

Validation of a peak endocardial acceleration-based algorithm to optimize cardiac resynchronization: early clinical results

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Aims Cardiac resynchronization therapy (CRT) involves time-consuming procedures to achieve an optimal programming of the system, at implant as well as during follow-up, when remodelling occurs. A device equipped with an implantable sensor able to measure peak endocardial acceleration (PEA) has been recently developed to monitor cardiac function and to guide CRT programming. During scanning of the atrioventricular delay (AVD), PEA reflects both left ventricle (LV) contractility (LV dP/dt_{max}) and transmitral flow. A new CRT optimization algorithm, based on recording of PEA (PEA_{area} method) was developed, and compared with measurements of LV dP/dt_{max} , to identify an optimal CRT configuration.

Methods and results We studied 15 patients in New York Heart Association classes II–IV and with a QRS duration > 130 ms, who had undergone implantation of a biventricular (BiV) pulse generator connected to a right ventricular (RV) PEA sensor. At a mean of 39 ± 15 days after implantation of the CRT system, the patients underwent cardiac catheterization. During single-chamber LV or during BiV stimulation, with initial RV or LV stimulation, and at settings of interventricular intervals between 0 and 40 ms, the AVD was scanned between 60 and 220 ms, while LV dP/dt_{max} and PEA were measured. The area of PEA curve (PEA_{area} method) was estimated as the average of PEA values measured during AVD scanning. A $\geq 10\%$ increase in LV dP/dt_{max} was observed in 12 of 15 patients (80%), who were classified as responders to CRT. In nine of 12 responders (75%), the optimal pacing configuration identified by the PEA_{area} method was associated with the greatest LV dP/dt_{max} .

Conclusion The concordance of the PEA_{area} method with measurements of LV dP/dt_{max} suggests that this new, operator-independent algorithm is a reliable means of CRT optimization.

Introduction

Cardiac resynchronization therapy (CRT) is an established therapy for patients with advanced, congestive heart failure (CHF) associated with cardiac dyssynchrony. The mechanisms of action of CRT are complex, as it interacts with several electromechanical variables, including atrioventricular (AV), interventricular (VV), intraventricular,

and intramural delays. Information regarding the optimal programming and follow-up of these devices are limited.

Left ventricular (LV) dP/dt_{max} and several non-invasive indices have been used to optimize the functions of CRT devices, in particular AV delay (AVD) and VV configuration,^{1–6} and recent clinical experience has confirmed the need for, and benefits of their long-term reprogramming, as their optimal stimulation settings might change over time.^{7–10}

A direct assessment of changes in systolic function (LV dP/dt_{max}) determined to CRT requires invasive measurements,

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which are neither practical, nor ethically acceptable as a routine procedure.

As a consequence, in clinical practice, the optimization of CRT is usually achieved with the assistance of non-invasive echocardiographic procedures, which can only be performed with the patient supine, and are costly, time-consuming, and operator-dependent.

A haemodynamic sensor integrated in a CRT pulse generator, which automatically calculates and optimizes the programmable settings of the device, might be an objective means of assessing and adjusting therapy, also during activities or exercise.

As the myocardium contracts isometrically, it generates muscular and valve vibrations (endocardial accelerations) that are transmitted throughout the heart and thus measured with an implantable microaccelerometer located inside the tip of a conventional unipolar pacing lead. These vibrations, in their audible component, are responsible for the first heart sound. A pacing system equipped with a microaccelerometer sensor (PEA sensor), able to measure the peak of the endocardial acceleration during the isovolumic contraction phase (first component of the signal here defined as 'PEA'), has been previously developed and clinically evaluated.^{11,12} The system allows monitoring of myocardial function by means of PEA, which was identified as an expression of cardiac contractility.¹³ Till now, several clinical applications and tools based on PEA assessment have been proposed.¹⁴⁻¹⁷

A new CRT-P device (The New Living™ CHF, Sorin Group CRM, Saluggia, Italy) equipped with an implantable PEA sensor has been recently developed to monitor cardiac function and guide CRT programming in patients affected by CHF.

This study examined the performance of a new CRT optimization algorithm based on PEA measurements (PEA_{area} method) in the identification of the optimal CRT pacing configuration, compared with direct measurements of LV pressure (LV dP/dt_{max}).

Methods

Patient population

The study included 15 patients (mean age = 72 ± 8 years, 13 men) with indications of CRT in accordance with standard international guidance. They were in New York Heart Association (NYHA) CHF functional class II-IV, despite stable optimal medical therapy, including β -adrenergic blockers ($n = 14$) and angiotensin-converting enzyme-inhibitors or angiotensin II blockers ($n = 13$). All patients were in sinus rhythm. Their mean echocardiographic LV ejection fraction (EF) was $\leq 35\%$ (mean = $23 \pm 8\%$) and QRS duration > 130 ms (mean = 170 ± 16 ms). The underlying heart disease was ischaemic in eight and non-ischaemic in seven patients. Exclusion criteria were: possible surgical treatment (myocardial revascularization or valve replacement), life-threatening ventricular arrhythmias, right ventricular (RV) dimension superior to LV dimension, myocardial infarction, coronary artery bypass grafting (CABG) within last 3 months, patient already implanted with a conventional pacemaker. The study protocol was approved by our institutional review committee, and all patients granted their informed consent before enrolment.

Implantation of the cardiac resynchronization system

All patients underwent implantation of Living™ CHF or NewLiving™ CHF CRT pulse generators (Sorin Group CRM), connected to standard atrial and LV pacing leads. The LV lead was inserted transvenously through the coronary sinus, preferably into a lateral or postero-lateral cardiac vein. A pacing lead (BEST™, Sorin Group CRM) with a micro-accelerometer sensor inside its tip was implanted at the RV apex to record the PEA signal. At implant, all pulse generators were programmed in dual chamber atrioventricular synchronous (DDD) mode and simultaneous biventricular (BiV) stimulation ($VV = 0$), and the AVD was adjusted to ensure full electrical pre-excitation of the ventricles during DDD pacing. The average AVD was 154 ± 20 ms.

Catheterization procedure

At a mean interval of 39 ± 15 days after implantation of the CRT system, the patients underwent cardiac catheterization under mild sedation. Haemodynamic measurements were performed using a 7F pigtail catheter equipped with a high-fidelity pressure transducer (CD-Leycom, Zoetermeer, The Netherlands). The catheter was advanced into the LV from the left femoral artery and connected to a signal-conditioning module (Sentron, Roden, The Netherlands) to record pressure.

Stimulation protocol

After placement of the pressure catheter, the heart was stimulated programming the device with a PMP 2000T external programmer (Sorin Group CRM).

The protocol included single LV and BiV stimulation, either simultaneously (BiV0), or sequentially at VV intervals of 12 or 40 ms, with LV (LR12, LR40) or RV (RL12, RL40) preactivation, in a random order. At each of these configurations, the AVD was scanned between the shortest 60 ms and the longest 220 ms interval, with four increments of AVD_{step} calculated as $(PR - 90)/4$ ms. The five tested AVD intervals were: 60 ms, $60 + 1 \times AVD_{step}$ ms, $60 + 2 \times AVD_{step}$ ms, $60 + 3 \times AVD_{step}$ ms, and $60 + 4 \times AVD_{step}$ ms. The AVD scans performed for each patient are listed in *Table 1*.

Data sampling and analysis

PEA signals, LV pressure with LV dP/dt_{max} calculation, and analog electrocardiographic signals were recorded simultaneously, using a MP100 acquisition system (Biopac System Inc., Goleta, CA, USA) at a sampling rate of 1000 Hz for each channel. For each pacing configuration, a 10-s programming period was required and a 30-s recording period was preceded by a stabilization period of 30 s (i.e. a total of 70 s for each configuration). According to the stimulation protocol, six pacing configurations were tested (RL40, RL12, BiV0, LR12, LR40, LV), performing AVD scanning over five AVD intervals. Thus, the total time needed to find the optimal pacing configuration with the new PEA_{area} method was approximately 35 min (2100 s), calculated as $(70 \text{ s}) \times (6) \times (5) = 2100 \text{ s}$.

For PEA recordings, the voltage signal generated by the acceleration was measured from peak to peak in gravity ($1g = 9.8 \text{ m/s}^2$). LV dP/dt_{max} and PEA were measured at steady state, cycle-by-cycle, using the AcqKnowledge 3.8.1 analysis software (Biopac System Inc., Goleta, CA, USA),

Table 1 Scans of the atrioventricular delay

Patient no.	Atrioventricular delay (ms)											
	60	80	90	100	110	120	140	150	160	180	220	
1	X		X			X	X	X		X		
2	X			X			X			X	X	
3	X			X						X	X	
4	X		X			X		X		X		
5	X		X			X		X		X		
6	X		X			X	X	X		X		
7	X			X						X	X	
8	X		X			X		X		X		
9	X		X			X		X		X		
10	X		X			X		X		X		
11	X	X			X				X		X	
12	X		X			X		X		X		
13	X		X			X	X	X		X		
14	X			X						X	X	
15	X		X			X		X		X		

Each scan was performed during single chamber left ventricular (LV) stimulation and during biventricular stimulation at 0, 12, and 40 ms VV intervals, with LV (LR12, LR40) or right ventricular (RL12, RL40) preactivation.

and values, sampled over approximately 30 s, were averaged. Cycles with failure to capture, affected by extra-systolic events and post-extrasystolic cycles were excluded from the analysis. LV dP/dt_{max} and PEA were first measured during intrinsic rhythm, used as the reference patient's status condition. The heart rate was kept constant by atrial pacing for all subsequent stimulation sequences.

Optimization of cardiac resynchronization

Response to CRT was defined as a $\geq 10\%$ increase in LV dP/dt_{max} , considered the gold standard to monitor cardiac function in clinical CRT studies,^{9,10} as it is reliable, reproducible, and not operator-dependent. For each patient, the optimal CRT configuration was determined by comparing the optimization criteria based on measurements of LV dP/dt_{max} (LV dP/dt_{max} method) vs. measurements of PEA (PEA_{area} method).

The new PEA_{area} method

Studies in animals have shown that the peak-to-peak value of acceleration of heart vibrations (PEA), recorded during LV isovolumic contraction with an accelerometer sensor, corresponds to the endocardial recording of the first heart sound (S1).¹⁸ LV contractility, as expressed by the maximum rate of rise of LV pressure (LV dP/dt_{max}), and the respective timing of atrial and ventricular systoles (the AVD), are both major and independent determinants of the amplitudes of S1 and PEA, in normal and in failing hearts.^{19–24} In normal hearts, shortening of the AVD causes a rapid increase in PEA amplitude, mainly determined by the degree of opening of the mitral valve leaflets, strictly related to an increase in transmitral flow during the A wave, while LV dP/dt_{max} remains relatively fixed. Similar results have been shown in clinical studies of CRT, where LV dP/dt_{max} remained nearly fixed with shortening of the AVD in case of successful resynchronization procedures, whereas it decreased with shortening of the AVD in case of unsuccessful resynchronization attempts.¹⁰

The new PEA_{area} method is, according to these results, based on measurements of the area under the PEA curve:

it is expected to have a lower PEA_{area} in case of unsuccessful resynchronization attempts, because of LV dP/dt_{max} decreasing for short AVDs, with respect to successful resynchronization procedure in which LV dP/dt_{max} remained nearly fixed. For each tested VV interval setting, the area of PEA curve was estimated, using a simplified formula, as the average of PEA values measured during AVD scanning (Figure 1A–D). Thus, the PEA_{area} is an index of both contractility variations and transmitral flow variations, and we assumed that an increase in the area reflects an increase in overall haemodynamic benefit achieved by the programmed configuration.

Statistical analysis

The mean values of LV dP/dt_{max} , calculated over a period of 10 respiratory cycles at each pacing configuration, were compared, using the Student-Newman-Keuls test for comparison of multiple variables. This specific *t*-test for comparison of paired variables belonging to a group, takes into account, for each paired comparison, the influence of all variables included in the group. A value of $\alpha \tau < 0.05$ was considered statistically significant.

Results

Responder patients were identified by a $\geq 10\%$ increase in LV dP/dt_{max} . Among the 15 patients included in this study, 12 (80%) were responders, a proportion consistent with other clinical studies of CRT.^{9,10} In 9 out of the 12 responders (75%), the results of the LV dP/dt_{max} and PEA_{area} methods were concordant (Table 2). The haemodynamic responses (LV dP/dt_{max} and PEA_{area} trends) for different pacing configurations are shown in Figure 2A–D for the same four representative patients used for showing the PEA_{area} curve during AVD scanning in Figure 1A–D.

The overall means and standard deviations for LV dP/dt_{max} and PEA_{area} values for pacing configuration for each patient were reported in Table 3.

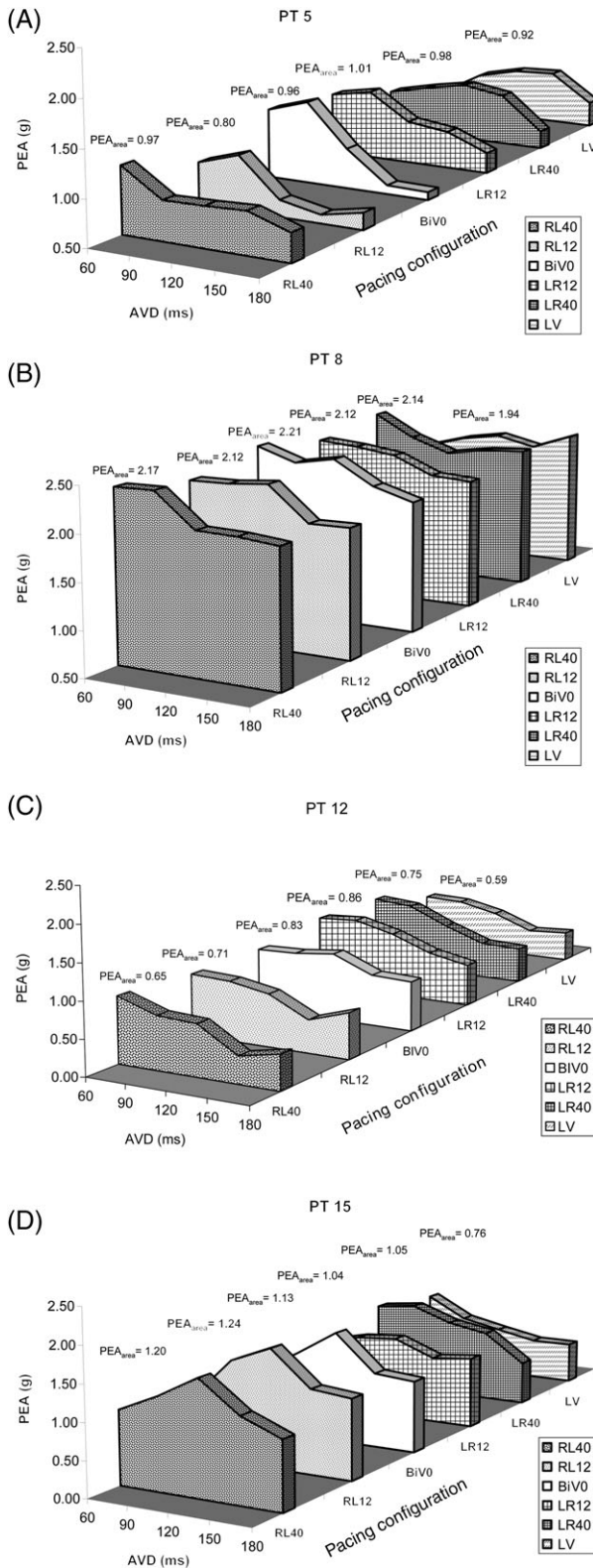


Figure 1 (A–D) Representative examples among cardiac resynchronization therapy responder patients of (peak endocardial acceleration) PEA_{area} curve measured during atrioventricular delay scanning for different pacing configurations [RL40: sequential biventricular pacing with 40 ms of right ventricular (RV) preactivation; RL12: sequential biventricular pacing with 12 ms of RV preactivation; LR12: sequential biventricular pacing with 12 ms of left ventricular (LV) preactivation; LR40: sequential biventricular pacing with 40 ms of LV preactivation; BiV0: simultaneous biventricular pacing].

Table 2 Concordance of the optimal pacing configuration identified by the LV dP/dt_{max} vs. PEA_{area} methods

Patient no.	Optimal configuration		Concordance
	LV dP/dt_{max}	PEA _{area}	
1	LR40, LV	LR40	+
2	BiV0, RL40, RL12, LR12	BiV0	+
3	NR	NR	NR
4	NR	NR	NR
5	LR12, BiV0, LV, LR40	LR12	+
6	NR	NR	NR
7	LV	RL12	–
8	BiV0, LR12	BiV0	+
9	RL12	RL12	+
10	RL12	LR40	–
11	LV, RL12	LV	+
12	LR12, LR40	LR12	+
13	LR40, LV	LR40	+
14	LR40	LR12	–
15	RL12, BiV0, LR12	RL12	+

+, concordant; –, non-concordant; NR, non-responder.

Both methods identified the greatest haemodynamic improvement with LV preactivation or single-chamber LV stimulation in six, RV preactivation in three, and simultaneous biventricular stimulation in two responders. LV preactivation or single chamber LV stimulation was associated with the greatest haemodynamic improvement by at least one method in nine, RV preactivation in five, and BiV stimulation in four responders. Finally, in eight responders, more than one optimal stimulation configuration (range 2–4) were identified by the LV dP/dt_{max} method (including opposite ventricular preactivation in two patients), whereas the PEA_{area} method identified a single optimal configuration in all responders (Table 2).

For each patient, the values of LV dP/dt_{max} increase in % for the optimal pacing mode, compared with PEA_{area} variations in % for the optimal pacing mode, were summarized in a scatter diagram plot (Figure 3).

Discussion

With the currently available CRT pulse generators, the AVD and the VV interval have become programmable, and their optimization is generally recommended, as an appropriate selection of VV interval might further optimize LV function, at implant as well as during follow-up.^{25–32} Therefore, a direct comparison of a new method of CRT optimization, based on PEA measurements, with LV dP/dt_{max} , the haemodynamic gold standard, was of particular interest. LV dP/dt_{max} has been used previously as an index of LV performance in CRT.^{27–29} However, it is influenced by heart rate, preload, LV synchronization, and degree of mitral regurgitation. Furthermore, when applied to optimize CRT, it requires an invasive procedure, and its value is limited to short-term observations. On the contrary, the optimization of CRT based on individual adjustments of heart rate, AVD, VV interval, and mode of stimulation can be accomplished non-invasively in the long term, with the assistance of haemodynamic sensors integrated in the implanted devices. The perspective of being able to re-adjust CRT, with an

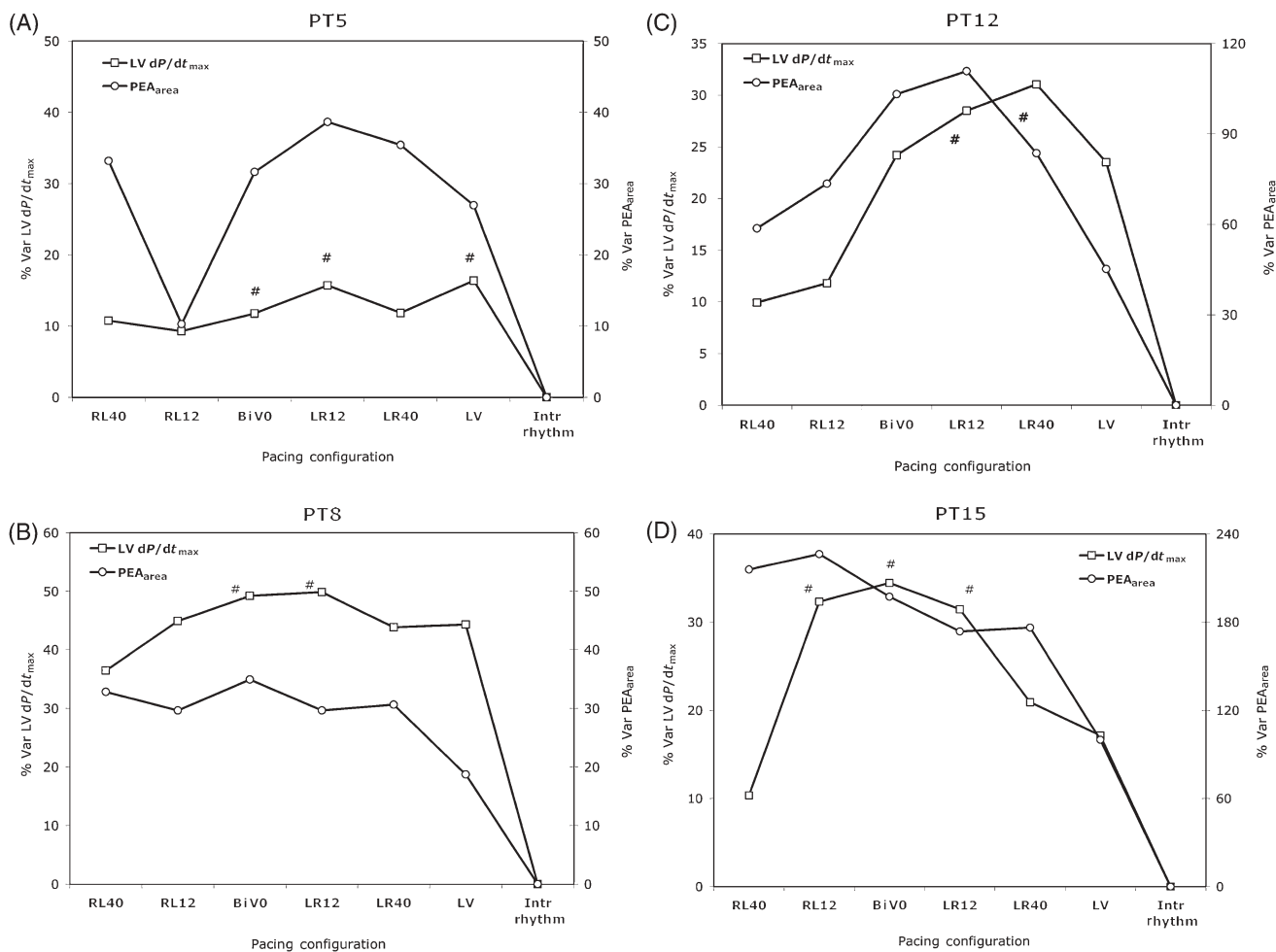


Figure 2 (A–D) Comparison between (peak endocardial acceleration) PEA_{area} method and LV dp/dt_{max} method in identifying the optimal stimulation configuration for the same representative responder patients reported in Figure 1. Measurements made during intrinsic rhythm were used as baseline to calculate % variation of PEA_{area} and LV dp/dt_{max} indexes. Symbol # indicates absence of significant difference between the two or more cardiac resynchronization therapy configurations by Student-Newman-Keuls analysis.

automatic on board function for periodic CRT optimization by PEA, at rest and during lifetime exercise activity, is attractive and preferable to the echocardiographic procedures that are currently applied in clinical practice only at follow-up. Moreover, the echocardiographic method is not so sensitive and might not be able to detect subtle changes in LV systolic function. Therefore, the consistent results obtained with the PEA_{area} method, validated by the direct measurements of LV dp/dt_{max}, strongly support the introduction of this new operator-independent method of CRT optimization into clinical practice and implantable devices.

Study limitations

The absence of an automated stimulation protocol and data analysis system limited the number of AVD used to calculate the area of PEA curve and VV intervals we were able to test. However, we believe that for preliminary evaluation of the new PEA-based method a five-step AVD scanning may be enough to provide meaningful data to estimate area under the PEA curve.

The number of patients included in the present study was relatively small, even if the rate of CRT responders was comparable with data reported in literature.³³

Furthermore, our method, based on the measurement of PEA during scanning of the AVD, is not applicable to patients presenting with atrial fibrillation.

Among 12 responders, according to the LV dp/dt_{max} measurement, three patients showed no concordant results between LV dp/dt_{max} and PEA_{area} method indications. For one patient, during the procedure, we encountered some problems with the pressure catheter that required its repositioning. Even if we used the same calibrating procedure, the obtained LV dp/dt_{max} trend could have been altered because of LVP recordings assessed before and after catheter repositioning.

For the other two patients, the optimal CRT configuration indicated by PEA_{area} method is ‘adjacent’ to the best configuration indicated by LV dp/dt_{max}. This means that the optimal configuration indicated by LV dp/dt_{max} corresponds to the ‘second optimal’ configuration indicated by PEA_{area} slightly lower than the optimal PEA_{area} value. Small differences can be observed between the optimal and the ‘second optimal’ CRT configurations indicated by PEA_{area}; consequently, for these two patients we can say that, even if PEA_{area} and LV dp/dt_{max} methods does not provide exactly the same CRT best mode, however it is clear that both identified the same optimal range of CRT configurations

Table 3 Means and standard deviation (SD) for LV dp/dt_{max} and PEA_{area} values for each pacing configuration, for each patient

Patient no.	LV dp/dt_{max} (mmHg/s)		PEA_{area} (g)		
	Configuration	Mean \pm SD	Configuration	Mean \pm SD	
1	RL40	680 \pm 33	RL40	0.68 \pm 0.09	
	RL12	695 \pm 25	RL12	0.68 \pm 0.09	
	BiV0	724 \pm 38	BiV0	0.68 \pm 0.08	
	LR12	711 \pm 22	LR12	0.73 \pm 0.09	
2	LR40	777 \pm 35	LR40	0.77 \pm 0.07	
	LV	778 \pm 59	LV	0.63 \pm 0.06	
	RL40	1429 \pm 39	RL40	1.63 \pm 0.16	
	RL12	1434 \pm 57	RL12	1.62 \pm 0.17	
	BiV0	1440 \pm 37	BiV0	1.65 \pm 0.16	
	LR12	1425 \pm 38	LR12	1.45 \pm 0.17	
	LR40	1341 \pm 38	LR40	1.19 \pm 0.17	
	LV	1270 \pm 32	LV	0.84 \pm 0.10	
3	NR	NR	NR	NR	
4	NR	NR	NR	NR	
5	RL40	1289 \pm 43	RL40	0.97 \pm 0.10	
	RL12	1272 \pm 64	RL12	0.80 \pm 0.10	
	BiV0	1301 \pm 99	BiV0	0.96 \pm 0.05	
	LR12	1347 \pm 57	LR12	1.01 \pm 0.07	
	LR40	1301 \pm 86	LR40	0.98 \pm 0.08	
	LV	1355 \pm 102	LV	0.92 \pm 0.05	
	6	NR	NR	NR	NR
	7	RL40	1269 \pm 22	RL40	1.24 \pm 0.13
RL12		1257 \pm 28	RL12	1.33 \pm 0.12	
BiV0		1233 \pm 33	BiV0	1.26 \pm 0.11	
LR12		1216 \pm 27	LR12	1.23 \pm 0.12	
LR40		1271 \pm 68	LR40	1.00 \pm 0.11	
LV		1303 \pm 61	LV	0.56 \pm 0.07	
8	RL40	644 \pm 29	RL40	2.17 \pm 0.28	
	RL12	683 \pm 26	RL12	2.12 \pm 0.45	
	BiV0	704 \pm 26	BiV0	2.21 \pm 0.34	
	LR12	707 \pm 20	LR12	2.12 \pm 0.27	
	LR40	678 \pm 19	LR40	2.14 \pm 0.33	
	LV	680 \pm 39	LV	1.94 \pm 0.22	
9	RL40	1388 \pm 35	RL40	0.31 \pm 0.03	
	RL12	1509 \pm 64	RL12	0.32 \pm 0.02	
	BiV0	1292 \pm 59	BiV0	0.29 \pm 0.02	
	LR12	1221 \pm 42	LR12	0.29 \pm 0.01	
	LR40	1285 \pm 51	LR40	0.26 \pm 0.02	
	LV	1257 \pm 41	LV	0.30 \pm 0.02	
10	RL40	1160 \pm 24	RL40	0.11 \pm 0.01	
	RL12	1195 \pm 38	RL12	0.10 \pm 0.01	
	BiV0	1137 \pm 26	BiV0	0.08 \pm 0.01	
	LR12	1161 \pm 28	LR12	0.08 \pm 0.01	
	LR40	1121 \pm 21	LR40	0.08 \pm 0.01	
	LV	1094 \pm 23	LV	0.09 \pm 0.01	
11	RL40	825 \pm 21	RL40	0.51 \pm 0.08	
	RL12	845 \pm 45	RL12	0.51 \pm 0.07	
	BiV0	479 \pm 21	BiV0	0.56 \pm 0.08	
	LR12	779 \pm 24	LR12	0.64 \pm 0.07	
	LR40	815 \pm 22	LR40	0.73 \pm 0.06	
	LV	840 \pm 27	LV	0.74 \pm 0.07	
12	RL40	888 \pm 22	RL40	0.65 \pm 0.08	
	RL12	903 \pm 50	RL12	0.71 \pm 0.11	
	BiV0	1004 \pm 31	BiV0	0.83 \pm 0.07	
	LR12	1038 \pm 76	LR12	0.86 \pm 0.14	
	LR40	1059 \pm 51	LR40	0.75 \pm 0.05	
	LV	998 \pm 36	LV	0.59 \pm 0.06	
13	RL40	1271 \pm 46	RL40	0.45 \pm 0.03	
	RL12	1259 \pm 36	RL12	0.38 \pm 0.03	

*Continued***Table 3** *Continued*

Patient no.	LV dp/dt_{max} (mmHg/s)		PEA_{area} (g)	
	Configuration	Mean \pm SD	Configuration	Mean \pm SD
	BiV0	1265 \pm 30	BiV0	0.39 \pm 0.03
	LR12	1298 \pm 31	LR12	0.43 \pm 0.04
	LR40	1332 \pm 53	LR40	0.47 \pm 0.02
	LV	1341 \pm 58	LV	0.46 \pm 0.03
	14	RL40	901 \pm 21	RL40
RL12		910 \pm 30	RL12	0.61 \pm 0.08
BiV0		954 \pm 20	BiV0	0.66 \pm 0.07
LR12		944 \pm 28	LR12	0.67 \pm 0.06
LR40		989 \pm 20	LR40	0.66 \pm 0.05
15	LV	964 \pm 20	LV	0.43 \pm 0.05
	RL40	1140 \pm 31	RL40	1.20 \pm 0.17
	RL12	1367 \pm 49	RL12	1.24 \pm 0.11
	BiV0	1389 \pm 44	BiV0	1.13 \pm 0.12
	LR12	1358 \pm 52	LR12	1.04 \pm 0.11
	LR40	1249 \pm 56	LR40	1.05 \pm 0.11
	LV	1210 \pm 113	LV	0.76 \pm 0.11

Bold denotes optimal pacing configuration.

(RV preactivation—RL12, RL40—in one case, and LV preactivation—LR12, LR40—for the other). Moreover, for sequential BiV stimulation we performed a VV interval scanning with only two increments of VV step (12 ms, 40 ms). Probably, a more refined VV interval scanning (e.g. four increments of VV step, from 12 to 40 ms) would have helped in determining the optimal configuration for these two 'no concordant' patients, as for both LV dp/dt_{max} and PEA_{area} methods the best pacing mode could correspond to a configuration with VV interval included in the range of 12–40 ms.

We are working towards implementing the CRT-P device as an automated stimulation protocol and PEA_{area} calculations during AVD scanning in order to provide a more practical and systematic method to apply for a more large and complete clinical study. With this automated PEA_{area} algorithm implemented in the device, the time needed to find the optimal pacing configuration can be reduced up to 10–15 min, minimizing the programming and the recording periods.

Finally, the outcomes of CRT optimization based on the PEA_{area} method might not be predicted over an intermediate or long-term follow-up. Thus, the long-term performance of the PEA_{area} index must be clinically validated.

In the next clinical study, we are planning to validate the method; results obtained with the automated PEA_{area} algorithm implemented in the device will be compared with clinical non-invasive measurements of cardiac performance and CRT outcome (e.g. the 6 min-walk test), at implant and during periodic follow-up (three or six months after implant).

Conclusions

Recent clinical studies have shown that CRT might require reprogramming during follow-up. The proposed method, based on measurements of the area under the PEA curve during scanning of the AVD with different CRT configurations, might be the answer to the need of automatic CRT optimization at implant and during follow-up. The attainment of concordant results with invasive haemodynamic

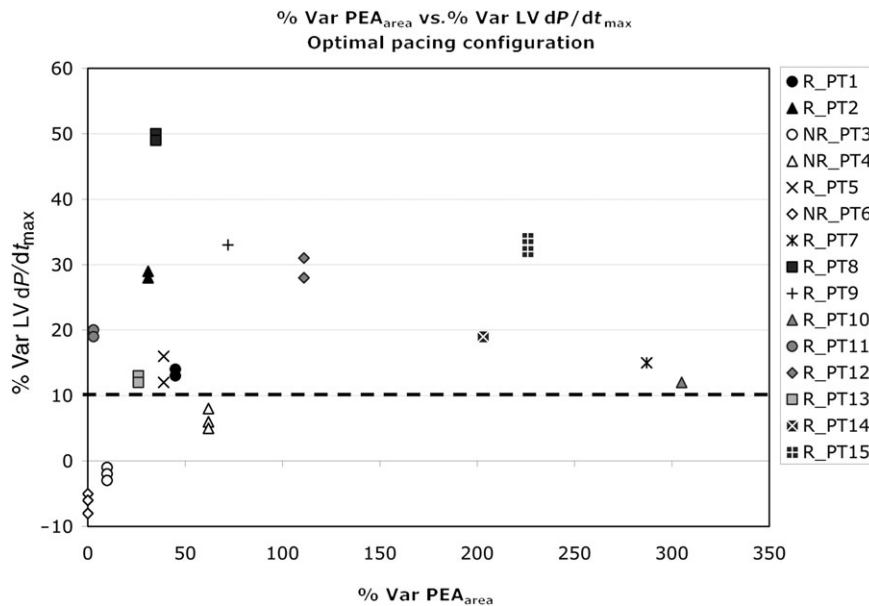


Figure 3 Scatter diagram plot of LV dP/dt_{max} % variations vs. (peak endocardial acceleration) PEA_{area} % variations, for each patient in the optimal pacing configuration.

measurements in the majority of responders warrant further testing of this operator-independent and expeditious method of CRT optimization in a larger patient population.

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