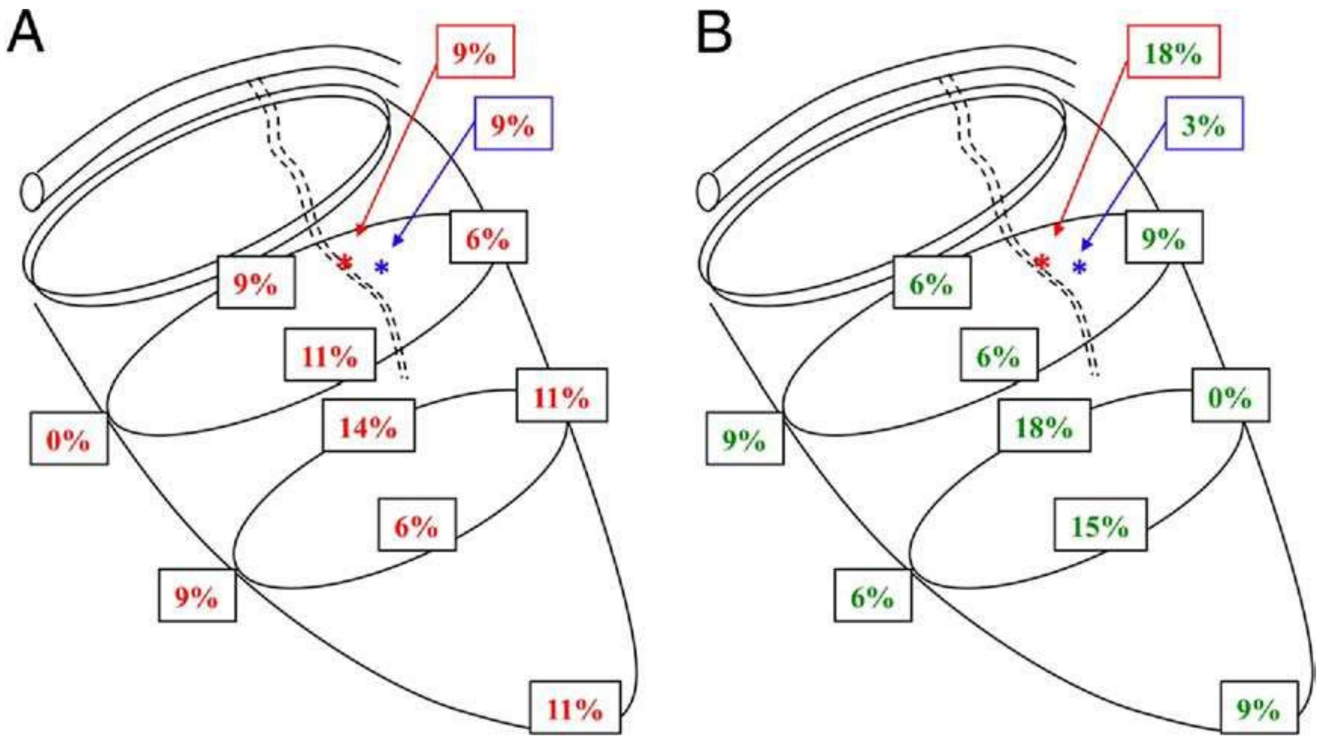
Important factor to determine CRT response and lead location position at implant

Varma N et al. Card Electrophysiolo Clin 2015.



LV Lead Position: Hemodynamics

Distribution of Best (A) and Worst (B) Sites



- Stimulation from the best LV endocardial site resulted in a 2x ↑dP/dt
- Site was widely distributed

Conclusion - Practice of fixed single site in lateral wall will not capture hemodynamically best site- this requires individualization

Derval JACC 2010

LV Pacing and Location: *Patient Specific* LV Lead placement

Need to "personalize" LV final site How to determine "best"

LV site

- Site of latest electrical activation Guided by QLV, Electrical
  - mapping
- Site of latest mechanical activation
  - Guided by hemodynamic data
  - Guided by imaging (ICE/3 D Echo/Tissue speckle tracking, MRI, CT scan, SPECT Nuclear)

How to arrive at "best" LV site

- Transvenous vs Epicardial vs Endocardial

LV Pacing and Location

Non-apical LV lead location better than apical

Target the site of maximal electrical delay: QLV >95 ms,
Body surface mapping

Target the site of maximal mechanical delay: Tissue speckle tracking (TARGET Trial), Cardiac MRI, SPECT (Guide-CRT)

Quadripolar LV leads better than bipolar leads

Multisite (MPP) LV lead pacing maybe better than single site

LV endocardial pacing maybe better than epicardial pacing

Imaging

Targeted Left Ventricular Lead Placement to Guide Cardiac Resynchronization Therapy

The TARGET Study: A Randomized, Controlled Trial

Fakhar Z. Khan, MA,* Mumohan S. Virdee, MD,* Christopher R. Palmer, PHD,† Peter J. Pugh, MD,‡
Denis O'Halloran, BCH,‡ Maros Elsik, PHD,* Philip A. Read, MD,* David Begley, MD,*
Simon P. Fynn, MD,* David P. Dutka, DM‡

Cambridge, United Kingdom

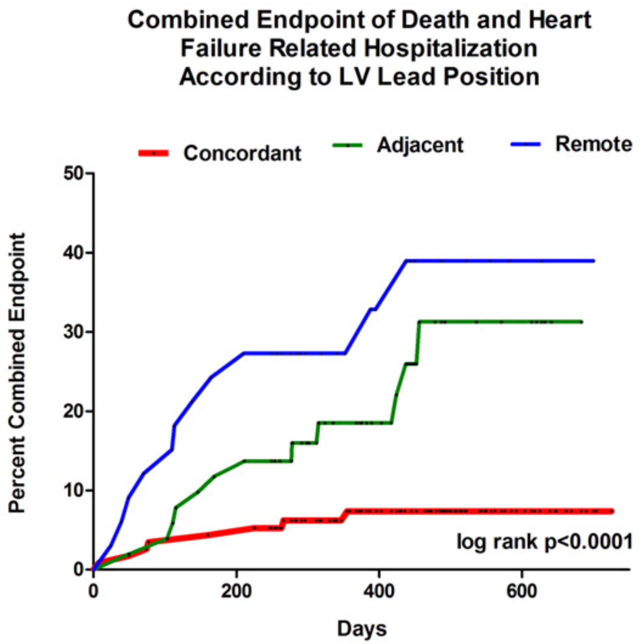
Objectives This study sought to assess the … resynchronization therapy (CRT)

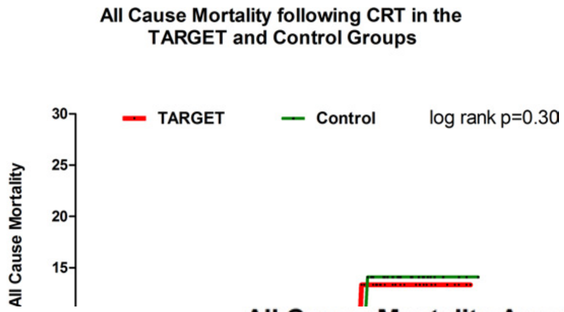
Background Placement of the LV lead to the la… conducted a randomized, controlle…

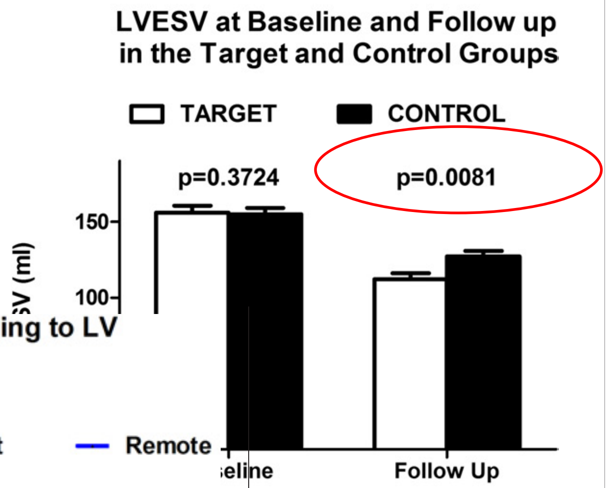
Methods A total of 220 patients schedul… radial strain imaging and were … Lead Placement to Guide Cardi… peak contraction with an ampli… went standard unguided CRT. P… concordant (at optimal site), ad… was a ≥15% reduction in LV en… improvement in New York Hear… tality and heart failure–related …

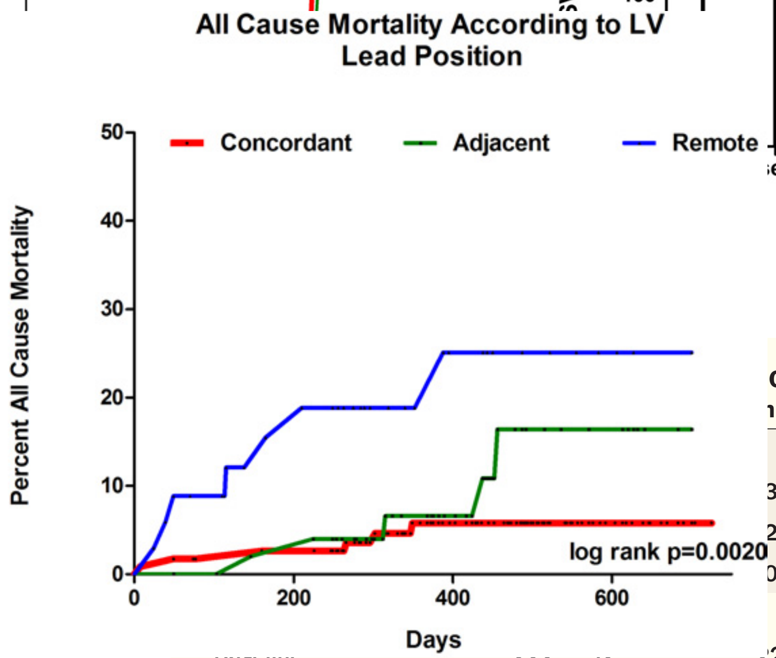
Results The groups were balanced at ra… at 6 months (70% vs. 55%, p = … fidence interval: 2% to 28%). Co… 65%, p = 0.003) and lower rates of the combined endpoint (log-rank test, p = 0.031).

Conclusions Compared with standard CRT treatment, the use of speckle-tracking echocardiography to the target LV lead placement yields significantly improved response and clinical status and lower rates of combined death and heart failure–related hospitalization. (Targeted Left Ventricular Lead Placement to Guide Cardiac Resynchronization Therapy [TARGET] study); ISRCTN19717943) (J Am Coll Cardiol 2012;59:1509–18) © 2012 by the









		Control (n = 104)	p Value
		3.1 ± 0.3	
		2.3 ± 0.7	
		0.8 ± 0.7	0.002
Baseline		229 ± 95	
Follow-up	282 ± 101	268 ± 112	
Change	61 ± 76	38 ± 76	0.011
MLHFQ			
Baseline	55 ± 21	53 ± 20	
Follow-up	33 ± 21	38 ± 22	
Change	−22 ± 20	−16 ± 19	0.024

Khan FZ et al. J Am Coll Cardiol 2012;59:1509–18

Influence of Pacing Site Characteristics on Response to Cardiac Resynchronization Therapy

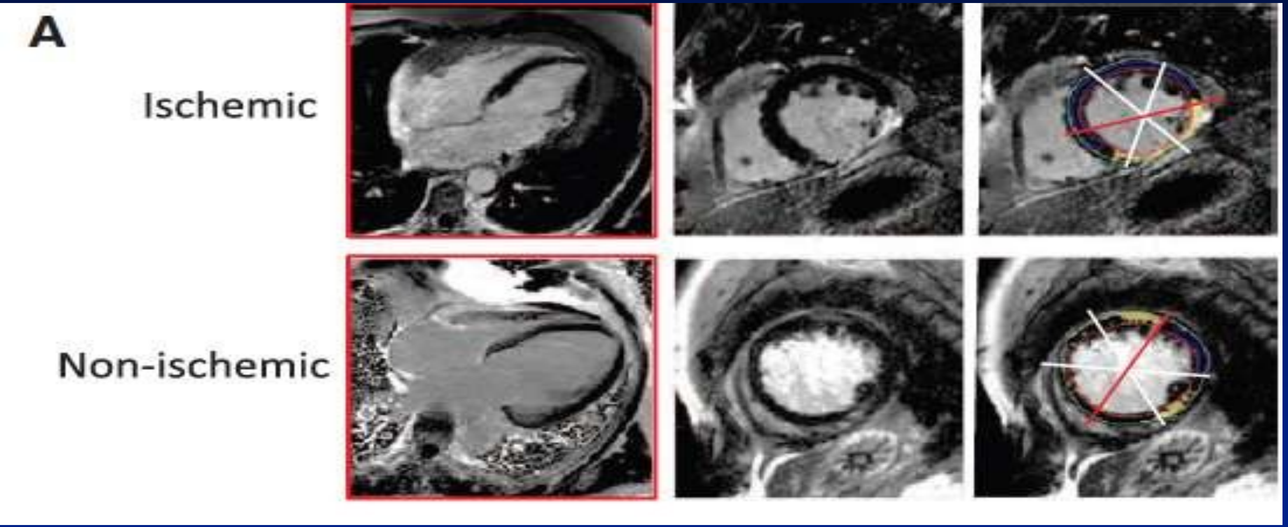
Jorge A. Wong, MD; Raymond Yee, MD; John Stirrat, BMSc; David Scholl, BSc; Andrew D. Krahn, MD; Lorne J. Gula, MD, MSc; Allan C. Skanes, MD; Peter Leong-Sit, MD; George J. Klein, MD; David McCarty, MB BCh; Nowell Fine, MD; Aashish Goela, MD; Ali Islam, MD; Terry Thompson, PhD; Maria Drangova, PhD; James A. White, MD

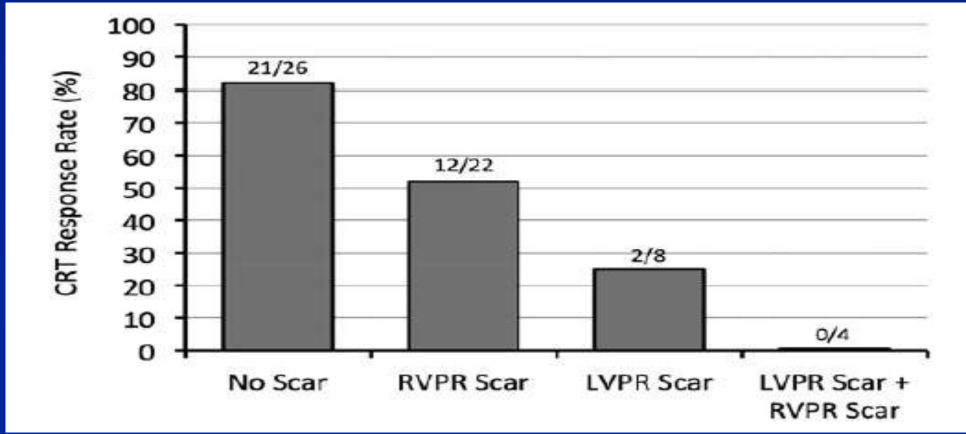
(*Circ Cardiovasc Imaging*. 2013;6:542-550.

Evaluated scar (RV/LV) distribution in 60 CRT pts using LGE-MRI/cardiac CT scan

Assessed CRT response at 6M by echo (reduction of LVESV >15%)

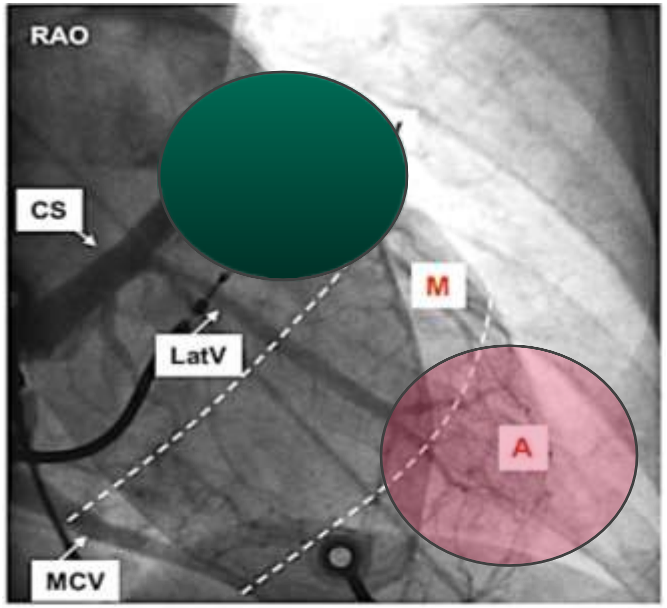
Significant scar
13% LV pacing regions
37% RV pacing regions





Non-Apical LV Lead Location Better

Apical placement may enhance lead stability but is associated with worse outcomes (MADIT-CRT) [1,2]



Distal LV lead placement: 1.64 increased risk of death or HF hospitalization & a 2.6 increased risk of mortality

1. Singh, J.P. et al. Circulation 2011 Mar 22;123(11):1159-66.
2. Merchant, F.M. et al. Heart Rhythm 2010;7:639 – 644

Positioning of Left Ventricular Pacing Lead Guided by Intracardiac Echocardiography with Vector Velocity Imaging During Cardiac Resynchronization Therapy Procedure

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From the *Texas Cardiac Arrhythmia Institute at St. David's Medical Center, Austin, Texas, USA; †Electrophysiology Division, Central Baptist Hospital, Lexington, Kentucky, USA; ‡UOC Cardiologia, Policlinico Casilino ASL/RMB, Rome, Italy; §Division of Cardiovascular Medicine, Gill Heart Institute, University of Kentucky, Lexington, Kentucky, USA; ‖Department of Internal Medicine, Tong-Ji Hospital, Tong-Ji Medical College, Huazhong University of Science and Technology, Wuhan, China; ¶Department of Cardiology, University of Foggia, Foggia, Italy; #Division of Cardiology, Stanford University, Palo Alto, California, USA; ††Department of Biomedical Engineering, University of Texas, Austin, Texas, USA; ‡‡School of Medicine, Case Western Reserve University, Cleveland, Ohio, USA

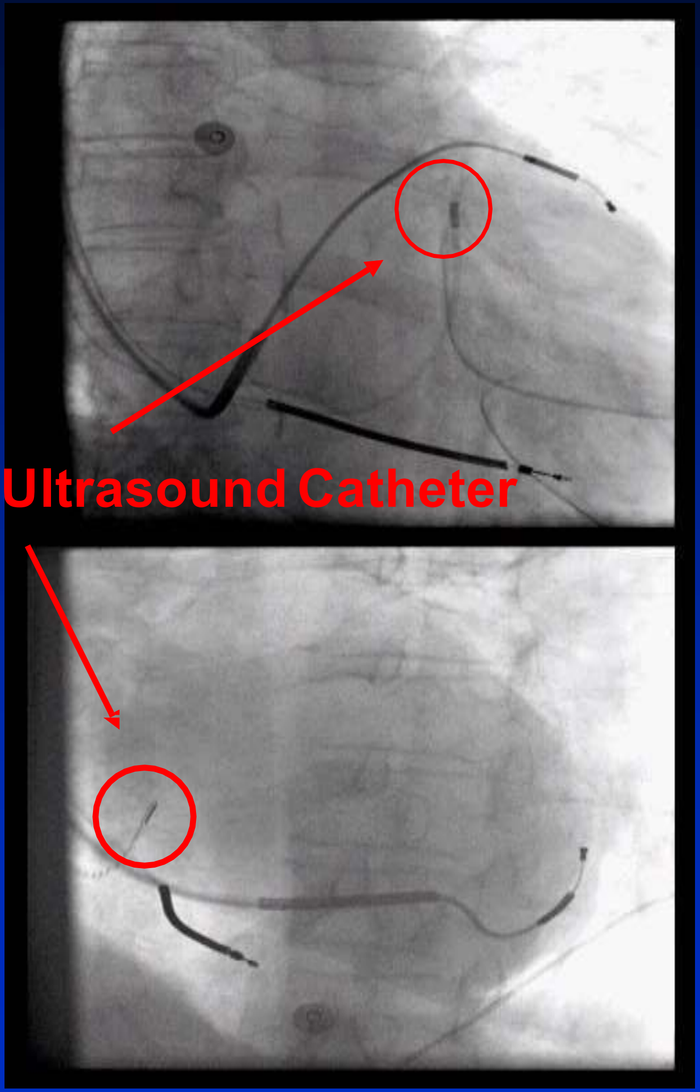
LV Lead Positioning Guided by ICE With Vector Velocity Imaging. ***Introduction*: Intra-operative modality for "real-time" left ventricular (LV) dyssynchrony quantification and optimal resynchronization is not established. This study determined the feasibility, safety, and efficacy of intracardiac echocardiography (ICE), coupled with vector velocity imaging (VVI), to evaluate LV dyssynchrony and to guide LV lead placement at the time of cardiac resynchronization therapy (CRT) implant.**

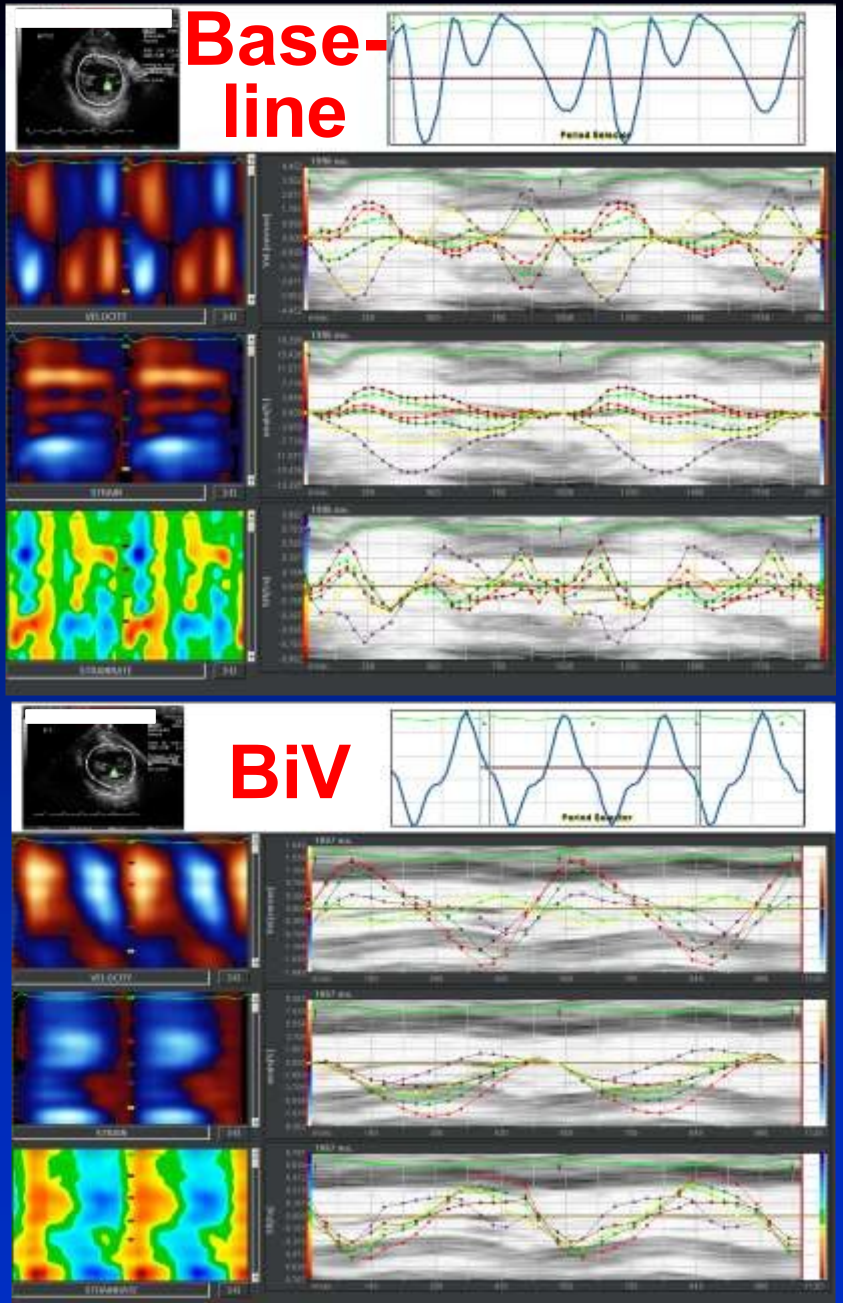
***Methods*: One hundred and four consecutive heart failure patients undergoing ICE-guided (Group 1, N = 50) or conventional (Group 2, N = 54) CRT implant were included in the study. For Group 1 patients, LV dyssynchrony and resynchronization were evaluated by VVI including visual algorithms and the maximum differences in time-to-peak (MD-TTP) radial strain. Based on the findings, the final LV lead site was determined and optimal resynchronization was achieved. CRT responders were defined using standard criteria 6 months after implantation.**

***Results*: Both groups underwent CRT implant with no complications. In Group 1, intraprocedural optimal resynchronization by VVI including visual algorithms and MD-TTP was a predictor discriminating CRT response with a sensitivity of 95% and specificity of 89%. Use of ICE/VVI increased number of and predicted CRT responders (82% in Group 1 vs 63% in Group 2; OR = 2.68, 95% CI 1.08–6.65, P = 0.03).**

***Conclusion*: ICE can be safely performed during CRT implantation. "Real-time" VVI appears to be helpful in determining the final LV lead position and pacing mode that allow better intraprocedural resynchronization. VVI-optimized acute resynchronization predicts CRT response and this approach is associated with higher number of CRT responders.** *(J Cardiovasc Electrophysiol, Vol. 22, pp. 1034-1041, September 2011)*

Intracardiac ultrasound guided LV lead implant





Positioning of left ventricular pacing lead guided by intracardiac echocardiography with vector velocity imaging during cardi ac resynchronization therapy procedure. Bai R, et al. J Cardiovasc Electrophysiol. 2011 Sep;22(9):1034-41

Multimodality imaging-guided left ventricular lead placement in cardiac resynchronization therapy: a randomized controlled trial

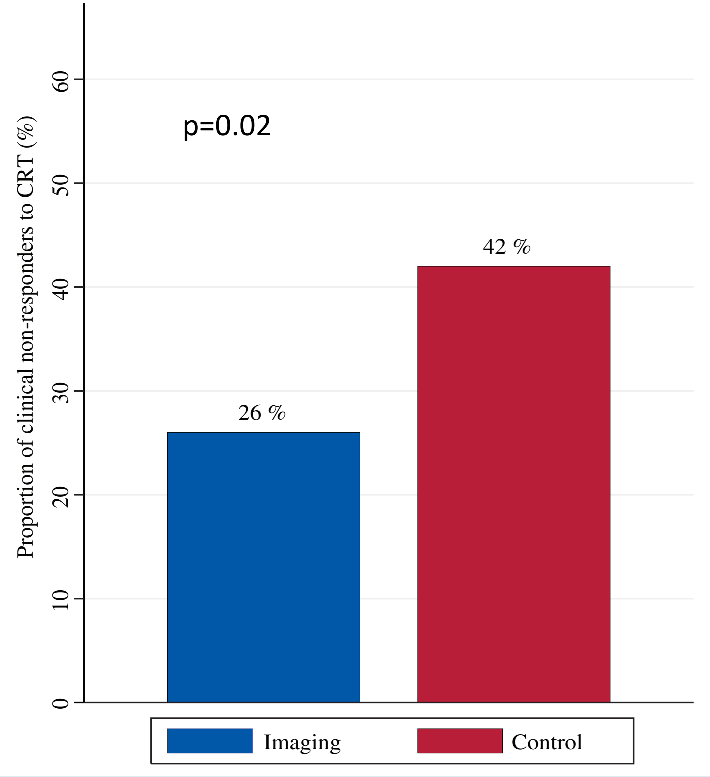
Anders Sommer[1]*, Mads Brix Kronborg[1], Bjarne Linde Nørgaard[1], Steen Hvitfeldt Poulsen[1], Kirsten Bouchelouche[2], Morten Böttcher[3], Henrik Kjærulf Jensen[1], Jesper Mø... des[1], ... Mortense

Aim

Methods and results

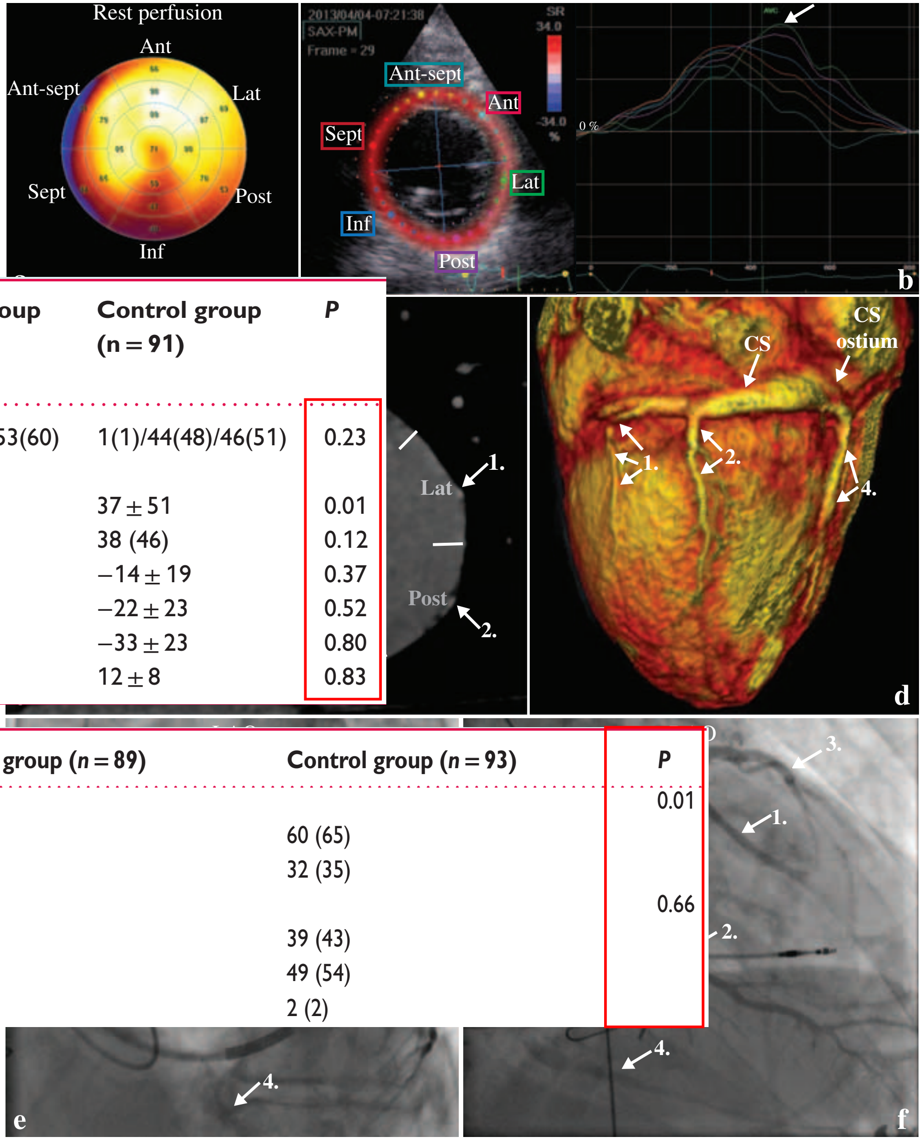
no improvement in New York Heart Association class

Conclusions



	Imaging group (n = 88)	Control group (n = 91)	*P*
NYHA class: worse/unchanged/ improved	0(0)/35(40)/53(60)	1(1)/44(48)/46(51)	0.23
6MWT:			
Change, m	65 ± 73	37 ± 51	0.01
>10 % increase	44 (59)	38 (46)	0.12
MLHFQ change	−16 ± 18	−14 ± 19	0.37
LV EDV: relative change, %	−24 ± 20	−22 ± 23	0.52
LV ESV: relative change, %	−34 ± 23	−33 ± 23	0.80
LV EF: absolute increase, %	12 ± 9	12 ± 8	0.83

	Imaging group (*n* = 89)	Control group (*n* = 93)	*P*
Relationship of LV lead to optimal CS branch			0.01
1. priority	74 (83)	60 (65)	
2. or 3. priority	15 (17)	32 (35)	
Relationship of LV lead to optimal pacing site			0.66
Concordant	43 (49)	39 (43)	
Adjacent	44 (50)	49 (54)	
Remote	1 (1)	2 (2)	

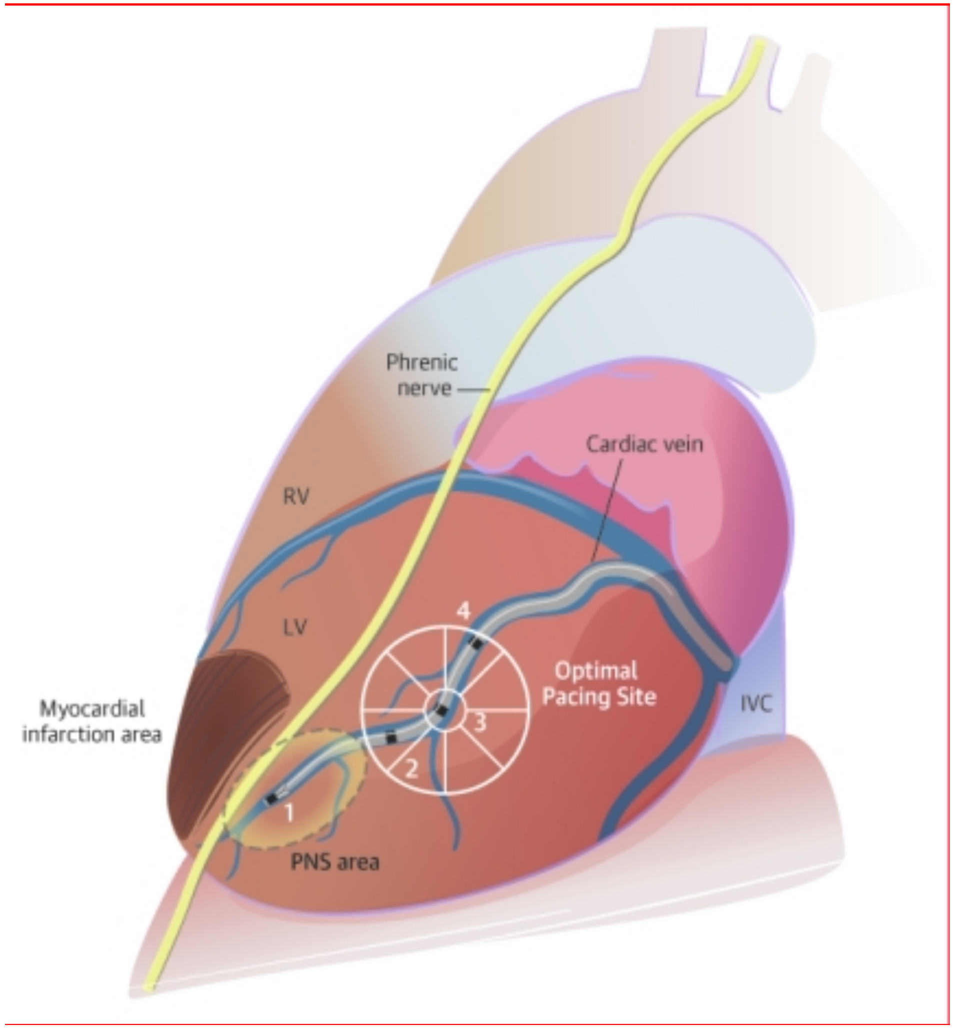


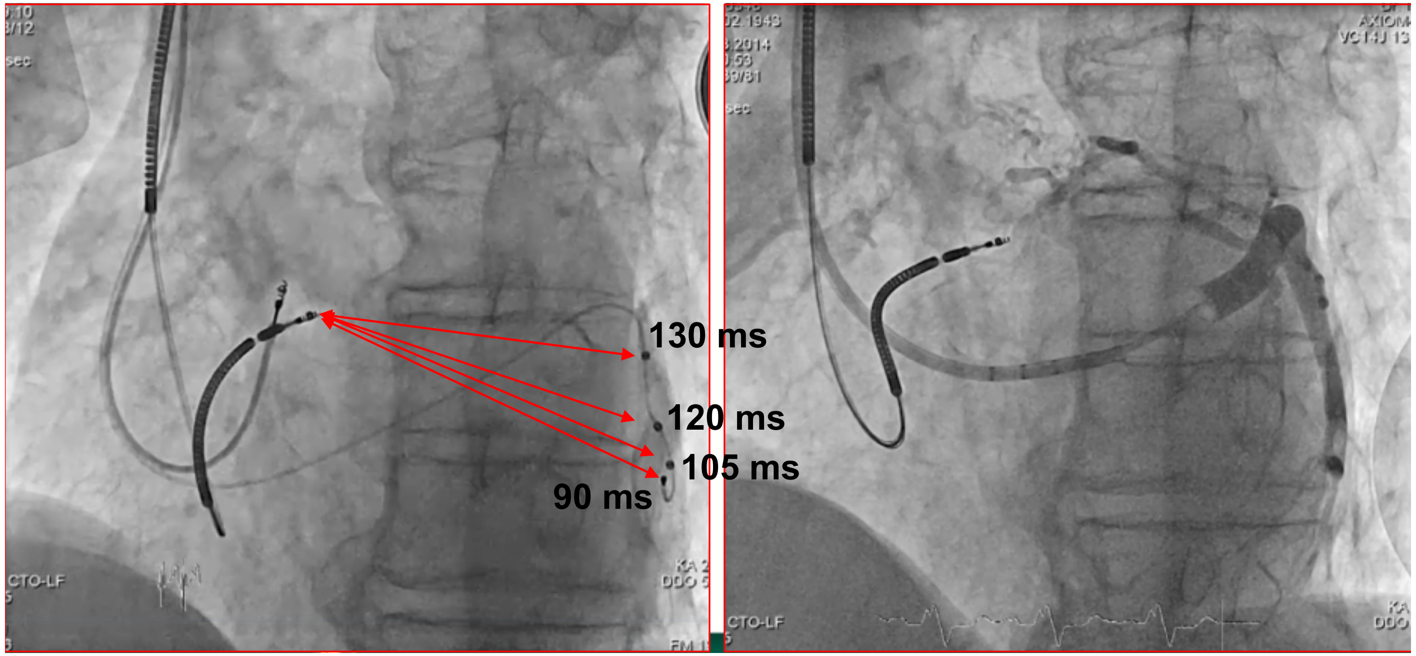
Sommer A et al. Eur J Heart Fail. 2016 Nov;18(11):1365-1374

Multipoint pacing

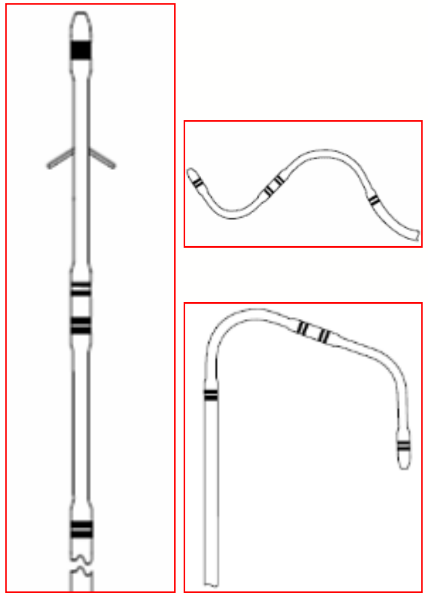
LV lead

- multipoint stimulation -

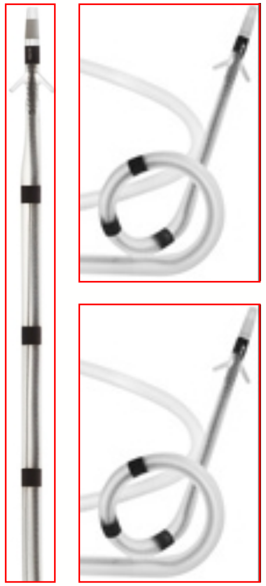




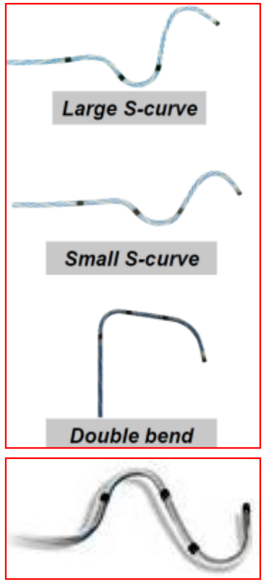
Biotronik Sentus



Medtronic Attain Performa



Boston-Scientific Acuity X4



SJM Quartet

Acute echocardiographic optimization of multiple stimulation configurations of cardiac resynchronization therapy through quadripolar left ventricular pacing: A tailored approach

Leonardo Calò, MD, FESC, Annamaria Martino, MD, Ermenegildo de Ruvo, MD, Monia Minati, MD, Simona Fratini, MD, PhD, Marco Rebecchi, MD, Chiara Lanzillo, MD, PhD, Alessandro Fagagnini, MD, Alessio Borrelli, MD, Lucia De Luca, MD, PhD, and Luigi Sciarra *Rome, Italy*

Background Cardiac resynchronization therapy (CRT) is ineffective in approximately 30% of recipients, in part due to sub-optimal left ventricular (LV) pacing location. The Quartet LV lead, with 2 additional electrodes proximal to conventional bipolar lead electrodes, enables 10 different pacing configurations at four independent LV locations. In a CRT patient cohort, we sought to evaluate the spectrum of echocardiographic and electrocardiographic response over these 10 configurations, to select the optimal one in each patient. Moreover, we sought to evaluate the 6-months clinical and echocardiographic response to a "tailored approach" in which the optimal LV pacing configuration for CRT was determined by echocardiographic measures, QRSd and pacing capture thresholds.

Methods Twenty-two consecutive CRT indicated patients were implanted with a quadripolar CRT system (St. Jude Medical). Optimal LV pacing configuration was determined by echocardiographic measures, including velocity time integral (VTI), myocardial performance index (MPI) and mitral regurgitation (MR), and an electrocardiographic measure (QRS duration) during pacing from each of the configurations at pre-discharge. The optimal LV pacing vector was chosen for every patient. Clinical and echocardiographic assessment was repeated after 6 months.

Results Various configurations provided different VTI, MPI, MR and QRSd values. Conventional bipolar vectors (ie, D1-M2, D1-RVc, M2-RVc) were rarely associated with the best echocardiographic improvements and provided significantly worse VTI, MR, MPI, and QRSd values than the best configuration for every patient ($P = .005$, $P = .05$ and $P = .03$ for VTI; $P = .01$, $P = .005$ and $P = .001$ for MPI; $P = .003$, $P = .01$ and $P = .005$ for MR, $P > .5$, $P = .01$ and $P = .05$ for QRSd) Conversely, "unconventional" proximal configurations (ie, making use of P4 and M3 electrodes) were generally characterized by higher acute VTI, MR and MPI improvements. CRT devices were reprogrammed with an "unconventional" LV pacing configuration in 50% of patients. A significant improvement in New York Heart Association class (81%), LV ejection fraction (76%), end-diastolic and end-systolic volumes was observed after 6 months ($P = .02$, $P < .001$, $P = .02$ and $P = .003$, respectively).

Conclusions In this study, conventional bipolar vectors of quadripolar-CRT were rarely associated with the best echocardiographic improvements. Quadripolar CRT utilizing optimal LV pacing configuration was associated with a significant improvement in New York Heart Association class and LV ejection fraction after 6 months. (Am Heart J 2014;0:1-9.)

A Meta-Analysis Of Quadripolar Versus Bipolar Left Ventricular Leads On Post-Procedural Outcomes

Mohit K. Turagam, MD[1], Muhammad R. Afzal, MD[2], Sandia Iskander, MD[2], Madhu Reddy, MD[2], Luigi Di Biase, MD[3], Andrea Natale, MD[4], Dhanunjaya Lakkireddy, MD, FHRS[2]

Abstract

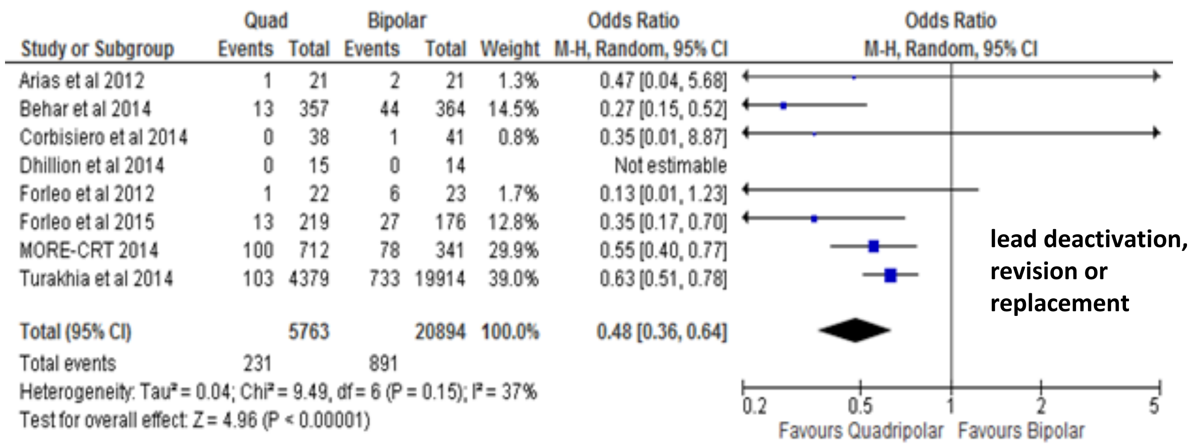
Objective: We aimed to perform a meta-analysis from eligible studies to analyze the true impact of QL when compared with BL with regard to post-procedural outcomes including lead deactivation, revision or replacement.

Background: Many observational and retrospective studies showed that quadripolar left ventricular leads (QL) are associated with better outcomes and fewer complications when compared with bipolar leads (BL).

Methods: We performed a comprehensive literature search through June 30, 2015 using: quadripolar, bipolar, left ventricular lead and CRT in Pubmed, Ebsco and google scholar databases.

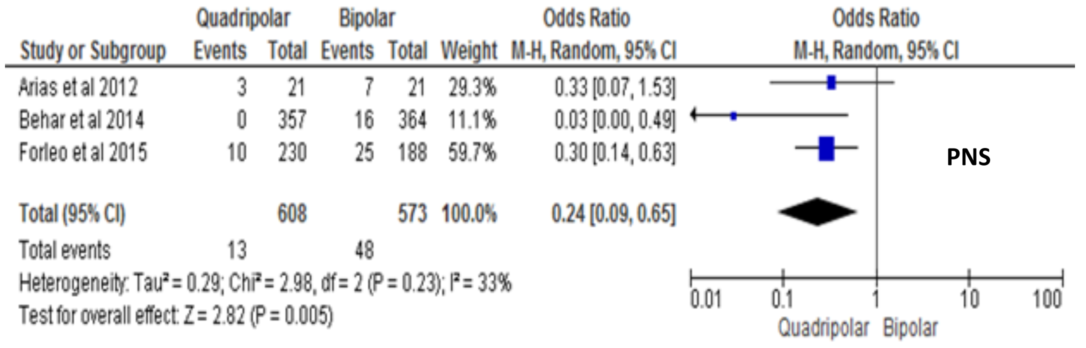
Results: The analysis included 8 studies comparing QL and BL implantation. Post-procedural outcomes such as lead deactivation, revision or replacement were used as primary outcome and assessed with Mantel–Haenszel risk ratio (RR). Secondary outcomes included total fluoroscopy/procedure time, occurrence of phrenic nerve stimulation (PNS) and all-cause mortality on follow up. Follow-up duration for the studies ranged from 3 to 60 months. Compared with BL, the use of QL is associated with 52 % reduction (relative risk 0.48; 95% CI: 0.36-0.64, p=0.00001) in the risk of deactivation, revision or replacement of the LV lead. QL had significantly lower fluoroscopy/procedure time, PNS and all-cause mortality when compared with BL.

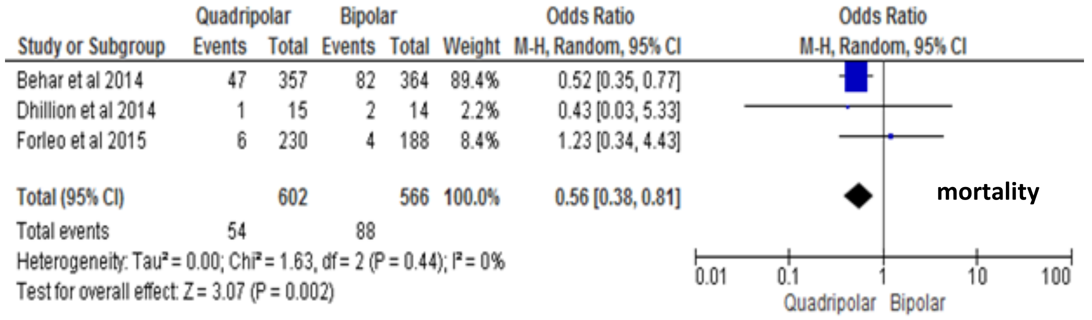
Conclusion: Our meta-analysis shows that QL implantation was associated with decreased risk of LV lead deactivation, revision or replacement when compared with BL.



Cost-Effectiveness Analysis of Quadripolar Versus Bipolar Left Ventricular Leads for Cardiac Resynchronization Defibrillator Therapy in a Large, Multicenter UK Registry

	Quadripolar (n = 319)		Bipolar (n = 287)		
	n	Cost (£)	n	Cost (£)	p Value
ACS	35	115,029	21	67,544	0.13
Arrhythmia	59	51,218	65	55,557	0.23
Heart failure	51	137,695	75	195,841	0.003
System explantation and reimplantation	5	121,122	6	136,788	0.76
Generator replacement	9	142,026	19	273,276	0.03
RA/RV lead revision	27	88,918	24	69,840	0.21
LV lead revision	5	16,466	15	43,650	0.02
Total episodes/cost	191	672,474	225	842,484	<0.001

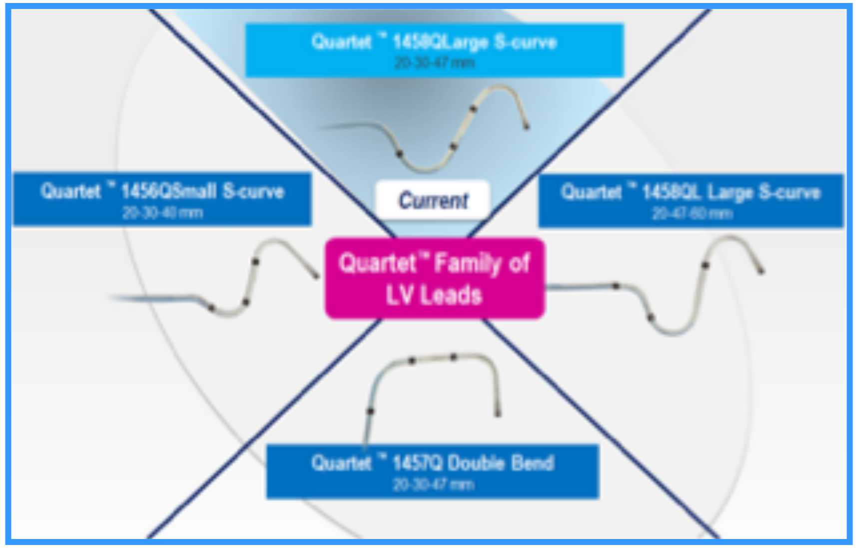




Turagam MK et al. J Atr Fibrillation. 2016 Aug-Sep; 9(2): 1472
Behar JM et al. JACC Clin Electrophysiol. 2017 Feb;3(2):107-116

Elettrocatetere Quadripolare sinistro

- Tutte le aziende hanno un elettrocatetere sx quadripolare



+10
anni di esperienza

+100
pubblicazioni

+100K
impianti nel mondo

41% **RIDUZIONE DEL RISCHIO RELATIVO** rispetto ai sistemi CRT bipolari.[1]

18%

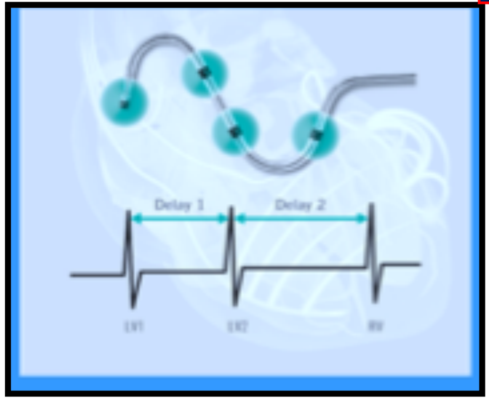
18% **RIDUZIONE RELATIVA DELLA MORTALITÀ PER QUALSIASI CAUSA** a 18 mesi rispetto ai sistemi di CRT bipolari.[2]

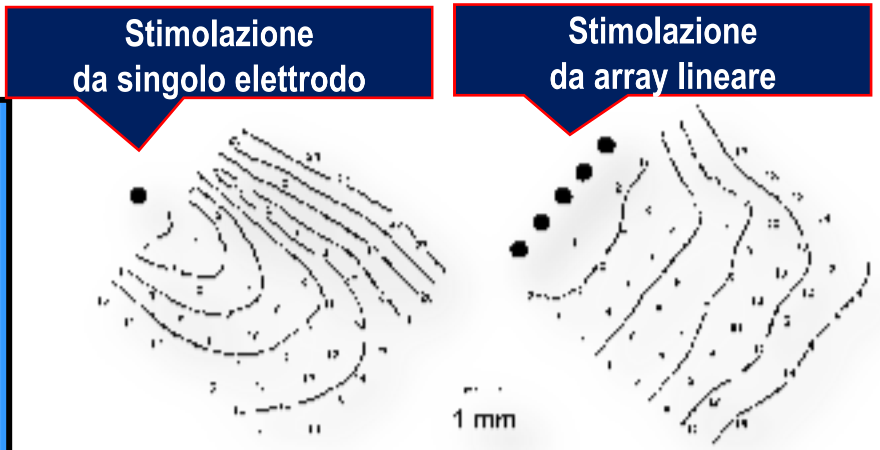
87% **IN MENO SUI COSTI DI RICOVERO** nei primi 100 giorni dopo l'impianto.[3]

1. Boriani et al., Cardiac resynchronization therapy with a novel quadripolar lead decreases complications at six months: preliminary results of the MORE-CRT trial, ESC 2014, FP# 887.
2. Turakhia M, et al. Reduced Mortality with Quadripolar Versus Bipolar Left Ventricular Leads in Cardiac Resynchronization Therapy. PO01-51. HRS 2014. Dati di analisi retrospettiva.
3. Corbisiero R, et al. Reduced Costs Post CRT with Quadripolar LV leads compared to Bipolar LV leads. 2014 PO01-195. HRS 2014. San Francisco, California. 7-10 maggio 2014.

MultiPoint Pacing:

Razionale





I numeri rappresentatno i tempi di attivazione in ms relativi al punto più precoce

Resultati:

- Mappe ottiche di attivazione ottenute con laser scanning
- Dimostrano che la stimolazione da singolo elettrodo genera un fronte d'onda più ellittico, mentre la stimolazione da array lineare genera un fronte d'onda più piatto
- La maggior curvatura del fronte d'onda più ellittico provoca una minor velocità di conduzione del **13,3%**.

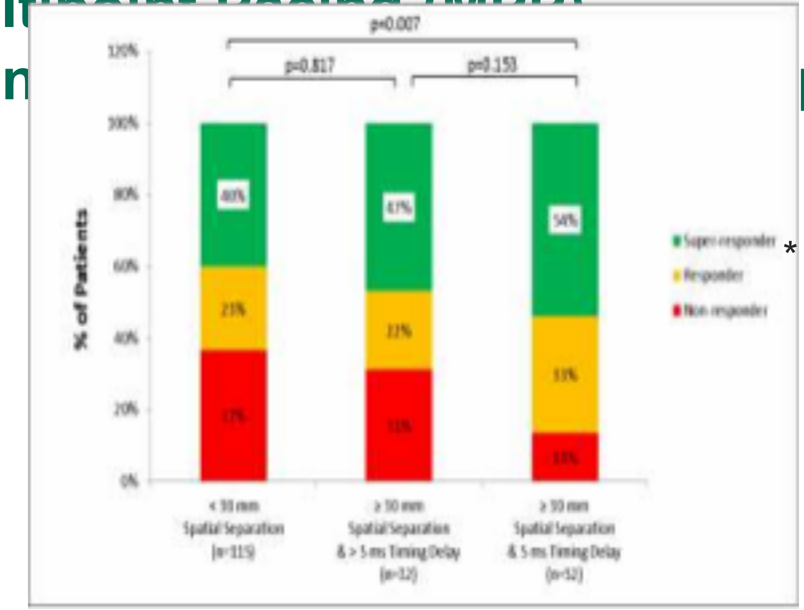
Fast et al., Cardiovascular Research 1997; 33: 258–271

Mult... (MPP)
Convert Non-respon... ponder?

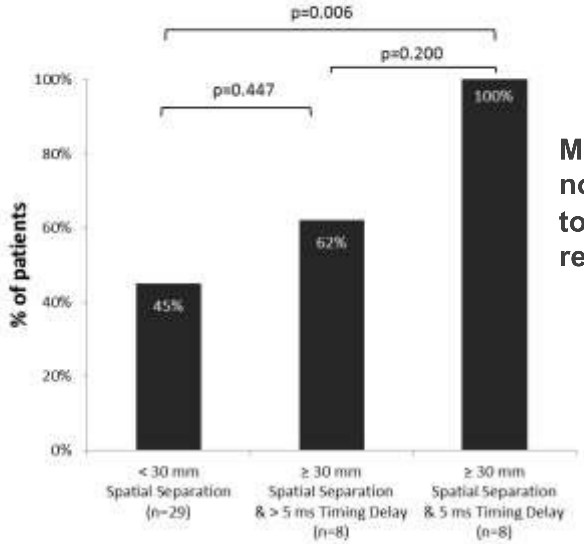
Poor CRT response due to significant number of factors with complex interactions

MPP:

- Decreased LV total activation by ~50%
- Reduced TDI measured dyssynchrony
- Improved LV ESV, LV EF, and pressure volume loops
- In USA IDE Trial
  - Converted non-responders to responders
  - Increased both super-responder & responder rates



*



MPP: 3-Month non-responder to 9-Month responder rate

Menardi E, et al. Heart Rhythm 2015; 12(8):1762-9
Rinaldi CA, et al. J Card Fail. 2013; 19(11):731-8
Pappone C, et al. Heart Rhythm 2014; 11(3):394-401
Tomassoni F, et al. LBCT Abstract HRS 2016

Stimolazione Multisito

MultiPoint Pacing:

Evidenze Cliniche

Autore	# Pazienti	Metodo	Risultati	Pubblicazione
Thibault et al.	19 (21)	Misurazione in acuto del dp/dt	Miglioramento del dp/dt nel 72% dei pazienti	Europace, 2013
Rinaldi et al.	41 (52)	Misurazione in acuto della dissincronia (TDI)	Riduzione della dissincronia nel 64% dei pazienti	Journal of Cardiac Failure, 2013
Rinaldi et al.	41 (52)	Misurazione in acuto della dissincronia (TDI)	Riduzione della dissincronia nel 64% dei pazienti. Incremento del VTI LVOT (valutato in 13 pazienti)	J Interv Card Electrophysiol, 2014
Pappone et al.	44	Misurazione in acuto con P-V Loop	Miglioramento dei parametri emodinamici	Heart Rhythm, 2014
Osca et al.	27	Misurazione in acuto della dissincronia (radial strain) e di parametri emodinamici (LVEF e CI)	Riduzione della dissincronia e incremento della LVEF e del CI	Europace 2015
Zanon et al.	29	Misurazione in acuto del dp/dt	Miglioramento del dp/dt nel 90% dei pazienti	Heart Rhythm, 2015
Menardi et al.	10	Misurazione in acuto del dp/dt; misurazione del tempo di attivazione endocardico	20% di incremento relativo del dp/dt; 15% di riduzione relativa del tempo totale di attivazione	Heart Rhythm, 2015
Sohal et al.	16	Misurazione tempo di attivazione e dp/dt in acuto	Miglioramento del dp/dt e del tempo di attivazione specialmente nei pazienti non LBBB puri	Heart Rhythm, 2015
Pappone et al.	44	Misurazione echo a 12 mesi	33% di incremento del numero di pazienti responder	Heart Rhythm, 2015
Forleo et al.	313	Misurazione durata del QRS e frazione di eiezione LVEF	Significativa riduzione del QRS	Europace 2015
Zanon et al.	110	Valutazione ESVi, Classe NHYA e PACKER's score a 12 Mesi	Miglioramento dell' outcome clinico nel 90% dei pazienti	Heart Rhythm Journal - August 2016
Tomassoni et al.	506	Valutazione della sicurezza e dell'efficacia	Sicuro ed efficace. 87% di responder. 100% dei non responder trasformati in responder	Late Breaking Clinical Trial Session, HRS 2016

MPP

MIGLIORA L'EMODINAMICA

MIGLIORA LA MECCANICA

MIGLIORA L'ATTIVAZIONE ELETTRICA

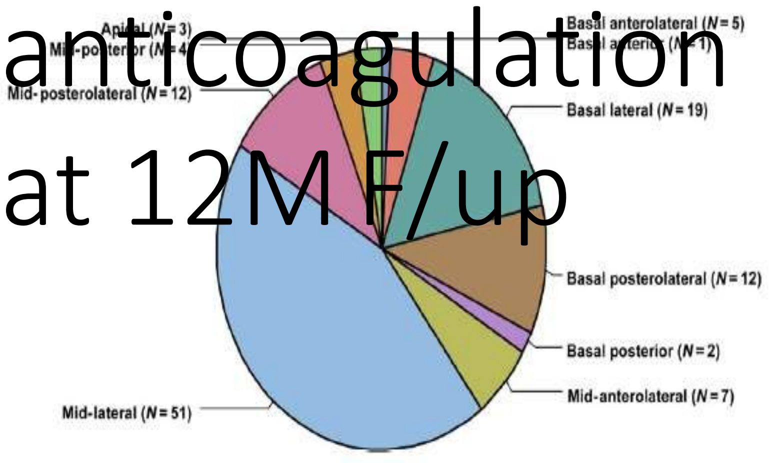
Menardi et al. Heart Rhythm 2015

Stimolazione endocardica

ALternate Site Cardiac ResYNChronization (ALSYNC): a prospective and multicentre study of left ventricular endocardial pacing for cardiac resynchronization therapy

European Heart Journal (2016) 37, 2118–2127

138 failed/non-response CRT pts) Lifelong anticoagulation Response at 12M F/up



Successful LV endocardial LV lead insertion: 89%

5 peri-procedural CVA
14 TIA's in 9 pts (86% low PT INR)
6 LV lead dislodgements

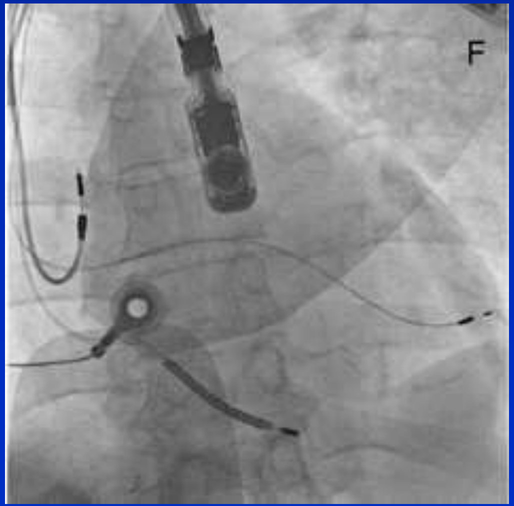


Table 3 Echocardiographic indices and clinical outcomes

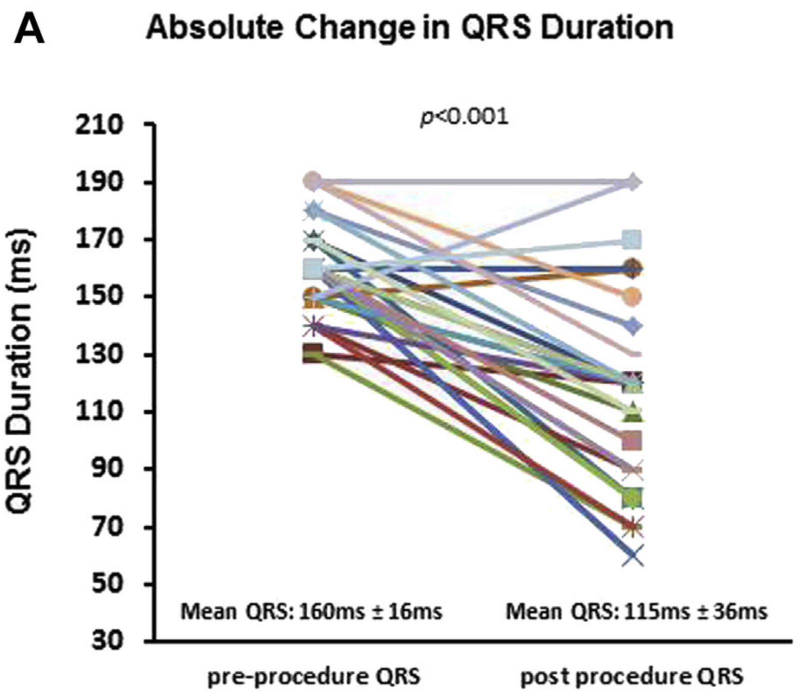
	Baseline (n = 118)	6 months (n = 105)	Change	P-value*	Response definition	Response rate for all patients (n = 118)	Response rate for non-responders with prior CRT (n = 31)
LVESV	149 ± 79 mL	121 ± 74 mL	29 ± 60 mL reduction	<0.0001	≥15% relative reduction	55%	47%
					≥30% relative reduction	33%	5%
LVEF	29 ± 10%	36 ± 12%	7 ± 10% increase	<0.0001	≥5% absolute increase	64%	61%
Mitral regurgitation	Moderate/severe: 41%	Moderate/severe: 30%		0.035	≥1 class improvement	33%	43%
NYHA class	I/II/III/IV: 3%/20%/69%/7%	I/II/III/IV: 19%/51%/28%/2%		<0.0001	≥1 class improvement	59%	52%
Six-minute walking test	332 ± 117 m	388 ± 135 m	47 ± 87 m increase	0.004	≥60 m increase	44%	42%

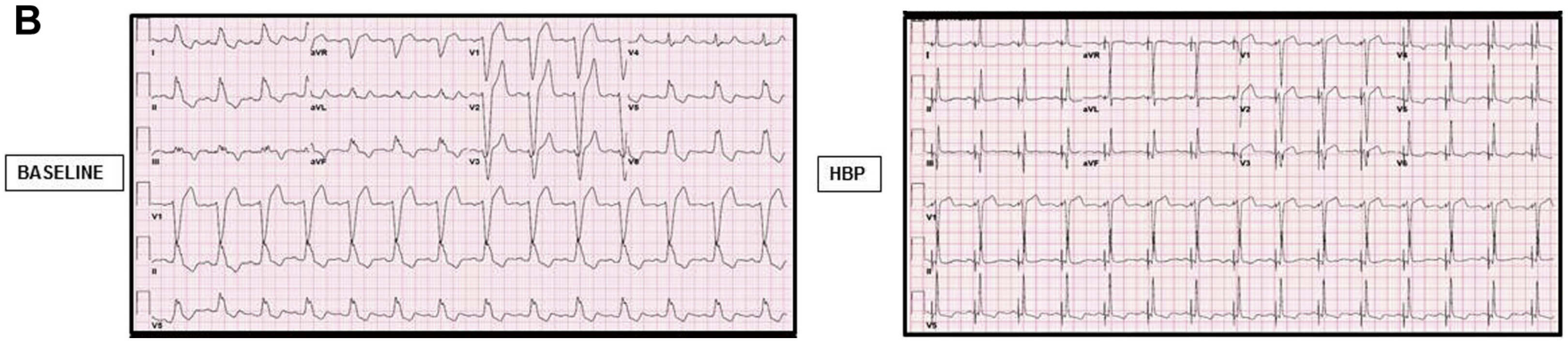
LVESV: left ventricular end-systolic volume; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; CRT: cardiac resynchronization therapy.
*P-value from repeated-measures linear or multinomial regression model.

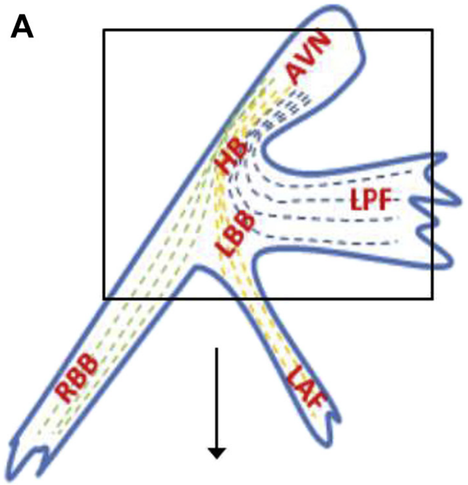
Usefulness of His Bundle Pacing to Achieve Electrical Resynchronization in Patients With Complete Left Bundle Branch Block and the Relation Between Native QRS Axis, Duration, and Normalization

Alexandra E. Teng, MD[a], Daniel L. Lustgarten, MD, PhD[b], Pugazhendhi Vijayaraman, MD[c], Roderick Tung, MD[d], Kalyanam Shivkumar, MD, PhD[a], Galen S. Wagner, MD[e], and Olujimi A. Ajijola, MD, PhD[a,*]

His Bundle pacing (HBP) restores electrical synchronization in left bundle branch block (LBBB); however, the underlying mechanisms are poorly understood. We examined the relation between native QRS axis in LBBB, a potential indicator of the site of block, and QRS normalization in patients with LBBB. Data from patients (n = 41) undergoing HBP at 3 sites were studied (68 ± 13 years, 13 women). Study criteria included strictly defined complete LBBB and successful implantation of a permanent HBP lead. Preprocedure and postprocedure electrocardiograms were reviewed independently by 2 blinded readers. QRS axis and duration were measured to the nearest 10° and 10 ms, respectively. QRS narrowing or normalization was the primary end point. Of 29 patients meeting study criteria, 9 had frontal plane QRS axes between −60° and −80°, 10 from −40° to 0°, and 10 from +1° to +90°. QRS narrowing occurred in 24 patients (83%, 44 ± 34 ms, $p < 0.05$). Percent QRS narrowing by axis were 26 ± 19%, 29 ± 25%, and 28 ± 23%, respectively. No correlation between prepacing QRS axis and postpacing narrowing was identified ($r^2 = 0.001$, p = 0.9). In patients with or without QRS normalization after HBP, mean QRS duration was 155 ± 21 vs 171 ± 8 ms, respectively, p = 0.014. HBP induces significant QRS narrowing in most patients and normalization in patients with shorter baseline QRS duration. In conclusion, the lack of correlation between native QRS axis and narrowing suggests that proximal His-Purkinje block causes most cases of LBBB, or that additional mechanisms underlie HBP efficacy. Further studies are needed to better understand how to predict those patients in whom HBP will normalize LBBB.







Teng AE et al. Am J Cardiol 2016;118:527-534.

Long-Term Results of Triventricular Versus Biventricular Pacing in Heart Failure

A Propensity-Matched Comparison

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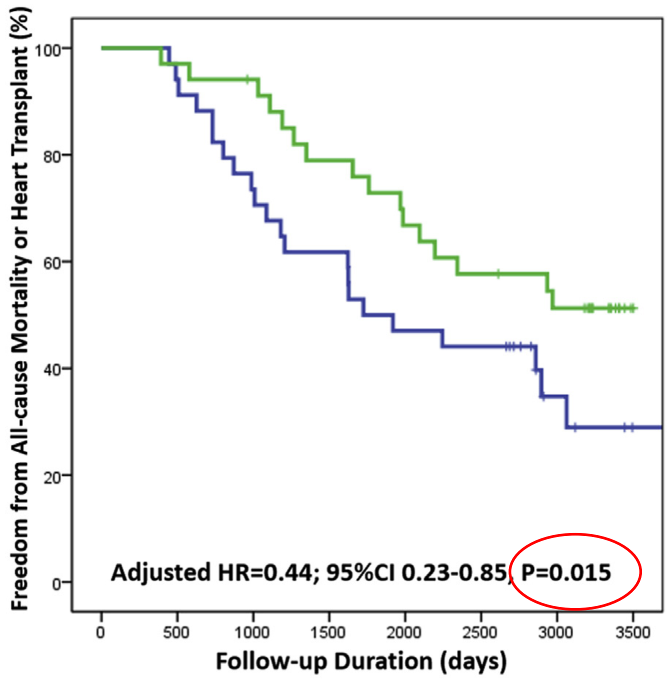
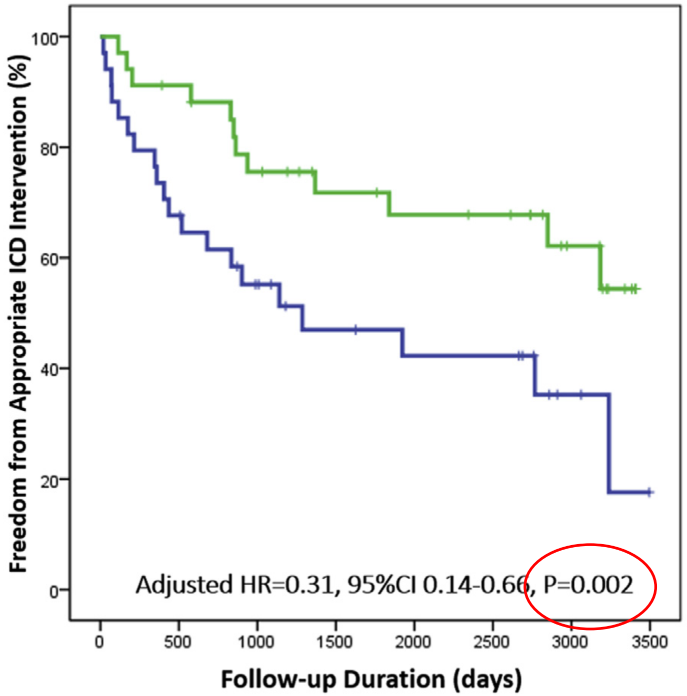
METHODS This single-center, propensity score–matched cohort study compared 34 patients with advanced heart failure who underwent implantation with Tri-V devices versus 34 control subjects treated with Bi-V pacing. Clinical outcomes during a median of 2,478 days (IQR: 1,183 to 3,214 days) were compared.

RESULTS Tri-V–treated patients compared with Bi-V–treated patients presented with a trend for shorter battery longevity (time to box change, 1,758 ± 360 days vs. 1,993 ± 408 days; p = 0.072). Incidence of lead dislodgement (Tri-V vs. Bi-V, 0.86 vs. 1.10 per 100 patient-years; p = 0.742), device-related infection (Tri-V vs. Bi-V, 1.83 vs. 1.76 per 100 patient-years; p = 0.996), and refractory phrenic nerve capture (Tri-V vs. Bi-V, 0.48 vs. 1.84 per 100 patient-years; p = 0.341) was comparable in the 2 groups. Episodes of ventricular arrhythmia requiring implantable cardioverter-defibrillator intervention occurred more frequently in the Bi-V group versus the Tri-V group (6.55 vs. 16.88 per 100 patient-years; adjusted hazard ratio: 0.31; 95% confidence interval: 0.14 to 0.66; p = 0.002). Lower all-cause mortality and heart transplant was observed in the Tri-V group compared with the Bi-V group (6.99 vs. 11.92 per 100 patient-years; adjusted hazard ratio: 0.44; 95% confidence interval: 0.23 to 0.85; p = 0.015).

CONCLUSIONS Tri-V displayed a similar safety profile compared with Bi-V and was associated with potential benefits regarding long-term survival and ventricular arrhythmia burden. (J Am Coll Cardiol EP 2016;2:825–35)

	Incidence (Per 100 Patient-Yrs)				
	Tri-V	Bi-V	Hazard Ratio	95% CI	p Value
Device-related infection	1.83 (0.71-4.60)	1.76 (0.60-5.05)	1.00	0.22-4.54	0.996
Lead failure	0.86 (0.24-3.09)	1.10 (0.30-3.91)	0.72	0.10-5.11	0.742
Lead dislodgement	1.91 (0.74-4.80)	2.03 (0.87-4.66)	0.73	0.19-2.72	0.635
Refractory phrenic nerve capture	0.48 (0.08-2.65)	1.84 (0.55-4.67)	0.33	0.04-3.20	0.341





Providencia R et al. J Am Coll Cardiol EP 2016;2:825–35

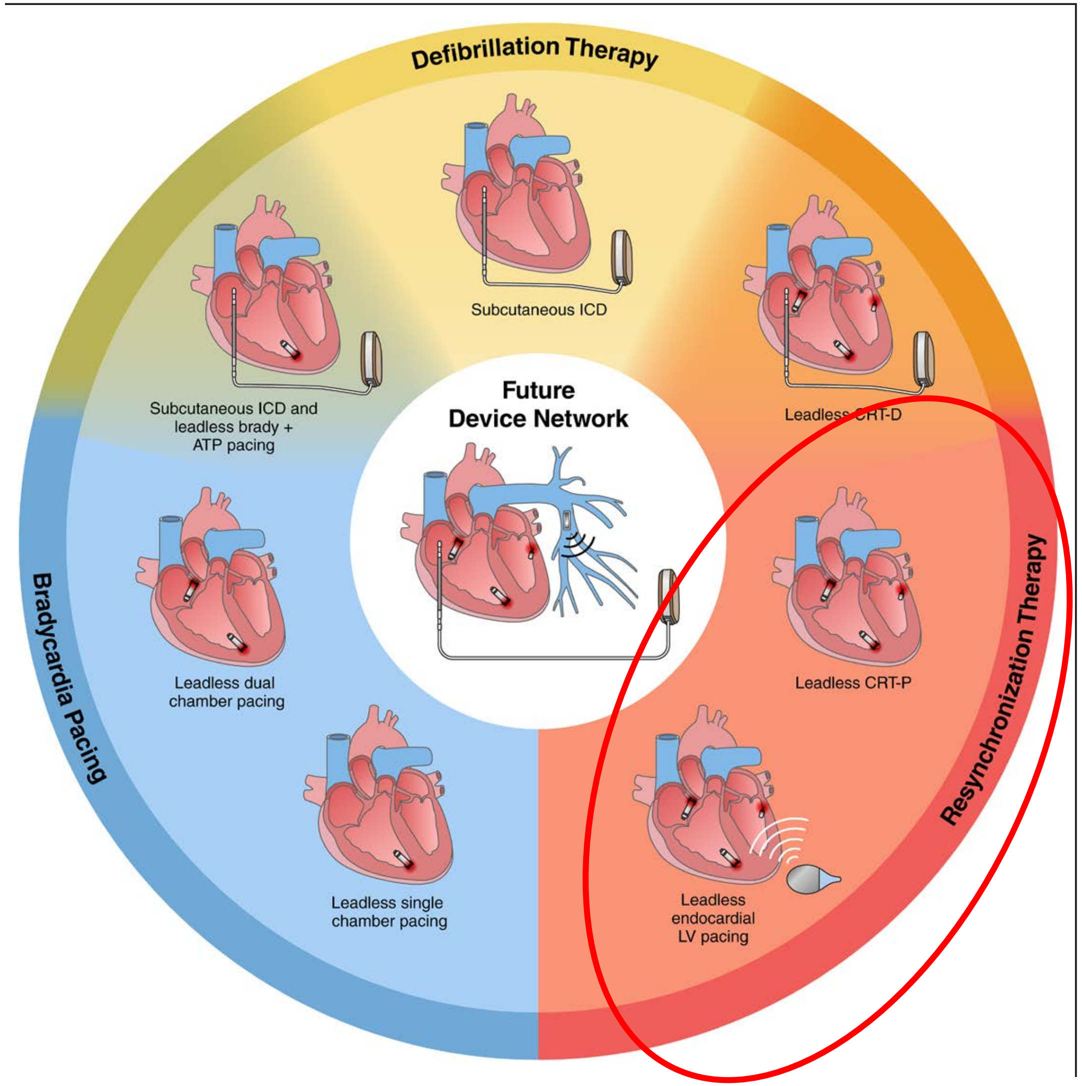
Leadless CRT

Permanent Leadless Cardiac Pacemaker Therapy

A Comprehensive Review

Although current leadless pacemakers are limited to right ventricular pacing, future advanced, communicating, multicomponent systems are expected to expand the potential benefits of leadless therapy to a larger patient population

Reddy V, Tjong FVJ – Circulation, 2017



Feasibility, safety, and short-term outcome of leadless ultrasound-based endocardial left ventricular resynchronization in heart failure patients: results of the Wireless Stimulation Endocardially for CRT (WiSE-CRT) study

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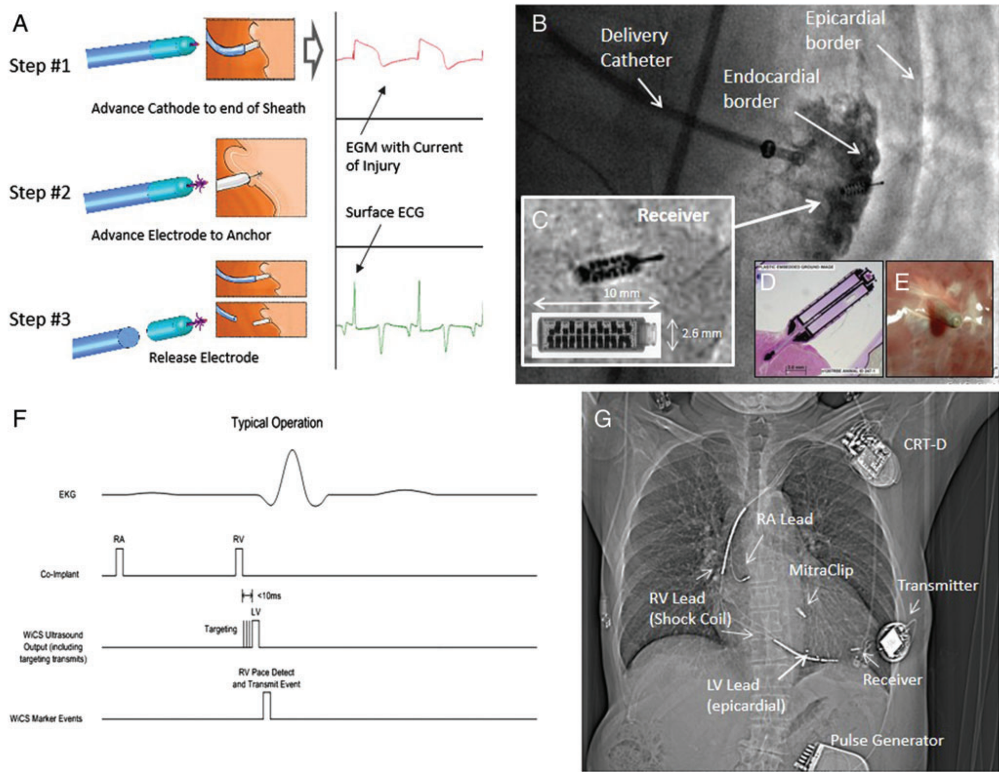
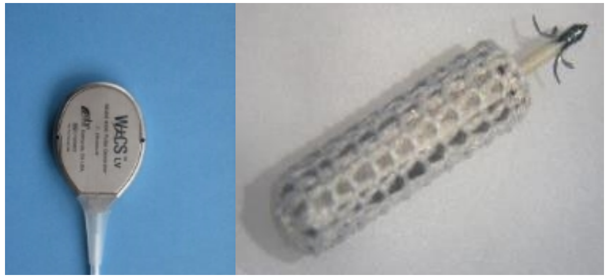
Methods and results Seventeen HF patients were enroled and categorized as: (i) patients in whom attempted coronary sinus lead implantation for CRT had failed (*n* = 7); (ii) patients with a previously implanted CRT device, not responding to CRT (*n* = 2); and (iii) patients with previously implanted pacemakers or implantable cardioverter-defibrillator and meeting the standard indications for CRT (*n* = 8). System implantation was achieved in 13 patients (76.5%); mean R-wave amplitude was 5.6 ± 3.2 mV and the mean pacing threshold was 1.6 ± 1.0 V, respectively. In one patient, no sufficient pacing thresholds were found; in three patients pericardial effusion occurred. Biventricular pacing was recorded in 83% and 92% of the patients at 1 month and 6 months, respectively. QRS duration was shorter during biventricular pacing compared with right ventricular pacing at 1 month (−41 ms; $P = 0.0002$) and 6 months (−42 ms; $P = 0.0011$), respectively. At the 6-month follow-up, two-thirds of the patients had at least one functional class change. Left ventricular ejection fraction significantly increased ($P < 0.01$) by 6 points at the 6-month follow-up.

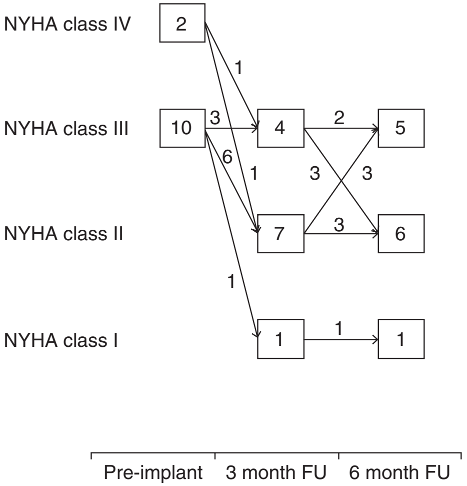
Conclusion The feasibility of providing an endocardial stimulation for CRT with a leadless technology was successfully demonstrated. Despite the promising results for a novel technology, further study is required to definitively conclude the safety and the performance of the system.

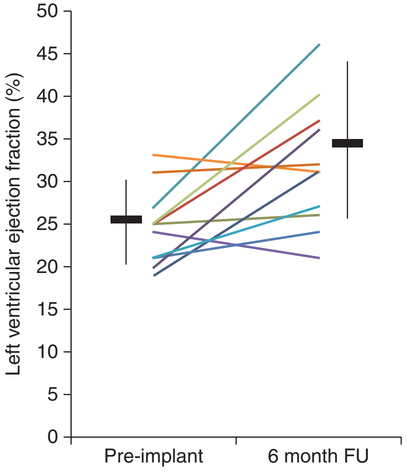




Safety

There were 19 SAE occurring within 6 months of the study procedures, most of these (12 events, 63%) were comorbidities that were neither procedure-related nor system-related. Seven of these events were adjudicated to be procedure-related in six patients (35%). As noted above, there were three peri-procedural pericardial effusion events that occurred; one patient death occurred with one of these events. One SAE occurred as a groin haematoma. In two events, a transmitter position revision was needed due to the loss of the biventricular pacing. One battery replacement was performed during one of the transmitter revisions. As noted above, one other battery replacement was needed but not performed.





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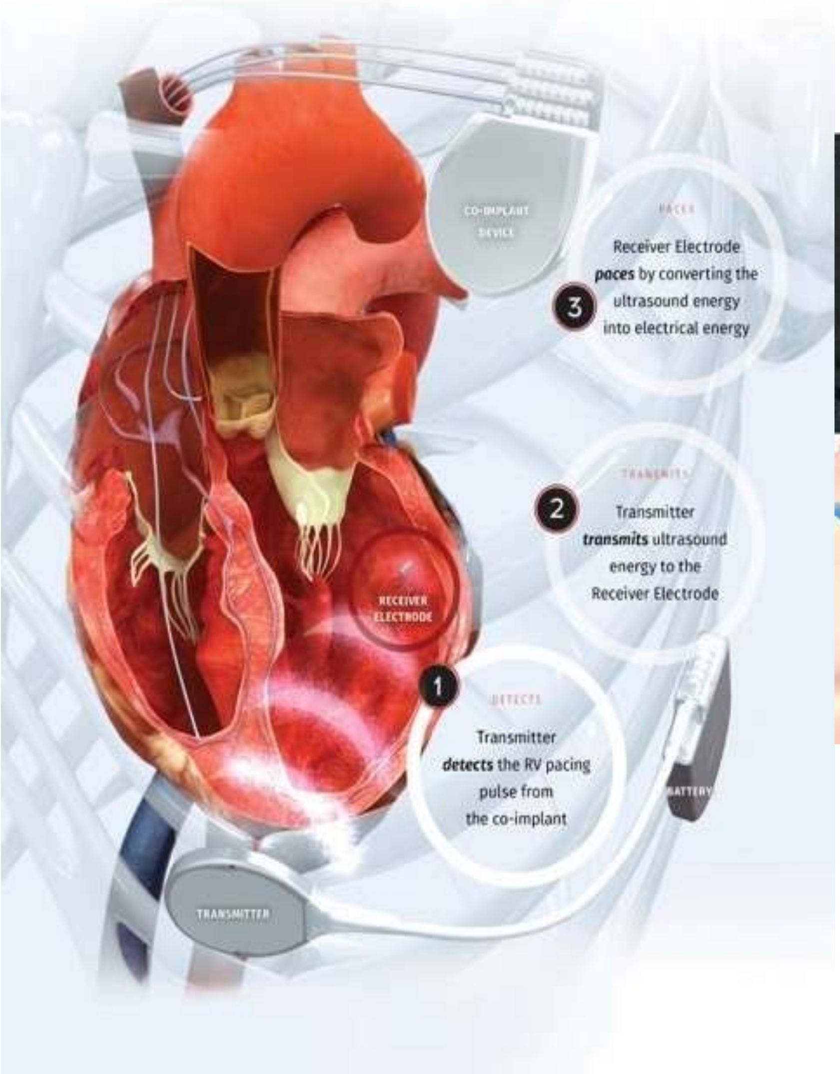
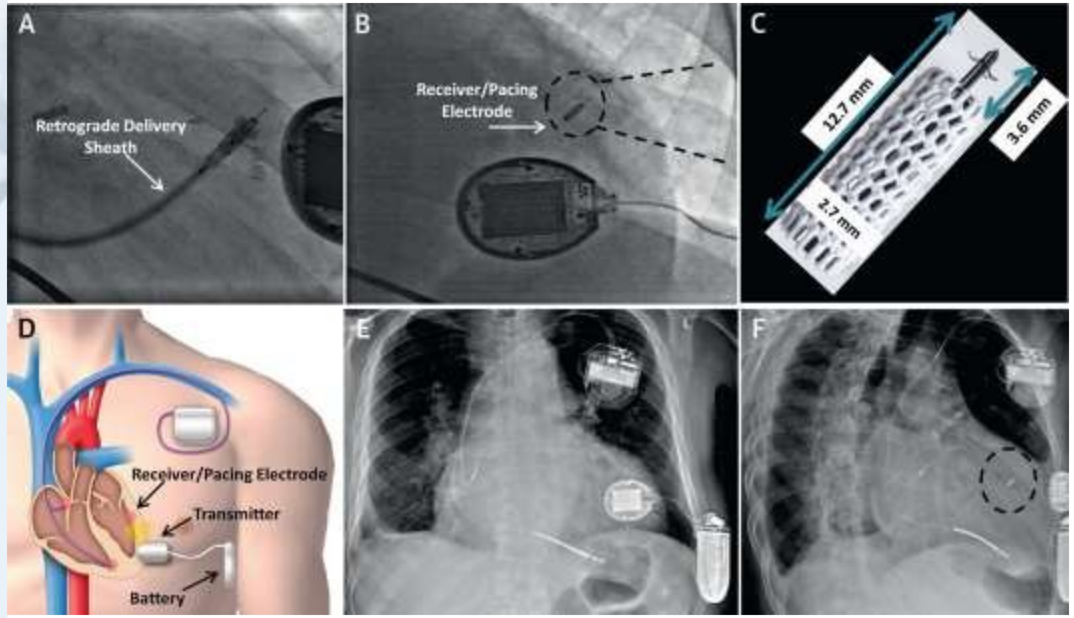


WISE (Wireless Stimulation Endocardially Technology) System



Wireless pacing by transmitting ultrasonic energy from pulse generator transmitter implanted SQ to a receiver electrode in the LV

WISE (Wireless Stimulation Endocardially Technology) System

Cardiac Resynchronization Therapy With Wireless Left Ventricular Endocardial Pacing

The SELECT-LV Study

JACC 2017 69;17.

Prospective multicenter 35 pts failed CRT implant/non-responders
Successful implant: 97%

Improvement in HF CCS in 85% pts
Positive CRT Echo (reduction in LVESV >15%): 52% pts at 6M

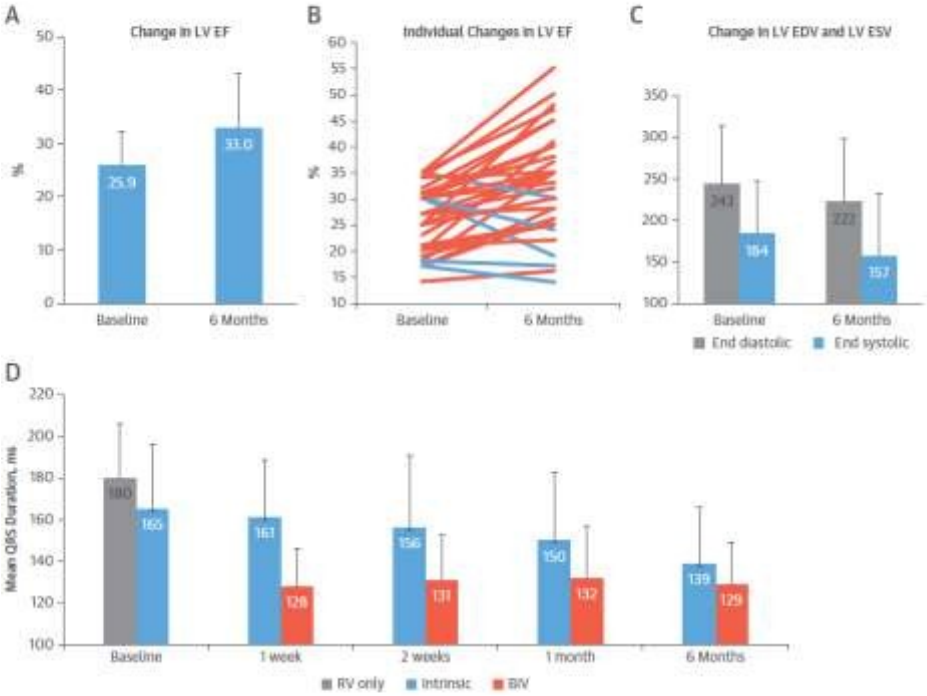


TABLE 3 Device- or Procedure-Related Adverse Events (n = 35)	
<24 h	3 (8.6%)
VF during catheter contact with LV endocardium	1
Electrode embolization to lower extremity	1
Femoral artery fistula (required surgical repair)	1
24 h to 1 month	8 (22.3)
Acute CVA (AF noncompliant with anticoagulation)	1
Femoral pseudoaneurysm	2
Pocket hematoma (generator)	1
Suspected infection (generator site)	3
Death (following VF during initial implant procedure)	1
1 to 6 months	3 (8.6)
Defective transmitter circuitry	3

Complications: 8.6% pts at 24 hrs
22% at 24 hr – 1M

Future of CRT

- Newer pacing strategies
  - Epicardial (Access to greater number of LV sites)
    - New leads (Xiphoid approach, Improved Thoracoscopic access)
  - Endocardial (More physiological activation of LV)
    - Improved transseptal/endocardial technology
    - WISE technology (SOLVE-CRT)
  - Multisite Pacing (Improve intra LV synchrony)
    - 2 CS leads (1 CS & 1 epicardial)
  - Multipoint Pacing (MORE CRT Trial, MPP registry)
- Integration of CRT pacing
  - CRT & LVAD, Cardiac contractility modulation (CCM), Baroreflex activation therapy

Summary

CRT Response: Inadequate and unpredictable

CRT Non-response can be attributed to many factors

LV lead placement is important

Patient specific not *anatomical* based LV Lead placement

Target the site of maximal electrical delay or maximal mechanical delay

Quadripolar LV leads: Standard of care

MPP or multisite LV lead pacing if single site not effective

Newer technologies may favor greater CRT response by LV endocardial pacing compared to standard transvenous CS pacing