Multisite Pacing (MSP)

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Background

- Many patients are still non responders to CRT (20-45%)
- CS anatomy quite variable
- Heterogeneity in patient population
  - Ischemic
  - Non-Ischemic
- What would be the “ceiling” in CRT response rate?

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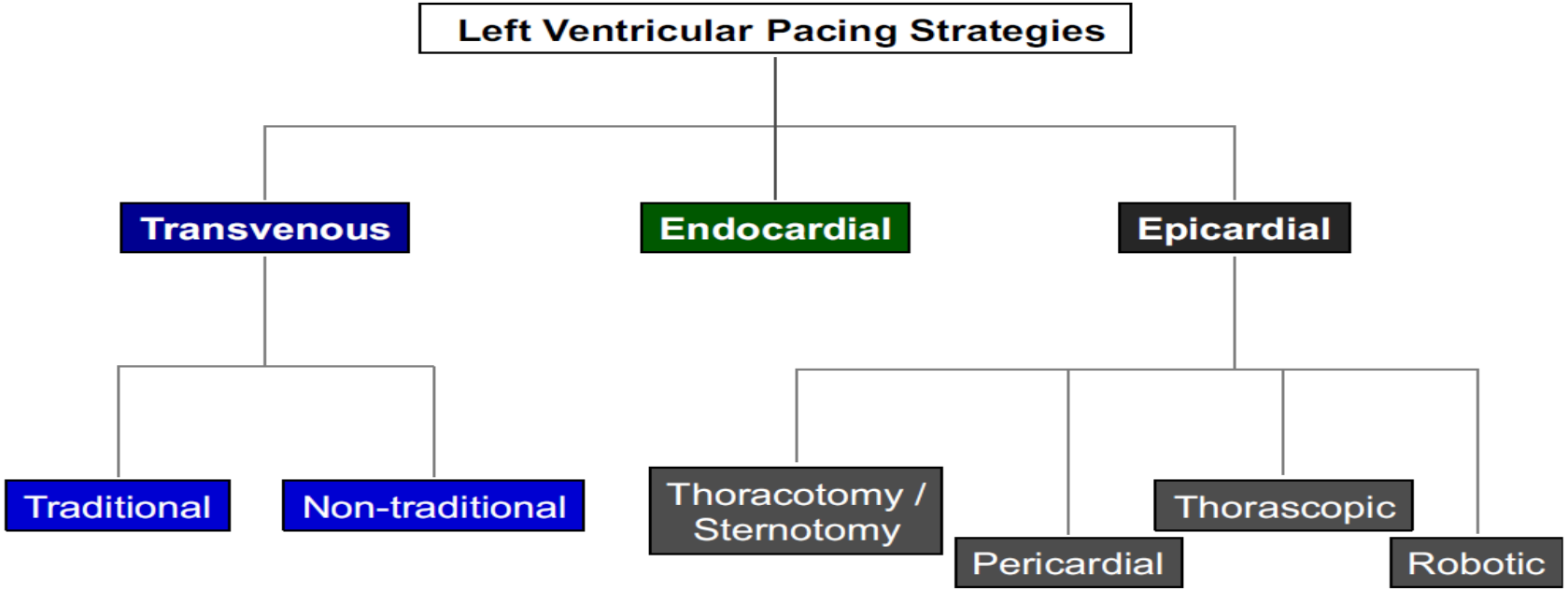

Figure 3 Graphic display of available left ventricular pacing strategies.

Heart Rhythm, Vol 9, No 8S, August Supplement 2012

Table 4 Advantages and disadvantages of the various methods of left ventricular lead placement

Method	Advantages	Limitations
Traditional transvenous	Abundant data on clinical outcomes	Technical challenges and unpredictable implant times
	Generally high implant success rate	Need for fluoroscopy
Nontraditional transvenous	Potential reduction in implant times	Few data available
	Greater choice of target sites	Potential for pericardial tamponade
Direct endocardial	More predictable implant times	Few data available
	Greater choice of target sites	Risks of embolic phenomenon and transseptal puncture
Transapical endocardial	Potential reduction in implant times	Few data available
	Greater choice of target sites	Risks of embolic phenomenon and apical puncture
Sternotomy/thoracotomy	Potential reduction in implant times	Few data available
	Greater choice of target sites	Risks from invasive procedure
Minimally invasive epicardial	More predictable implant times	Few data available
	Minimal or no fluoroscopy	Risks from invasive procedure
Percutaneous pericardial	Potential reduction in implant times	Few data available
	Greater choice of target sites	Risks of embolic phenomenon and apical puncture
Robotic epicardial	Greater choice of target sites	Highly specialized equipment
	Minimal or no fluoroscopy	Risks of invasive procedure

How to Improve Responders

- Better patient selection
- Better imaging before implant
  - Scar burden
  - Viability
  - Late activation
- LV lead location
  - Late, viable, non-apical, no phrenic, good thresholds, stable, etc
- Timing optimization
  - AV, VV, fusion, AdaptivCRT™, SonR™, QuickOpt ™, SmartDelay ™, etc
- **Multisite pacing (MSP)**
  - **2 RV leads, one LV lead**
  - **2 LV leads**
  - **Multipolar pacing with quadripolar leads**
- LV endocardial
- His bundle pacing in non responders

Table 1 Factors influencing response to cardiac resynchronization therapy

Patient	Device
Static	
• Gender	• Lead location
• Cause of LV dysfunction	• Right ventricular function
• Degree of dyssynchrony	• Pulmonary hypertension
Dynamic	
• Atrial fibrillation and other arrhythmias	• AV timing and VV timing
• Intercurrent illness (eg, anemia)	• Adequacy of LV capture
• Alteration/compliance with diet and medications	• True capture vs pseudocapture

AV = atrioventricular; LV = left ventricular; VV = interventricular.

Trial	Author (Year)	N	Comparator	Intervention(s)	Results
RHYTHM ID	Boriani et al[35] (2005)	121	Nominal VV settings	Echo-optimized VV timing	No difference in quality of life, NYHA class, or walk distance
DECREASE-HF	Rao et al[36] (2007)	306	Simultaneous VV pacing	Electrogram optimized VV timing	No difference in LV volumes or ejection fraction
FREEDOM	Abraham et al [37] (2010-abstract)	1800	Clinically optimized AV and VV timing	Serial electrogram optimized AV and VV timing	No difference in clinical outcomes or functional measures
CLEAR	Ritter (2010-abstract & 2012)[38]	186	Echo-optimized AV and VV timing	Automatic adjustment of AV delays via contractility sensor	Improved clinical response with the contractility sensor
SMART AV	Ellenbogen et al[39] (2011)	980	Fixed AV (120 ms) and VV (0 ms)	1. Echo-optimized AV and VV timing 2. Electrogram optimized AV and VV timing	No difference in LV volumes, ejection fraction, or functional measures among the 3 groups

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A Randomized Comparison of Triple-Site Versus Dual-Site Ventricular Stimulation in Patients With Congestive Heart Failure

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Rennes, Nantes, Paris, and Bordeaux, France; Stockholm, Sweden; Bad Rothenfelde, Germany; Eastbourne, United Kingdom; and Zaventem, Belgium

JACC Vol. 51, No. 15, 2008
April 15, 2008:1455–62

Methods

This multicenter, single-blind, crossover study enrolled 40 patients (mean age 70 ± 9 years) with moderate-to-severe heart failure despite optimal drug treatment, a mean LV ejection fraction of 26 ± 11%, and permanent atrial fibrillation requiring cardiac pacing for slow ventricular rate. A cardiac resynchronization therapy device connected to 1 RV and 2 LV leads, inserted in 2 separate coronary sinus tributaries, was successfully implanted in 34 patients. After 3 months of biventricular stimulation, the patients were randomly assigned to stimulation for 3 months with either 1 RV and 2 LV leads (3-V) or to conventional stimulation with 1 RV and 1 LV lead (2-V), then crossed over for 3 months to the alternate configuration. The primary study end point was quality of ventricular resynchronization (Z ratio). Secondary end points included reverse LV remodeling, quality of life, distance covered during 6-min hall walk, and procedure-related morbidity and mortality. Data from the 6- and 9-month visits were combined to compare end points associated with 2-V versus 3-V.

Results

Data eligible for protocol-defined analyses were available in 26 patients. No significant difference in Z ratio, quality of life, and 6-min hall walk was observed between 2-V and 3-V. However, a significantly higher LV ejection fraction (27 ± 11% vs. 35 ± 11%; $p = 0.001$) and smaller LV end-systolic volume (157 ± 69 cm^3 vs. 134 ± 75 cm^3; $p = 0.02$) and diameter (57 ± 12 mm vs. 54 ± 10 mm; $p = 0.02$) were observed with 3-V than with 2-V. There was a single minor procedure-related complication.

Conclusions

Cardiac resynchronization therapy with 1 RV and 2 LV leads was safe and associated with significantly more LV reverse remodeling than conventional biventricular stimulation. (J Am Coll Cardiol 2008;51:1455–62)

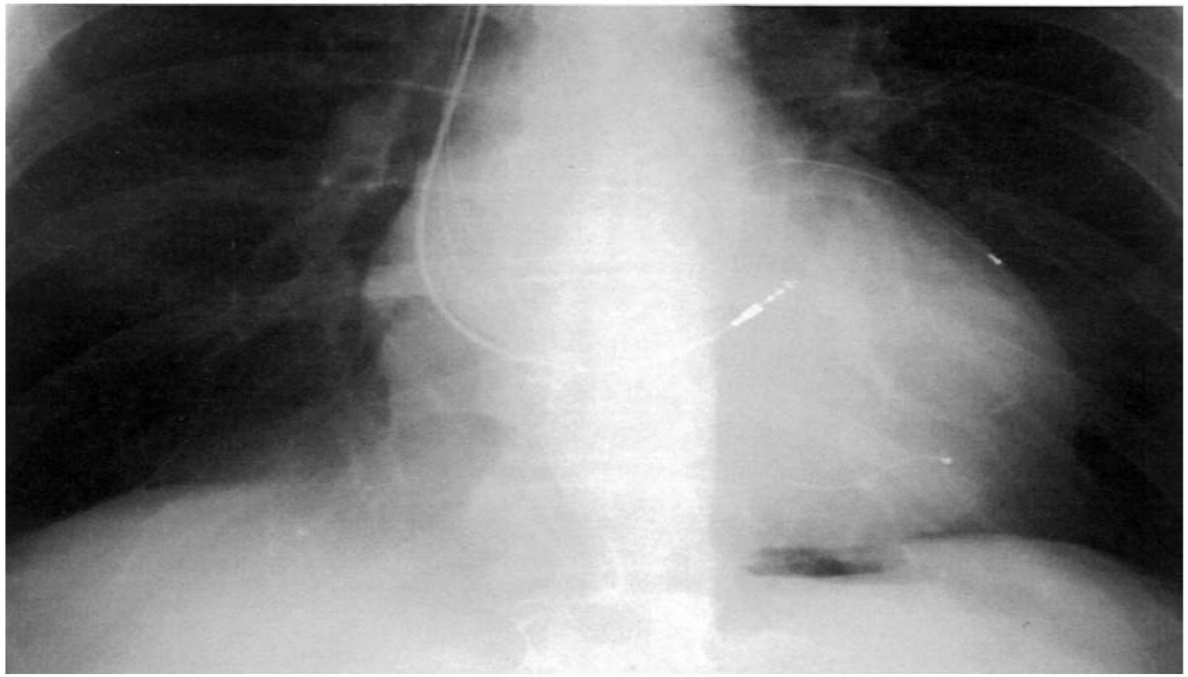

Figure 3 **Representative Frontal Roentgenographic View of the Leads of a Triple-Site, Biventricular Stimulation System**

JACC Vol. 51, No. 15, 2008
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J Interv Card Electrophysiol (2015) 42:135–142
DOI 10.1007/s10840-014-9971-2

Limitations of chronic delivery of multi-vein left ventricular stimulation for cardiac resynchronization therapy

Jonathan M. Behar · Julian Bostock · Matthew Ginks · Tom Jackson · Manav Sohal · Simon Claridge · Reza Razavi · Christopher Aldo Rinaldi

Conclusion Multisite epicardial LV lead placement may be acutely feasible and demonstrate beneficial hemodynamic results at implantation. Long-term delivery of this therapy is however problematic due to technical issues with pacing through the bifurcating adapter. This suggests the feasibility of *this* form of multisite CRT is limited.

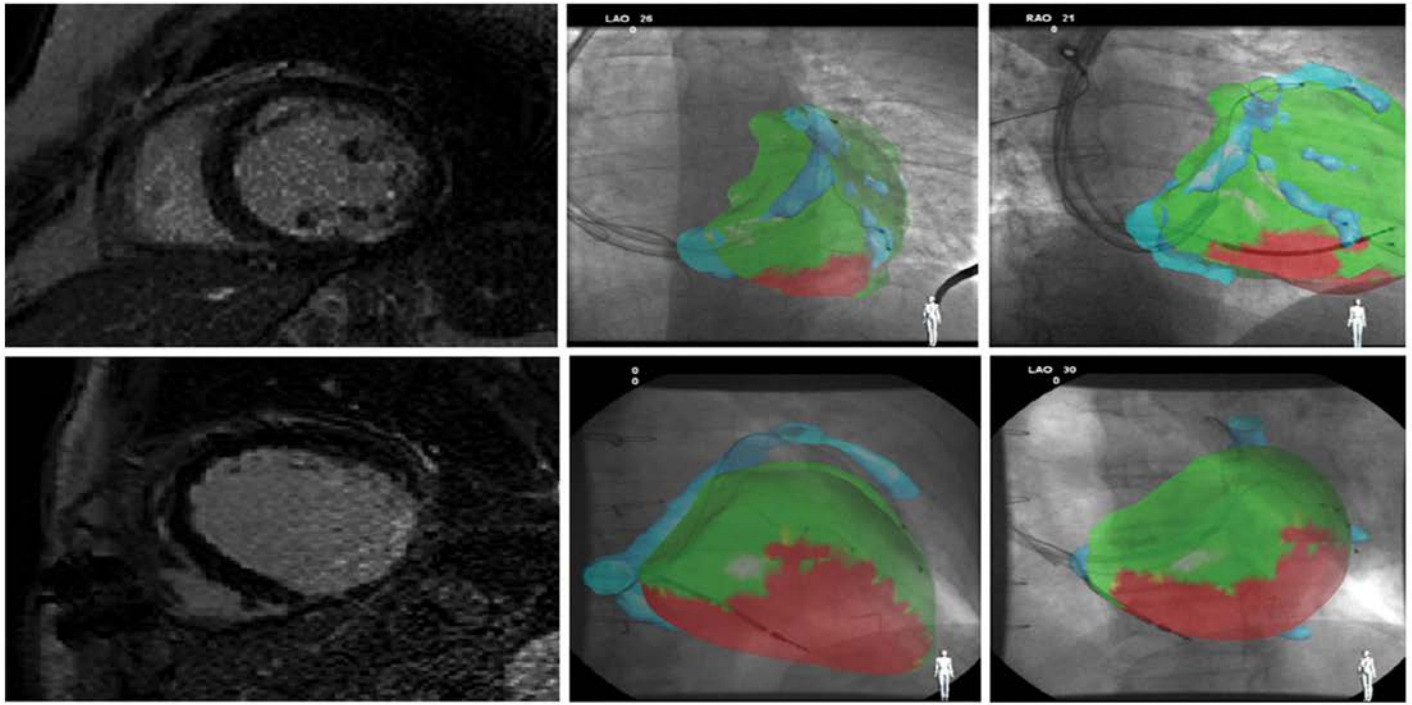

Fig. 1 Relationship of scar segmented from cardiac magnetic resonance imaging to lead position on fluoroscopy. *Left panel*: left anterior oblique projection; *right panel*: right anterior oblique projection. *Green shell* indicates three-dimensional left ventricular geometry; *red area* is scar in postero-lateral region. LV1 is seen to be positioned in the region of scar whereas LV2 lead is remote from scar. (Reprinted with permission from: Ginks MR, Duckett SG, Kapetanakis S, Bostock J, Hamid S, Shetty A, Ma Y, Rhode KS, Carr-White GS, Razavi RS, Rinaldi CA. Multisite left ventricular pacing as a potential treatment for patients with postero-lateral scar: insights from cardiac magnetic resonance imaging and invasive haemodynamic assessment. Europace. 2012;14:373–379, by permission of Oxford University Press) [19]

Clinical impact of an additional left ventricular lead in cardiac resynchronization nonresponders: the V^3 trial

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(Heart Rhythm 2018; ■:1–7)

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OBJECTIVE We assessed the feasibility and safety of adding a second LV lead to CRT nonresponders and its clinical impact.

METHODS Eighty-four recipients of a CRT system and considered as nonresponders as per clinical composite score (CCS) were enrolled in this multicenter study. They were randomized to the V^3 arm (implantation of an additional LV lead; n = 43) or control arm (no change; n = 41). Implant success rate, incidence of severe adverse events, CCS, and secondary clinical and echocardiographic end points were evaluated at 12 and 24 months.

RESULTS Positioning of a second LV lead was successful at first (90%) or second (10%) attempt. The perioperative complication rate (infection, system explant, pneumothorax, and hematoma) was high (20.4%). After 24 months, 35 systems (79.5%) were working properly. The multinomial logistic regression model showed that V^3 treatment had no significant influence (P = .27) on the CCS, number of HF hospitalizations, time to first HF hospitalization, New York Heart Association class, and LV ejection fraction at 12 and 24 months.

CONCLUSION Although addition of a second LV lead in CRT nonresponders is feasible with a high success rate, this approach is associated with a significant rate of severe adverse events and does not provide significant long-term clinical benefits (ClinicalTrials.gov Identifier No. NCT01059175).

(Heart Rhythm 2018;■:1–7)

Benefits of Endocardial and Multisite Pacing Are Dependent on the Type of Left Ventricular Electric Activation Pattern and Presence of Ischemic Heart Disease

Insights from Electroanatomic Mapping

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Circ Arrhythm Electrophysiol October 2012

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Acute Hemodynamic Study

Methods and Results—Ten patients (8 men and 2 women; mean [SD] age 63 [12] years; LV ejection fraction 246%; QRS duration 161 [24] ms) fulfilling conventional CRT criteria underwent an electrophysiological study, with assessment of acute hemodynamic response to conventional CRT as well as LV endocardial and multisite pacing. LV activation pattern was assessed using noncontact mapping. LV endocardial pacing gave a superior acute hemodynamic response compared with conventional CRT (26% versus 37% increase in LV dP/dt_{max}, respectively; $P<0.0005$). There was a trend toward further incremental benefit from multisite LV stimulation, although this did not reach statistical significance ($P=0.08$). The majority (71%) of patients with nonischemic heart failure etiology or functional block responded to conventional CRT, whereas those with myocardial scar or absence of functional block often required endocardial or multisite pacing to achieve CRT response.

Conclusions—Endocardial or multisite pacing may be required in certain subsets of patients undergoing CRT. Patients with ischemic cardiomyopathy and those with narrower QRS, in particular, may stand to benefit. (***Circ Arrhythm Electrophysiol*. 2012;5:889-897.**)

Type I and Type II Activation Patterns

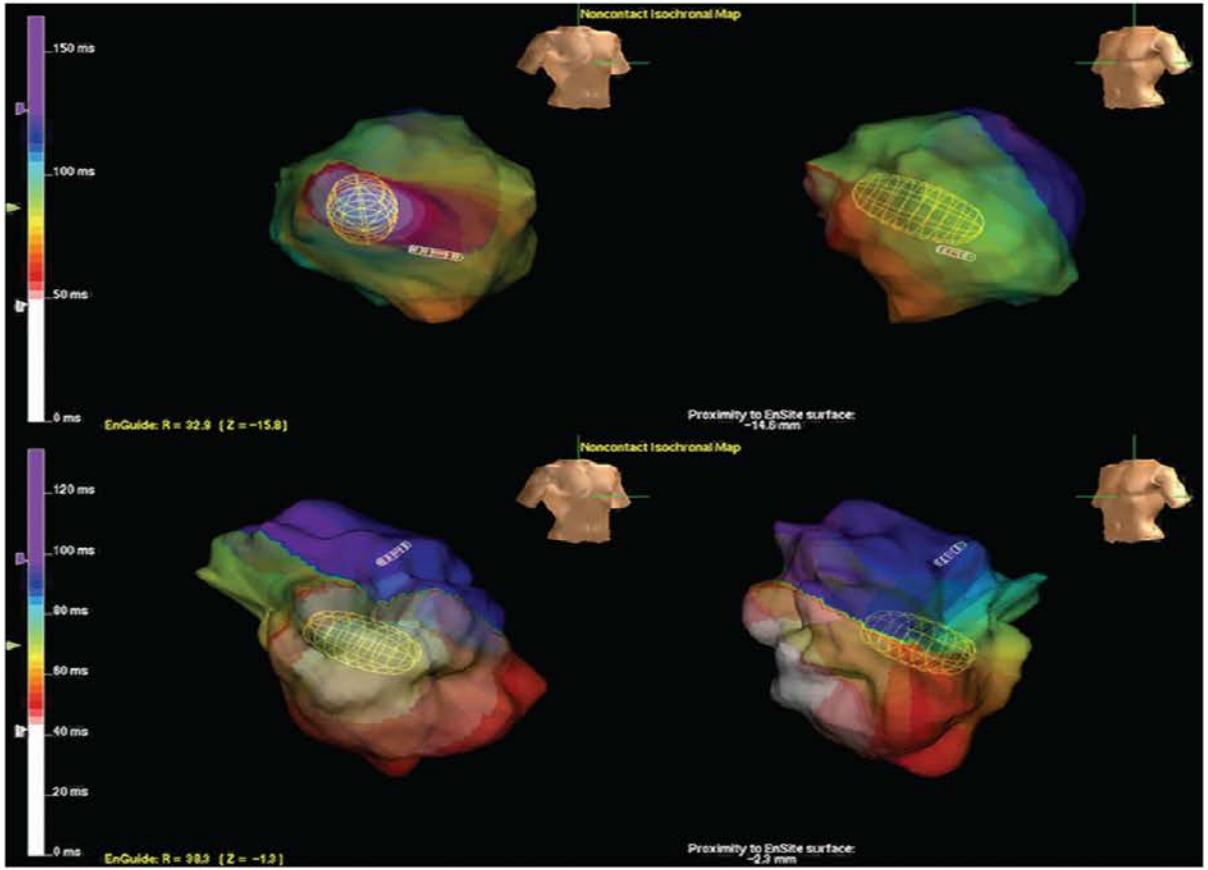

Figure 4. Activation patterns characterized by noncontact mapping. **Upper panel**: Type I activation pattern. The isochronal map shows a smooth propagation of the activation wave front from left ventricular (LV) septum to lateral wall. **Lower panel**: Type II activation pattern. The isochronal map shows a line of block in the anterior wall with the activation wave front passing around the inferior LV wall before it reaches the lateral wall.

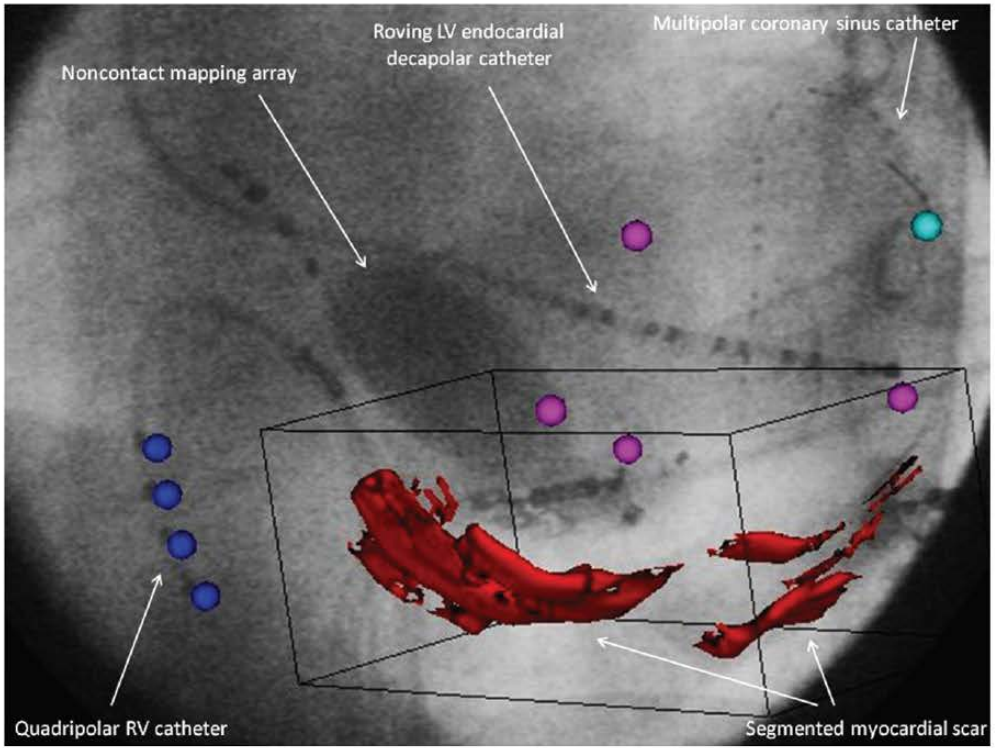

Figure 1. Left anterior oblique fluoroscopic image of noncontact mapping array and electrophysiological catheters in situ during a typical case. The color overlay shows left ventricular (LV) endocardial lead positions in **magenta**, right ventricular (RV) quadripolar electrodes in **blue**, tip of coronary sinus multipolar electrode in **cyan**, and scar segmented from cardiac magnetic resonance overlaid in **red** onto fluoroscopic image.

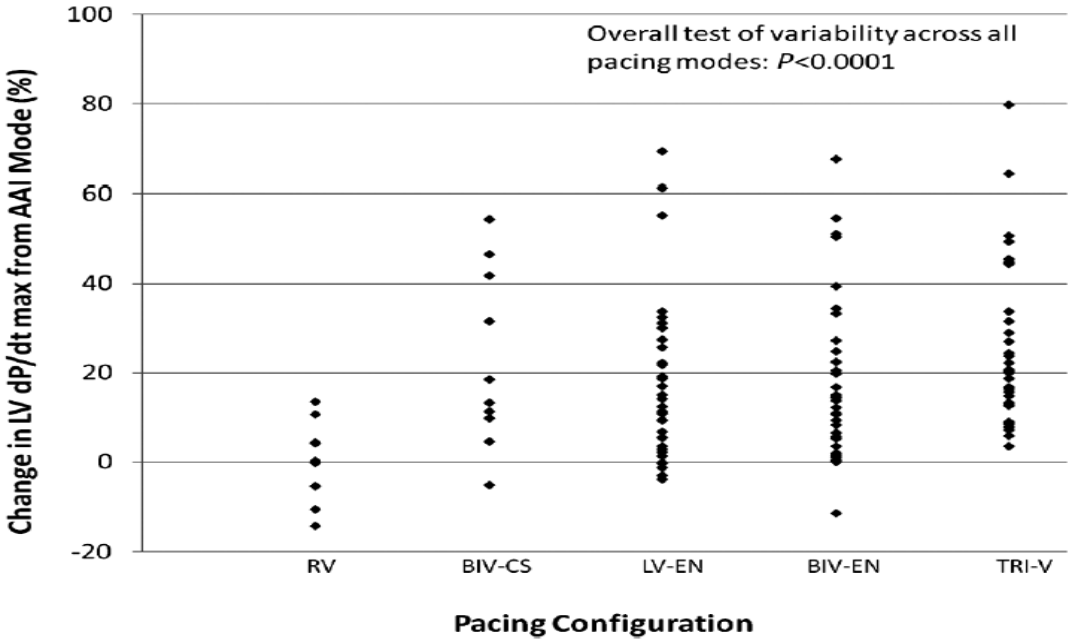

Figure 2. Mean dP/dt_{max} for all pacing modalities in all 10 patients. This is displayed as the change in mean peak dP/dt_{max} resulting from pacing at the optimal site in each pacing configuration, compared with baseline (AAI pacing). LV indicates left ventricular; RV, right ventricular; BIV, biventricular; TRI-V, simultaneous BIV-CS and LV endocardial (EN).

MSP Using a Standard Bipolar LV Lead

Acute Hemodynamic Effects of Single- and Dual-Site Left Ventricular Pacing Employing a Dual Cathodal Coronary Sinus Lead

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Conclusion: *Even with a relatively small distance of 20–21 mm between stimulation electrodes, there is a significant difference in acute hemodynamic effect from the single best and worst site. Dual-site LV pacing offers no hemodynamic benefit over the best single pacing site. The short electrode distance may have been a limitation and results may not be applicable to other forms of multisite pacing. (PACE 2015; 38:558–564)*

Medtronic bipolar 4196
St-Jude QuickFlex 1258T

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MSP Using 2 RV Leads and 1 LV Lead

Safety, feasibility, and outcome results of cardiac resynchronization with triple-site ventricular stimulation compared to conventional cardiac resynchronization

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METHODS Our pilot randomized trial was designed to assess the safety and feasibility of TRIV with 2 right ventricular leads and 1 left ventricular leads compared to conventional CRT. The primary end-point was the rate of severe adverse events at 6 months. Secondary end-points included functional improvement parameters, quality-of-life (QOL) score, and changes of echocardiographic indices at 6 and 12 months in a subset of patients.

(Heart Rhythm 2016;13:183–189)

RV septal connected to LV with a “Y” connector

RESULTS Seventy-six patients were enrolled at 11 centers and randomized to control or TRIV arm. All implant procedures but one were successful. At 6 months, there was no statistical difference between proportions of patients with at least 1 severe adverse event in both groups (34.1% vs 25.7%, $P = .425$). There also was no difference between functional improvement parameters, 6-minute walking distances ($P = .40$), QOL scores ($P = .27$), and echographic indices. At 12 months, the proportions of patients with a left ventricular ejection fraction gain of more than 5%, 10%, or 15% were significantly superior with TRIV.

CONCLUSION TRIV pacing is an effective and safe technique and may provide a greater benefit in ventricular remodeling than conventional CRT. Further studies are needed to assess its long-term benefit.

(Heart Rhythm 2016;13:183–189)

MSP
Quadripolar Leads

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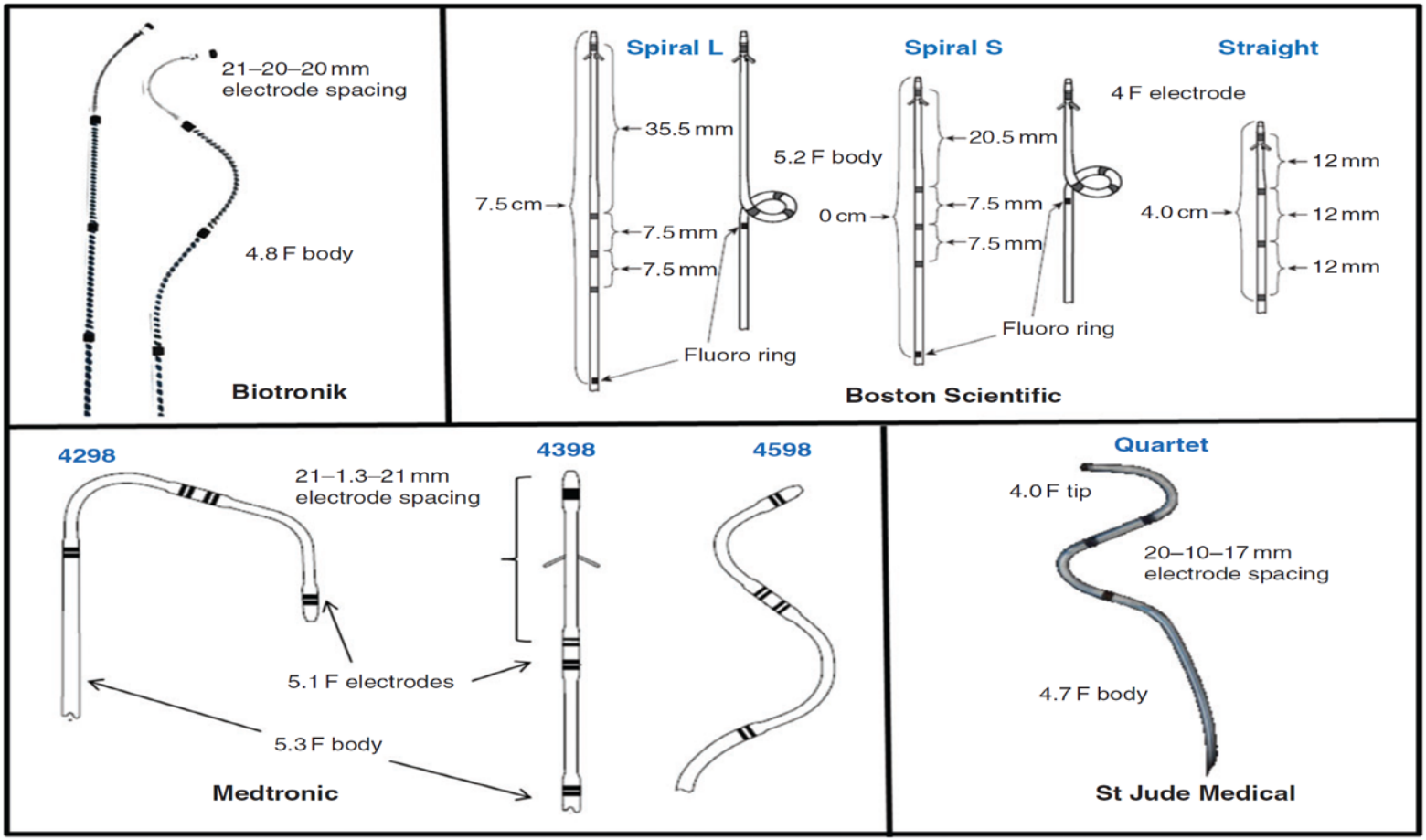
Table I Studies of MPS delivered by a quadripolar

Author, year	Number of patients	Study type	Findings
Thibault *et al.* (2013)	19 (21)	Acute comparative study Measurement: invasive haemodynamic evaluation (d*P*/d*t*)	72% of patients, MPP improved acute systolic function vs. conventional CRT. Pacing most distal and proximal electrodes most commonly yielded greatest LVd*P*/dt_{max}
Rinaldi *et al.* (2013)	41(52)	Comparative study after implant Measurement: echocardiographic dyssynchrony (TDI)	64% of patients MPP resulted in significant reduction in dyssynchrony vs. conventional CRT
Pappone *et al.* (2013)	44	Randomized comparative study at the time of implant Measurement: invasive haemodynamic evaluation (pressure–volume loops)	Main finding: CRT with MPP can significantly improve acute LV haemodynamic parameters assessed with PV loop measurements as compared with conventional CRT


21–20–20 mm
electrode spacing
4.8 F body
Biotronik
Spiral L
35.5 mm
7.5 cm
7.5 mm
7.5 mm
5.2 F body
Fluoro ring
Spiral S
20.5 mm
0 cm
7.5 mm
7.5 mm
Fluoro ring
Straight
4 F electrode
12 mm
4.0 cm
12 mm
12 mm
Boston Scientific
4298
21–1.3–21 mm
electrode spacing
4398
4598
5.1 F electrodes
5.3 F body
Medtronic
Quartet
4.0 F tip
20–10–17 mm
electrode spacing
4.7 F body
St Jude Medical

EUROPEAN SOCIETY OF CARDIOLOGY®

Europace (2013) **15**, 984–991
doi:10.1093/europace/eus435

CLINICAL RESEARCH
Pacing and resynchronization therapy

Acute haemodynamic comparison of multisite and biventricular pacing with a quadripolar left ventricular lead

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Acute Hemodynamic Study

Methods and results

In 21 patients receiving cardiac resynchronization therapy, a quadripolar LV lead and conventional right atrial and ventricular leads were connected to an external pacing system. A guidewire pressure sensor was placed in the LV for continuous d*P*/d*t* measurement. Four multisite pacing configurations were tested three times each and compared with BiV pacing using the distal LV electrode. Nineteen patients had useable haemodynamic data. Median increase in LV dP/dt_{max} with BiV vs. atrial-only pacing was 8.2% (interquartile range 2.3%, 15.7%). With multisite pacing using distal and proximal LV electrodes, median increase in LV dP/dt_{max} was 10.2% compared with atrial-only pacing (interquartile range 6.1%, 25.6%). In 16 of 19 patients (84%), two or more of the four multisite pacing configurations increased LV dP/dt_{max} compared with BiV pacing. Overall, 72% of all tested configurations of multisite pacing produced greater LV dP/dt_{max} than obtained with BiV pacing. Pacing from most distal and proximal electrodes was the most common optimal configuration, superior to BiV pacing in 74% of patients.

Conclusion

In the majority of patients, multisite pacing improved acute systolic function further compared with BiV pacing. Pacing with the most distal and proximal electrodes of the quadripolar LV lead most commonly yielded greatest LV dP/dt_{max}.

Europace (2013) **15**, 984–991

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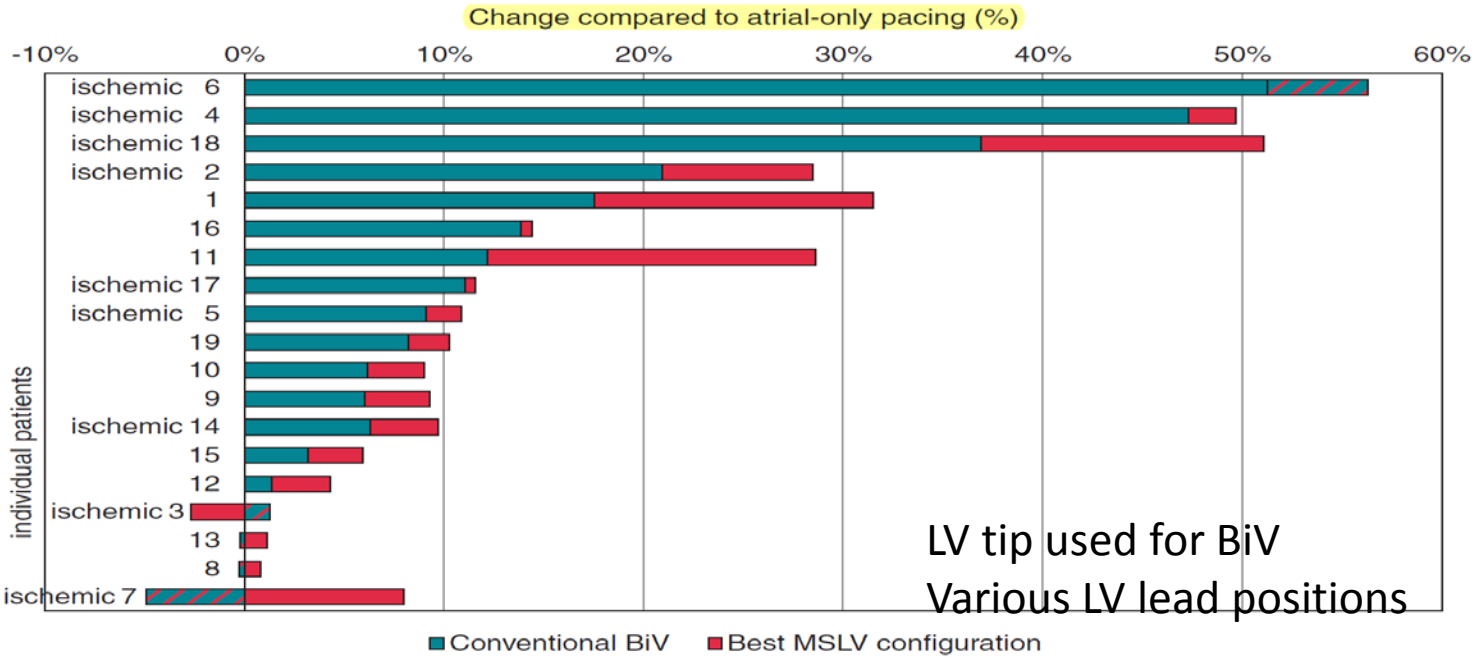
Table I Patient characteristics

Number of patients	$N = 21$
Age	60 ± 14 years
Gender	9 Female (43%), 12 male (57%)
Aetiology of heart disease	10 Ischaemic cardiomyopathy (48%), 11 dilated cardiomyopathy (52%)
NYHA functional class at time of implant	19 Class III (90%), 2 Class II (10%)
LV ejection fraction	22 ± 5%
Conduction delay	21 Left bundle branch block (100%)
Sensed QRS duration	144 ± 16 ms (18 patients without permanent ventricular pacing)
Arrhythmia history	9 Atrial (43%), 10 Ventricular (48%)
Pharmacological therapy	14 Angiotensin-converting enzyme inhibitor (67%), 7 angiotensin receptor blocker (33%), 21 β-adrenergic receptor antagonist (100%), 19 diuretic of any type (90%), 16 anti-platelet (76%), 10 cardiac glycoside (48%), 6 antiarrhythmic drug (29%), 2 calcium channel antagonist (10%), 7 nitrate (33%), 16 statin (76%)

Europace (2013) **15**, 984–991



LV tip used for BiV
Various LV lead positions

Figure 2 Percent change in LV dP/dt_{max} in each of the 19 patients compared with atrial pacing, using BiV and the best of four multisite pacing configurations. Results are sorted in descending order of acute haemodynamic response to BiV pacing. Horizontal bars show percentage improvement in LV dP/dt_{max} for BiV pacing (light blue) and incremental improvement from best of four multisite pacing configurations (red). Striped bars indicate change in direction from multisite pacing. Patients are identified according to category of response to BiV and multisite pacing.

Journal of Cardiac Failure Vol. 19 No. 11 2013

Acute Effects of Multisite Left Ventricular Pacing on Mechanical Dyssynchrony in Patients Receiving Cardiac Resynchronization Therapy

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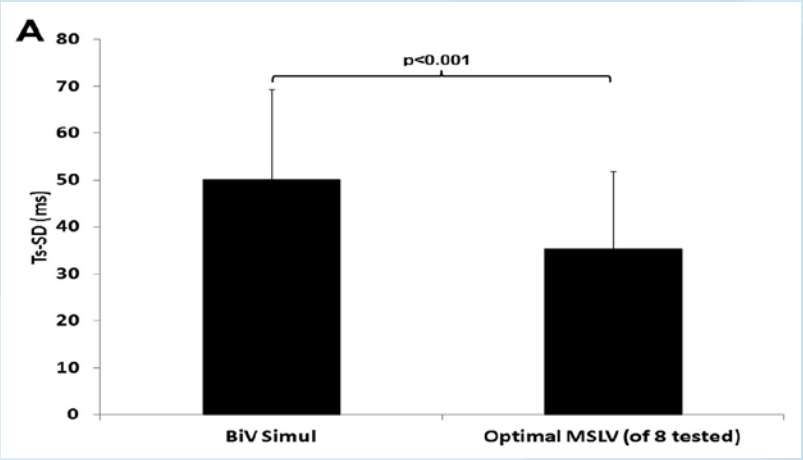
Acute Study - Tissue Doppler Imaging

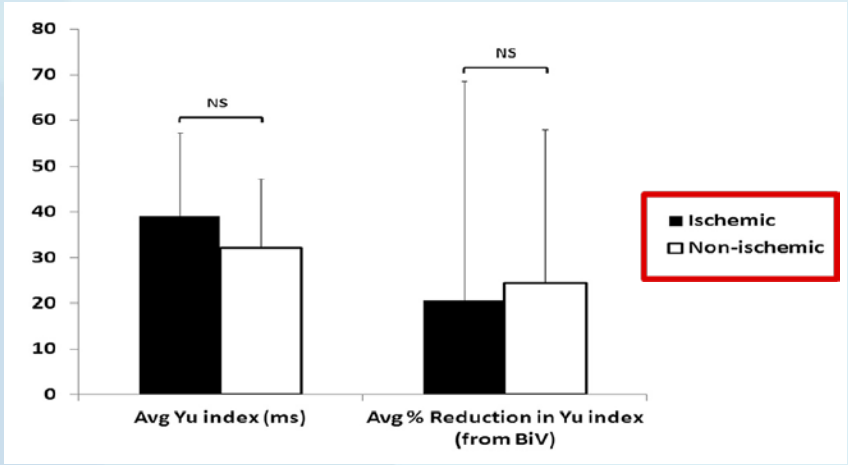
Methods and Results: Prospective multicenter study in 52 patients receiving CRT. An acute pacing protocol comprising 8 MSLV configurations covering a range of delays was compared with conventional CRT (baseline). Transthoracic tissue Doppler imaging (TDI) was used to measure the standard deviation of time to peak contraction of 12 LV segments (Ts-SD) and delayed longitudinal contraction. No ventricular arrhythmia occurred in any of the 52 patients. Complete TDI datasets were collected in 41 patients. Compared with baseline: 1) The mean Ts-SD was significantly lower for the optimal MSLV configuration (35.3 ± 36.4 vs 50.2 ± 29.1 ms; $P < .001$); 2) at least 1 MSLV configuration exhibited a significant dyssynchrony improvement in 63% of patients; and 3) the mean number of LV segments with delayed longitudinal contractions was significantly reduced with the optimal MSLV configuration (0.37 ± 7.99 vs 2.20 ± 0.19; $P < .001$).

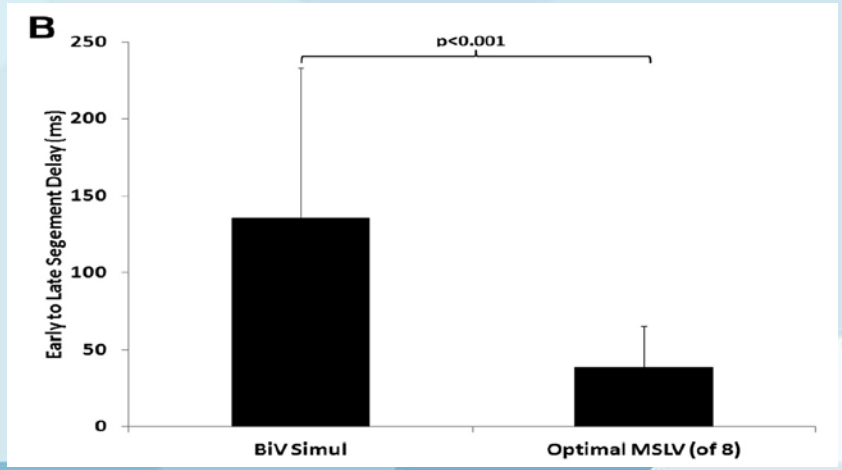
Conclusions: Acute MSLV was acutely safe, and a proportion of MSLV vectors resulted in a significant reduction in echocardiographic dyssynchrony compared with conventional CRT. (*J Cardiac Fail 2013;19:731–738*)

Table 2. Patient Demographics

Age, y	65.1 ± 9.7
Sex	
Male	83%
Female	17%
Clinical history	
Ischemic cardiomyopathy	39%
Nonischemic cardiomyopathy	51%
Etiology not reported	10%
Hypertension	7%
Valvular disease	12%
Left ventricular hypertrophy	2%
Prior myocardial infarction	37%
NYHA classification	2.6 ± 0.5
LVEF, %	24.9 ± 6.9
QRS duration, ms	156.4 ± 26.1
Ventricular arrhythmia history	20%
Supraventricular arrhythmia history	29%
Procedural history	
CABG	27%
PCTA	17%
LV lead position	
Anterior	5%
Anteriolateral	20%
Lateral	34%
Posterolateral	34%
Posterior	0%
Other	7%







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DOI 10.1007/s10840-014-9891-1

Improvement in acute contractility and hemodynamics with multipoint pacing via a left ventricular quadripolar pacing lead

C. Aldo Rinaldi · Christophe Leclercq · Wolfgang Kranig · Salem Kacet · Tim Betts · Pierre Bordachar · Klaus-Jürgen Gutleben · Anoop Shetty · Erwan Donal · Allen Keel · Kyungmoo Ryu · Taraneh G. Farazi · Marcus Simon · Tasneem Z. Naqvi

Conclusion MPP delivered via a quadripolar LV lead resulted in a significant improvement in acute cardiac contractility and hemodynamics compared to conventional CRT in the majority of patients studied.

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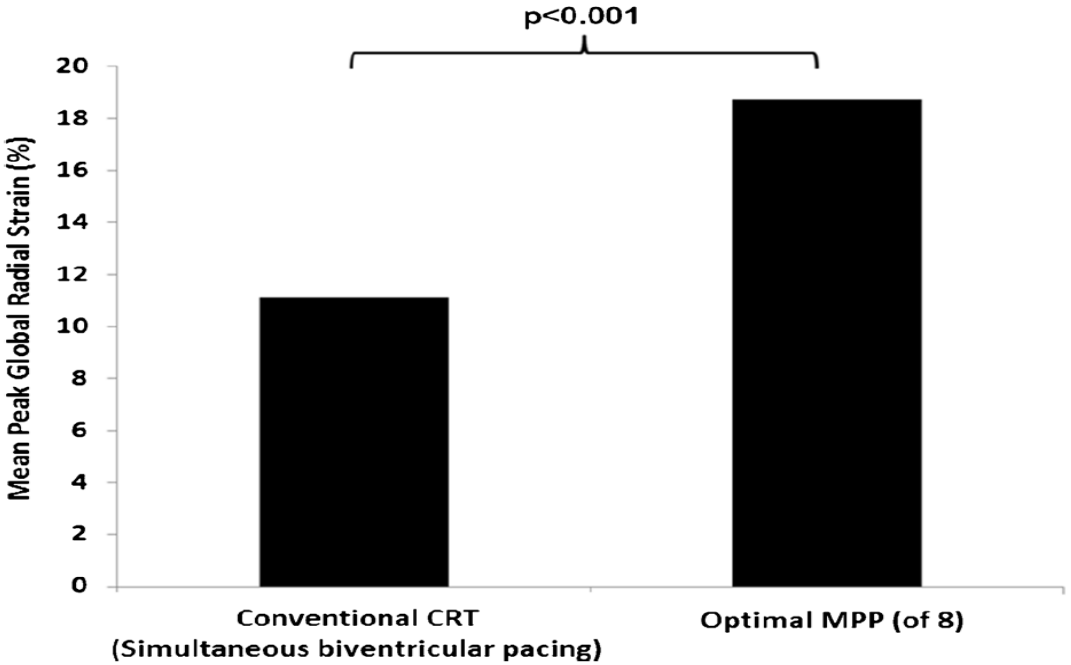
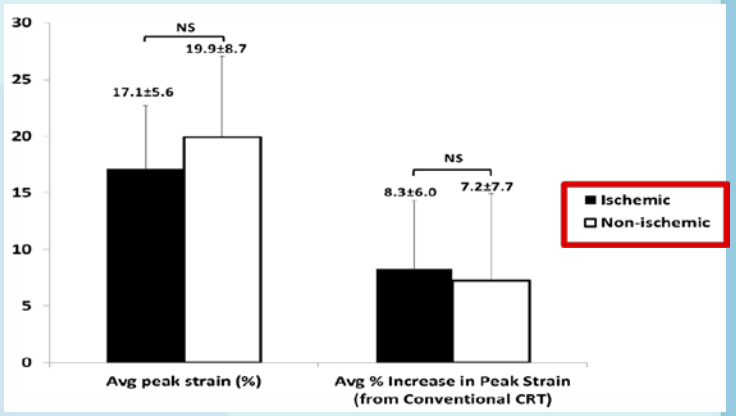


Fig. 1 Comparison of mean peak radial strain between MPP and conventional CRT—the mean global peak radial strain is higher with optimal MPP compared to conventional CRT



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J Interv Card Electrophysiol (2014) 40:75–80

% Patients with MPP Improving over BiV

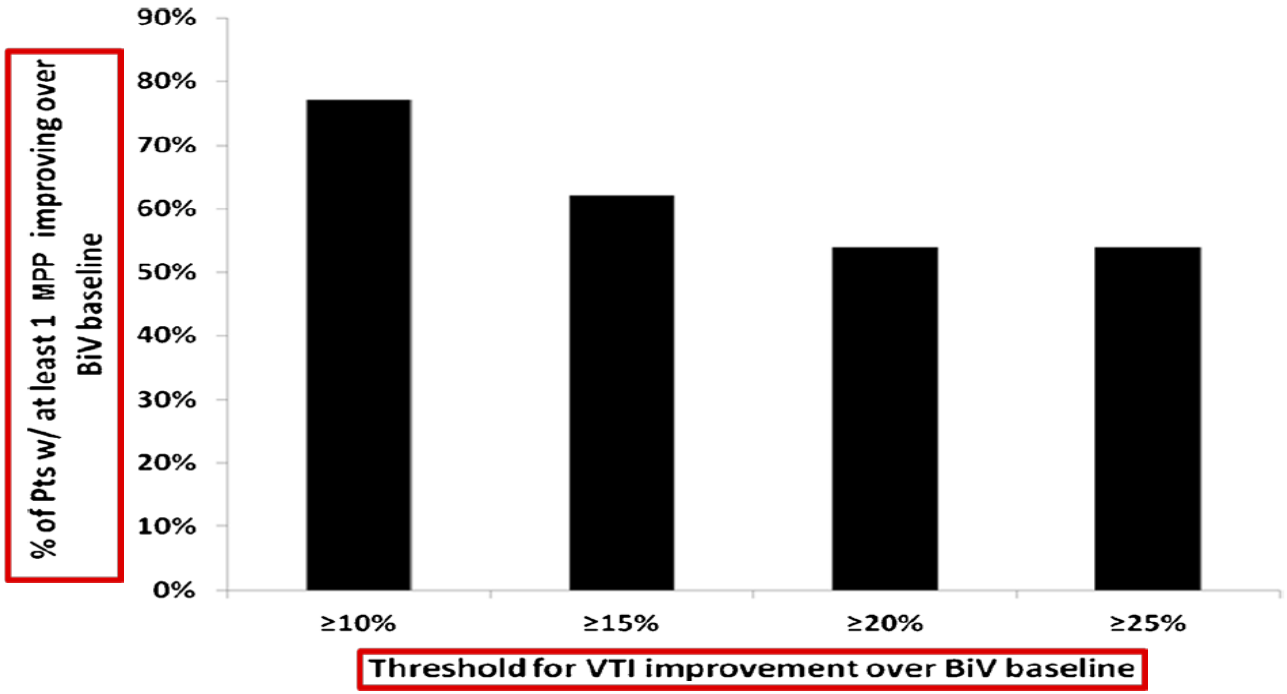

Fig. 4 Proportion of study patients who exhibited improvement in LVOT VTI with at least one MPP intervention over conventional CRT. Results shown for different thresholds of VTI improvement ranging from ≥10 to ≥25 %

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Europace (2014) **16**, 873–879
doi:10.1093/europace/eut420

CLINICAL RESEARCH
Pacing and cardiac resynchronization therapy

A comparison of left ventricular endocardial, multisite, and multipolar epicardial cardiac resynchronization: an acute haemodynamic and electroanatomical study

Anoop K Shetty[1,2]*, Manav Sohal[1,2], Zhong Chen[1,2], Matthew R Ginks[1,2], Julian Bostock[2], Sana Amraoui[1,2], Kyungmoo Ryu[3], Stuart P Rosenberg[3], Steven A Niederer[1], Jas Gill[1,2], Gerry Carr-White[1,2], Reza Razavi[1], and C Aldo Rinaldi[1,2]

Europace (2014) **16**, 873–879

Acute Study - Second Temporary LV Lead

Methods and results

Fifteen patients with a previously implanted CRT system received a second temporary CS lead and left ventricular (LV) endocardial catheter. A pressure wire and non-contact mapping array were placed into the LV cavity to measure LV$dP/dt_{max}$ and perform electroanatomical mapping. Conventional CRT, BV-Endo, and MSP were then performed (MSP-1 via two epicardial leads and MSP-2 via a single-quadripolar lead). The best overall AHR was found using BV-Endo pacing with a $19.6 \pm 13.6\%$ increase in AHR at the optimal endocardial site over baseline ($P < 0.001$). There was an increase in LV$dP/dt_{max}$ with MSP-1 and MSP-2 compared with conventional CRT, but this was not statistically significant. Biventricular endocardial pacing from the optimal site was significantly superior to conventional CRT ($P = 0.039$). The AHR achieved when BV-Endo pacing was highly site specific. Within individuals, the best pacing modality varied and was affected by the underlying substrate. Left ventricular activation times did not predict the optimal haemodynamic configuration.

Conclusion

Biventricular endocardial pacing and not MSP was superior to conventional CRT, but was highly site specific. Within individuals, however, different methods of stimulation are optimal and may need to be tailored to the underlying substrate.

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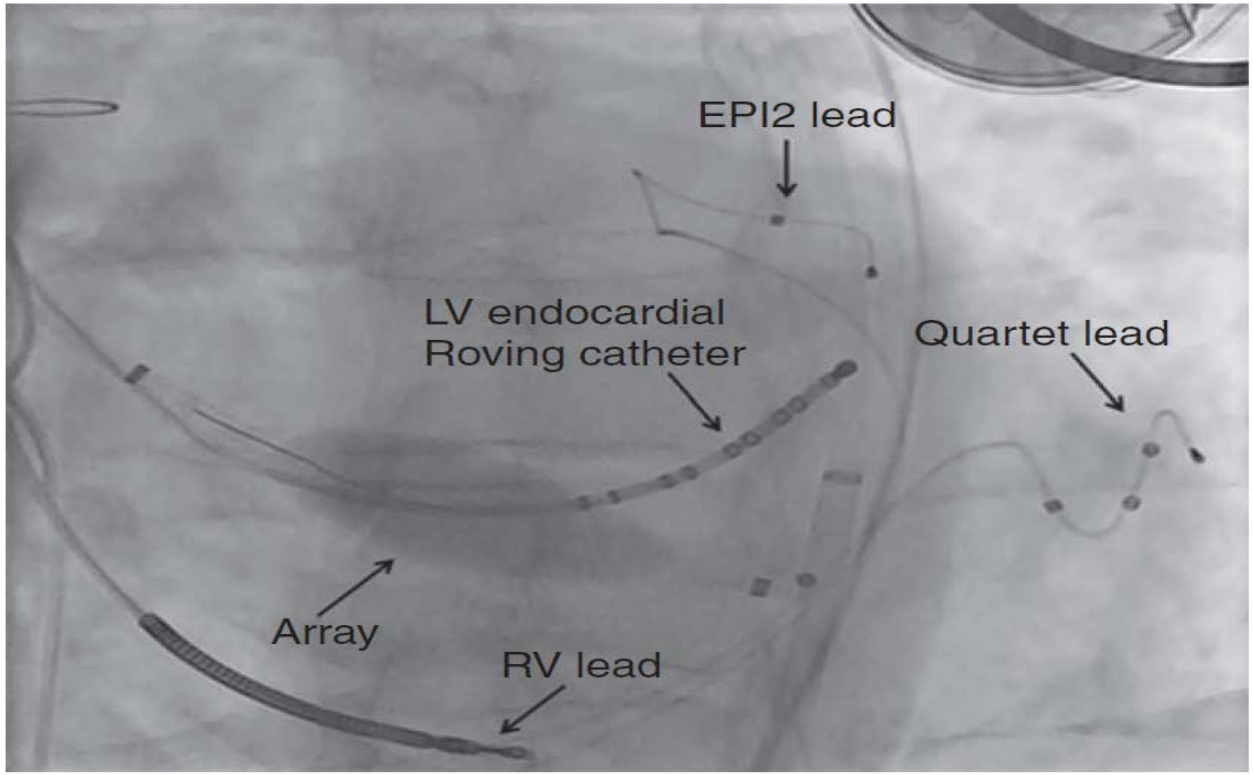

Figure 1 Postero-anterior fluoroscopic view of a typical invasive haemodynamic and electroanatomical study—A quadripolar quartet LV lead is in a posterolateral branch of the CS and a second temporary epicardial lead (EPI2) is in a proximal anterior branch of the CS. An LV endocardial catheter and NCM array are in the LV cavity and a permanent pacing lead in the RV apex.

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Table I Baseline characteristics of the study population

Parameter	Mean (SD) or numbers
Patients	15
Age (years)	64 ± 7
Male (%)	100
LVEF (%)	27 ± 9
NYHA Class (II/III)	2/13
Ischaemic/non-ischaemic (%)	10/5 (67/33)
Sinus rhythm/atrial fibrillation	13/2
QRS duration	160 ± 39 ms
QRS morphology (LBBB/non-specific IVCD)	13/2

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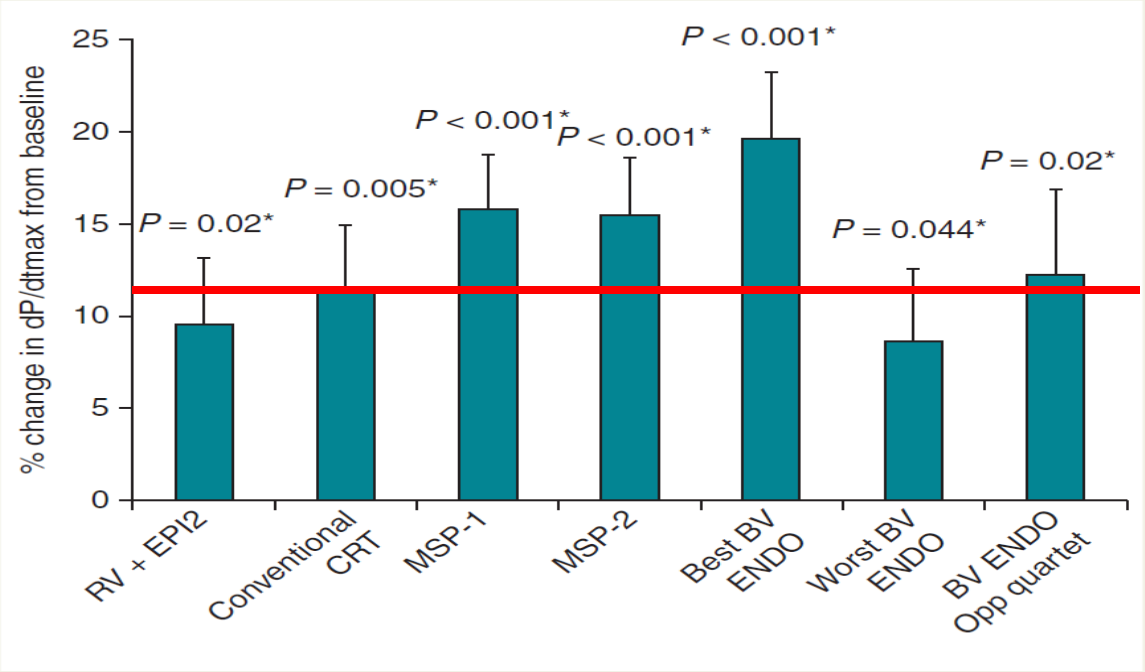

MSP-1: RV + EPI2 + V1 (one quadripolar lead vector, temporary epicardial lead and RV with 5 ms V–V delay)

MSP-2: RV + V1 + V2 (two quadripolar lead vectors and RV with 5 ms V–V delay)

Figure 2 Acute haemodynamic response achieved using different pacing modalities—AHR as percentage change in LVdP/dt_{max} over baseline (AAI/VVI pacing) on *y*-axis. Conventional CRT, chronic LV lead (RV + V1). BV Endo opp quartet, biventricular endocardial pacing at an endocardial site approximating the chronically implanted epicardial lead.

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doi:10.1093/europace/euv211

CLINICAL RESEARCH
Pacing and resynchronization therapy

The use of multisite left ventricular pacing via quadripolar lead improves acute haemodynamics and mechanical dyssynchrony assessed by radial strain speckle tracking: initial results

Joaquín Osca[1]*, Pau Alonso[1], Oscar Cano[1], Ana Andrés[1], Vicente Miro[2], María José Sancho Tello[1], Jose Olagüe[1], Luis Martínez[3], and Antonio Salvador[3]

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Methods and results

An open-label, non-randomized, single-centre, prospective study was designed. Twenty-seven consecutive patients were included. Evaluation of pacing configurations was performed in a random order. Transthoracic echocardiography was used to obtain haemodynamic and dyssynchrony parameters. Left ventricular ejection fraction (LVEF) was significantly superior in MPP compared with baseline ($38.4 \pm 1.8\%$ vs. $26.1 \pm 2.2\%$; $P < 0.001$), and in conventional pacing configuration compared with baseline ($33.2 \pm 1.8\%$ vs. $26.1 \pm 2.2\%$; $P = 0.007$). Cardiac index (CI) was increased by $21.8 \pm 5.4\%$ and $34.7 \pm 5.1\%$ in conventional and MPP configurations, respectively ($P = 0.19$). Percentage of acute responders (CI increase $\geq 10\%$) was 62.9 and 85.2% in conventional and MPP, respectively ($P < 0.001$). LV dyssynchrony was defined by radial strain rate parameters. Baseline anteroseptal-to-posterior wall time delay was 168 ± 21 ms. It was reduced until 70.4 ± 29 ms in conventional and -6.6 ± 11 ms in MPP (conventional vs. baseline $P = 0.04$; MPP vs. conventional $P = 0.05$). Standard deviation of the time-to-peak radial strain of the 6 LV basal segments was 101 ± 9.7, 80.3 ± 9.2, and 66 ± 8.03 ms in baseline, conventional, and MPP configurations, respectively (MPP vs. basal $P = 0.012$). Finally, we observed a positive correlation ($r = 0.69$) between reduction in dyssynchrony and CI increase ($P < 0.0001$).

Conclusion

MPP showed a further reduction in LV dyssynchrony compared with conventional biventricular pacing. Moreover, MPP resulted in an additional improvement in LVEF and in CI, and this was translated into a higher number of acute responders to CRT.

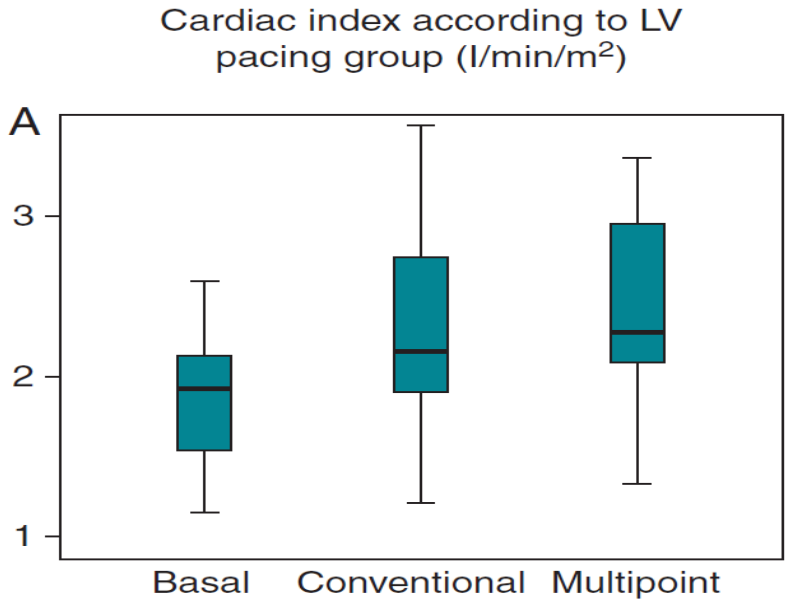
Europace (2016) **18**, 560–567

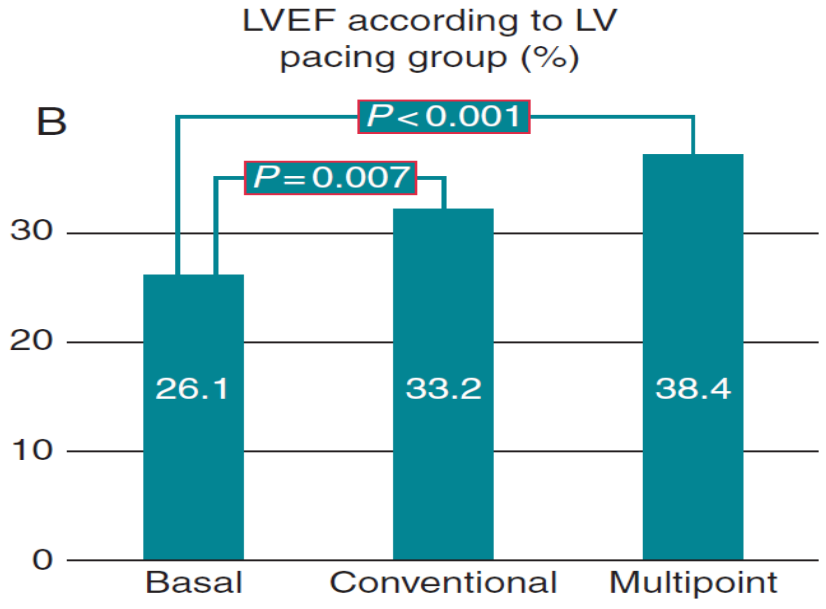
Quartet lead

Table 1 **Baseline characteristics of the study population ($n = 27$)**

Men, *n* (%)	21 (78)
Age (years)	65 ± 5
NYHA class	2.65 ± 0.16
II, *n* (%)	10 (37)
III, *n* (%)	16 (59)
IV, *n* (%)	1 (4)
Aetiology	
Ischaemic	11 (41)
Non-ischaemic	16 (59)
LVEF (%)	24.3 ± 1.8
Medical therapy	
ACE inhibitors, *n* (%)	23 (85)
β-Blockers, *n* (%)	24 (89)
Loop diuretics, *n* (%)	22 (81)
ARA, *n* (%)	13 (48)
QRS duration (ms)	165.6 ± 5.8
LBBB	23 (85)
Upgrading	4 (15)

Europace (2016) **18**, 560–567





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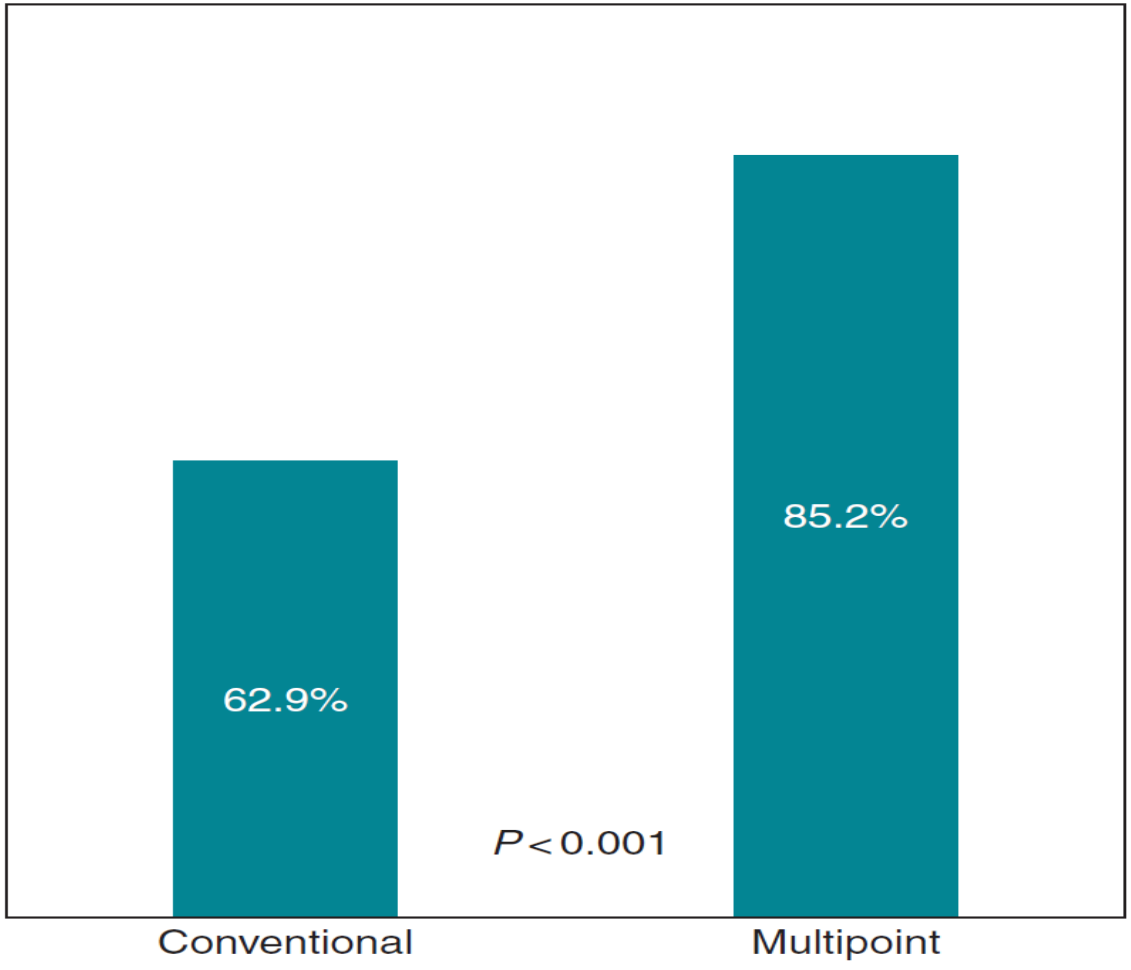
Europace (2016) **18**, 560–567

Percentage of acute haemodynamic responders to CRT



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Europace (2017) **0**, 1–7
doi:10.1093/europace/eux209

CLINICAL RESEARCH

Estimation of the effects of multipoint pacing on battery longevity in routine clinical practice

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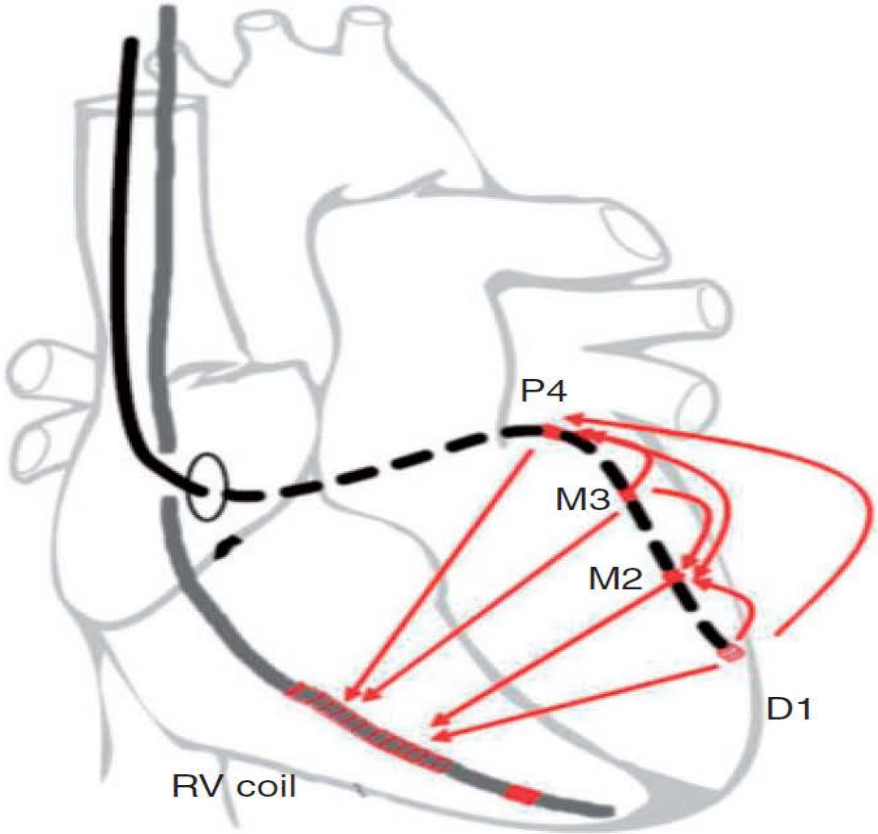
Methods and results

Patient ($n = 46$) and device data were collected from two centres at least 3 months after MPP-CRT device implantation. Multipoint pacing programming was based on the maximal possible anatomical LV1/LV2 separation according to three predefined LV pacing capture threshold (PCT) cut-offs (≤1.5 V; ≤4.0 V; and ≤6.5 V). Estimated battery longevity was calculated using the programmed lower rate limit, lead impedances, outputs, and pacing percentages. Relative to the longevity for conventional CRT using the lowest PCT (8.9 ± 1.2 years), MPP activation significantly shortened battery longevity for all three PCT cut-offs (≤1.5 V, -5.6%; ≤4.0 V, -16.9%; ≤6.5 V, -21.3%; *P*'s <0.001). When compared with conventional CRT based on longest right ventricle—LV delay (8.3 ± 1.3 years), battery longevity was significantly shortened for the MPP ≤ 4.0 V and ≤6.5 V cut-offs (-10.8 and -15.7%, respectively; *P*'s <0.001). Maximal LV1/LV2 spacing was possible in 23.9% (≤1.5 V), 56.5% (≤4.0 V), and 69.6% (≤6.5 V) of patients.

Conclusion

Multipoint pacing activation significantly reduces battery longevity compared with that for conventional CRT configuration. When reasonable MPP LV vector PCTs (≤4.0 V) are achieved, the decrease in battery longevity is relatively small which may prompt the clinician to activate MPP.

Europace (2017) **0**, 1–7



Available LV vectors (cathode–anode)	MPP cathode combinations (LV1/LV2)*
D1–M2	D1/P4
D1–P4	D1/M3
D1-RVCoil	D1/M2
M2-P4	M2/M3
M2-RVCoil	M2/P4
M3-M2	M3/P4
M3-P4	
M3-RVCoil	
P4-M2	
P4-RVCoil	

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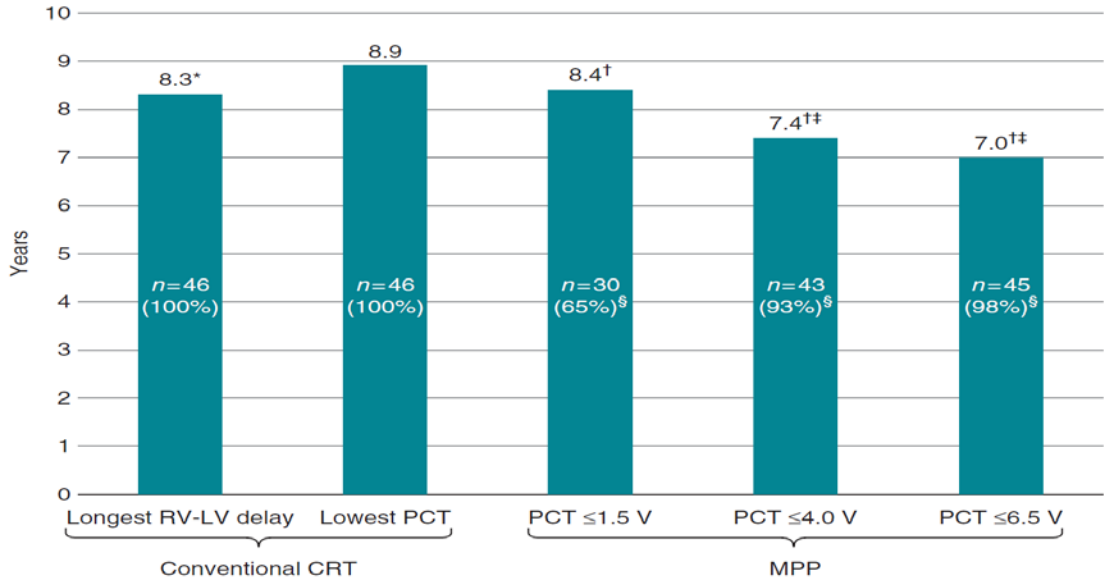

Figure 3 (Representative Figure) The estimated battery longevity based on device interrogation lead and programming data is shown for conventional (single left ventricle [LV] site) cardiac resynchronization therapy (CRT) and multipoint pacing (MPP) configurations. *$P = 0.001$ vs. conventional CRT using the lowest pacing capture threshold (PCT); †$P < 0.001$ vs. conventional CRT using the lowest PCT; ‡$P < 0.001$ vs. MPP PCT ≤ 1.5 V; and $P < 0.001$ vs. conventional CRT using the longest right ventricle (RV)-LV delay; §Patients with programmable MPP according to PCT cut-offs (proportion of the total cohort).

Table 4 Multipoint pacing (MPP) programmability and LV lead interelectrode spacing, *n* (%)

	MPP PCT ≤1.5 V	MPP PCT ≤4.0 V	MPP PCT ≤6.5 V
MPP not programmable	16 (34.8)	3 (6.5)*	1 (2.2)*,†
Interelectrode spacing[a]			
1	9 (19.6)	5 (10.9)	3 (6.5)
2	10 (21.7)	12 (26.1)	10 (21.7)
3	11 (23.9)	26 (56.5)*	32 (69.6)*,‡

LV, left ventricle; PCT, pacing capture threshold.

[a]Interelectrode cathode spacing for the following MPP vector combinations: 1 = D1/M2, M2/M3, or M3/P4; 2 = D1/M3 or M2/P4; and 3 = D1/P4.

*P <0.001 vs. MPP PCT ≤ 1.5 V.

†P = 0.5 vs. MPP PCT ≤ 4.0 V.

‡P = 0.031 vs. MPP PCT ≤ 4.0 V.

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	☐	Not yet recruiting	Heart Failure Study of **Multi-site Pacing** Effects on Ventriculoarterial Coupling	• Heart Failure	• Device: Activation of multi-site pacing capability on CRT devices	• First Department of Cardiology, Hippokration General Hospital Athens, Attiki, Greece
2	☐	Completed	**Multisite Pacing** With a Quadripolar Lead	• Heart Failure	• Device: Quadripolar LV lead (pacing configurations)	• Montreal Heart Institute Montreal, Quebec, Canada
3	☐	Not yet recruiting	Strategic Management to Improve CRT Using **Multi-Site Pacing** Post Approval Study (Reference # C1918)	• Left Ventricular Dysfunction	• Device: CRT-D	
4	☐	Completed	Characterization of Cardiac Hemodynamics During **MultiSite Pacing**	• Heart Failure		• Maria Cecilia Hospital Cotignola, Italy
5	☐	Completed	An Assessment of Dual Site Left Ventricular Endocardial **Pacing**	• Atrial Fibrillation • Ventricular Tachycardia • Heart Failure	• Procedure: Atrial Fibrillation/flutter (AF) or Ventricular Tachycardia (VT) ablation with multi-site pacing protocol	• Oxford University Hospitals NHS Trust Oxford, Oxfordshire, United Kingdom

ClinicalTrials.gov

More-CRT MPP

- After 6 months, evaluation of response
- If < 15% reduction in LVESV
  - Randomized to standard CRT or MPP programming

ENROLLMENT STATUS: 3556 out of 3796 patients have been enrolled (93.7% of the sample size) (Phase I and Phase II)
1634 out of 1898 patients have been enrolled (86.1% of the sample size) (Phase II only)

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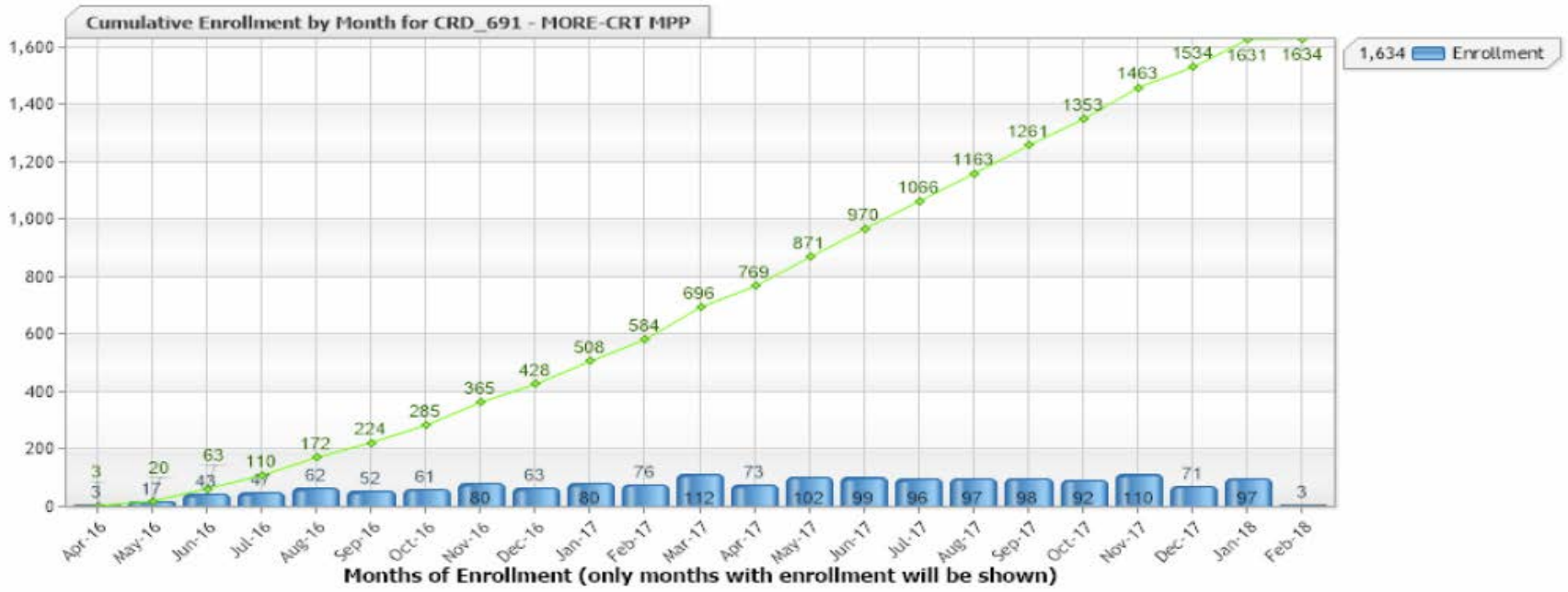
MORE-CRT MPP



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Conclusions

- MSP increases pacing loci with more rapid activation
- MSP showed promising results in acute studies
  - ↑ LV systolic function
  - ↓ Mechanical dyssynchrony
  - ↑ Radial strain
  - Improvement even in responders
  - Better in ischemic population with scar?
- MSP achieved with quadripolar leads seems the best option to test in large clinical trials for outcomes

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