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Abstract

Cardiac resynchronization therapy (CRT) is the therapy of choice for selected patients suffering from drug-refractory congestive heart failure and presenting an interventricular desynchronization. CRT is delivered by an implantable biventricular pacemaker, which stimulates the right atrium and both ventricles at specific timings. The optimization and personalization of this therapy requires to quantify both the electrical and the mechanical cardiac functions during the intraoperative and postoperative phases.

The objective of this paper is to evaluate the feasibility of the calculation of features extracted from endocardial acceleration (EA) signals and the potential utility of these features for the intraoperative optimization of CRT. Endocardial intraoperative data from one patient are analyzed for 33 different pacing configurations, including changes in the atrio-ventricular and inter-ventricular delays and different ventricular stimulation sites. The main EA features are extracted for each pacing configuration and analyzed so as to estimate the intra-configuration and inter-configuration variability. Results show the feasibility of the proposed approach and suggest the potential utility of EA for intraoperative monitoring of the cardiac function and defining optimal, adaptive pacing configurations.

INTRODUCTION

Heart failure (HF) is a multifactorial syndrome presenting one of the highest prevalence and incidence worldwide. Selected patients suffering from drug-refractory congestive heart failure (CHF) and presenting an inter-ventricular desynchronization are candidates for Cardiac Resynchronization Therapy (CRT) [1]. In CRT, a bi-ventricular stimulator is implanted in order to electrically stimulate the right atrium (RA), the right ventricle (RV) and the left ventricle (LV) at specific timings, so as to improve the ventricular filling phase and re-synchronize the mechanical function of both ventricles. Previous clinical trials, have demonstrated the efficacy of CRT, however, they have also shown a proportion of nonresponders to the therapy of around 30% [1].

Several factors may cause the nonresponse to CRT, including i) inappropriate patient selection, ii) sub-optimal lead positioning and iii) the inaccurate and non-adaptive programming of the stimulation instants of each lead, which are defined by the atrioventricular (AV) and interventricular (VV) delays (AVD and VVD respectively). The optimization of these factors, in a patient-specific manner, are thus a main priority in the context of CRT. This work is focused on a method that may assist the clinician in optimizing lead placement and the programming of AVD and VVD. It requires the ability to quantify both the electrical and the mechanical cardiac functions during the intra-operative and post-operative phases. We hypothesize that the joint analysis of intracardiac electrocardiographic and micro-acceleration signals could be useful for this optimization task.

The analysis of cardiac acoustic signals has been shown to be useful for the evaluation of the mechanical function of the heart. A variety of methods for the analysis of the phonocardiogram (PCG) or the seismocardiogram (SCG) have been proposed to extract useful information about the cardiac function and to estimate the main events of the cardiac cycle [2,3]. Although the arrival of Doppler echocardiography significantly reduced the clinical use of these signals, the quality of new miniaturized accelerometers and new signal-processing techniques have lead to a renewed interest in quantitative analysis of cardiac acoustic signals, especially in the field of CRT [4,5,6,7,8].

In this context, previous animal experimentation studies have shown that the analysis of endocardial acceleration (EA) signals may be valuable for an online follow-up of the inotropic state [9]. The EA signal is composed of two main components, denoted here EA1 and EA2, that are synchronous with the first and second heart sounds of the PCG, respectively. Plicchi et al. have particularly shown that changes in the peak-to-peak amplitude of EA1 (PEA1) were significantly correlated to changes on the positive peak of LV dP/dt [9].

Previous works from our group have demonstrated how the joint analysis of a set of features extracted from thoracic cardiac micro-acceleration signals may be useful for AV and VV delay optimization in CRT [5,7,8]. Recently, a right atrial lead integrating a

micro-accelerometer inside a hermetically-sealed capsule located in the tip of the pacing lead, has been approved for human use (SonRtip ™ lead, Sorin CRM SAS, Clamart, France). The objective of this work is to evaluate the feasibility of the calculation of features extracted from the EA, using the methods proposed in our previous works, that are sensitive to intraoperative changes on AVD, VVD or in pacing lead position. Data acquired during intraoperative CRT optimization from one clinical case will be analyzed and presented.

METHOD

Experimental Protocol

This paper is focused on data from one patient that were acquired during a clinical procedure using the recent SonRtip™ atrial lead. Leads on the RA, RV and LV were implanted using the standard procedure for a CRT system. The RA lead was implanted on the RA appendage or in the RA septum. Data acquired from the EA sensor represents thus a mixture of mainly the antero-posterior and coronal components of the mechanical cardiac function. Different pacing configurations during stable atrial pacing were applied intra-operatively to evaluate their impact on the acquired EA signal. Each configuration, denoted here P*k*, for $k \in$ [11,12,14,16,18,19,21,22,24,25,26], consisted of a combination of the following parameters:

- Pacing mode: All beats were initiated by an RA stimulation with a fixed heart rate of 90 beats per minute, in AAI mode. Three ventricular pacing modes were evaluated: i) spontaneous AV conduction and no ventricular pacing (P*k*-AAI), ii) pacing only the right ventricle (P*k*-RV) and iii) bi-ventricular pacing (P*k*-BiV).

- Atrio-ventricular delay (AVD): All configurations have been acquired with an AVD of 120 ms, except from the following configurations: P24, with an AVD = 100 ms; P25, with an AVD = 80 ms and P26, with an AVD = 140 ms.

- Position of ventricular stimulation sites: P11, P12, P14 and P16 have been acquired with the RV lead located at the apex. P18 and P19 where acquired with the RV lead at the outflow tract. Finally, the RV lead was located in the mid-septum for configurations P21 to P26. The LV lead was located at a middle position into the lateral coronary vein, for all configurations.

In summary, 33 different configurations were available for analysis (P*k*-AAI, P*k*-RV, P*k*-BiV, for all $k \in$ [11,12,14,16,18,19,21,22,24,25,26]). Records of 15 cardiac cycles, including a synchronous acquisition of the RA, RV and LV electrograms (EGM) and the EA signal were obtained for each pacing configuration, using a dedicated external system.

Analysis of intracardiac acceleration signals

EGM signals of each record were firstly analyzed, in order to detect the electrical activation time of the RA, RV and LV and to detect each beat. The earliest detection between the RV and LV electrical activation instants was used to trigger EA signal averaging. For each detected cardiac cycle, standard ensemble averaging was performed for each individual EA component (EA1 and EA2): i) the phase shifts that maximize the correlation between each cycle are calculated, ii) the cycles are aligned according to a reference component (first cycle of the analysis window) and iii) the two average components EA1 and EA2 are computed. Only the 7 highest correlated cycles with a normalized correlation coefficient greater than 0.6 were included in the averaging phase. The record was considered as noisy if there were less than 7 cycles with a correlation coefficient higher than 0.6. All data were analyzed offline.

Envelograms are computed from the average EA cycle and an optimal algorithm-switching method was applied to estimate the start and end instants of EA1 and EA2, their instant of maximum energy, and their global energy. The method is described in detail in [8]. In this work, we have adapted certain parameters of the signal-processing chain (cut-off frequencies of the filters, thresholds, etc.) to better fit the specificities of the intracardiac version of the signal.

Once the main EA features have been extracted, the intraconfiguration and interconfiguration variabilities of these features are analyzed. Intraconfiguration variability is evaluated on configurations P11-P16, which were acquired sequentially with the same AVD, VVD and the same LV and RV stimulation sites, in an 11 minutes interval. The standard deviation of each EA feature, for each pacing mode (spontaneous rhythm, RV, LV and BiV stimulation) will be considered as an indicator of the measurement error for that feature, using that particular pacing mode. This measurement error will be integrated in the analysis of interconfiguration modifications of the EA features.

RESULTS

After a description of the typical characteristics of the acquired intracardiac signals for two different pacing configurations, this section presents preliminary results on the stability and usefulness of the main features of the EA1 component, in the context of intraoperative CRT optimization.

General characteristics of the EA signal during CRT

Figure 1 show typical intracardiac signals obtained during the implant procedure for configuration P18 and two extremely different pacing modes: atrial stimulation with spontaneous ventricular activity (figure 1a) and bi-ventricular pacing (figure 1b). The signals shown are obtained after the application of the above-mentioned averaging method. Upper panels show the mean intracardiac electrograms acquired by the RA, RV and LV leads, while the lower panels present the mean EA signal.

EGMs in figure 1a clearly show the significant atrio-ventricular and inter-ventricular electrical activation delays in this patient. The RA to RV delay is of 275 ms and the RA to LV delay is of 375 ms (VVD = 100 ms). Note also the wide aspect of the LV deflection in the spontaneous case. The EA signal shows a wide EA1 component of more than 200 ms, with a rather low PEA1. Indeed, the desynchronized ventricular activation generates an increased AVD, abbreviating the diastolic filling time. The atrio-ventricular pressure gradient is low in this case at the moment of the closure of the AV valves, thus producing a low PEA1. The de-synchronization of both ventricles and the extended AVD may also contribute to the widening of the other EA components.

The case of a bi-ventricular pacing is shown in figure 1b. The AVD is still defined at 120 ms, but in this configuration, both ventricles are paced at the same time (VVD = 0). It should be noted that, since the LV lead is placed on the epicardium, the time from the LV pacing instant to the actual recruitment of LV myocardium is higher than for the RV, which is paced on the endocardium. Thus, even with this pacing configuration, LV activation and contraction is slower than that of the RV and both ventricles are still not mechanically synchronized. The EA signal shows in this case an even higher PEA1.

Exclusive ventricular stimulation of the RV or the LV produces a complex mix of the responses in figures 1a and 1b, as the AVD and VVD are modified. These examples show the difficulty associated with the intraoperative optimization of CRT, particularly when performed, as in most cases, without a marker of the mechanical cardiac response. The next section will be focused on the analysis of the EA1 component, so as to evaluate the intra- and inter-configuration variabilities of the features extracted from the EA signal.

EA modifications for different pacing configurations

The PEA1 and the duration of the EA1 component were automatically extracted from the mean EA signal of each record. An example of the EA1 segmentation obtained for all biventricular configurations is shown in figure 2. Here, the RV/LV stimulation spike was used as reference time (t=0), so the atrial component is seen for $t > 550$ ms.

Morphological differences on the EA signals can be observed for the different lead positions and AVD. P11 to P16 share the same configuration (AVD, VVD and lead locations) and show minor morphological differences. EA signals for P18 and P19 were acquired with a different RV lead location (outflow tract) and show a slightly larger EA1, with an earlier EA1 component and a higher EA2 amplitude. Configurations P24 to P26 show the effect of varying the AVD and moving the RV lead to the mid-septum, with significant modifications on EA1 and on the atrial component.

Intra and inter-configuration variability of EA1 features

Boxplots representing the intra-configuration variability for PEA1 and EA1 duration, for configurations P11-P16 (same AVD and lead locations), are proposed in figure 3. The median and standard deviation of each case are shown in Table I. The intra-configuration variability is generally lower than the variability due to changes in pacing mode, except for the differentiation between RV and BiV stimulation, using the EA1 duration.

Figure 4 presents a scatter plot showing EA1 duration vs. PEA1 for all the configurations analyzed for this patient. Ellipses represent the intra-configuration variability of one standard deviation, based on values from Table I. This graph shows that complementary information can be obtained from the joint analysis of PEA1 and EA1 duration, especially for distinguishing different AVD or lead positions, using the same pacing mode. The correlation coefficient between these variables equals $r=-0.61$. The inter-configuration variability in this bivariate plane is higher than on the corresponding univariate projections (see Figure 4). For instance, the different pacing modes for configuration P24 (red) could not be correctly differentiated with an univariate approach.

A particular attention should be paid to configuration P25 (cyan), which presents the lowest AVD. This configuration provoked an increased EA1 duration during RV and BiV, which may be due to the appearance of new components at the beginning and end of EA1 (see figure 2, for the BiV case). This configuration provoked also a loss in PEA1 during RV with respect to the AAI configuration, but a significant increase in PEA1 during BiV pacing. The shortest EA1 durations are obtained for the RV stimulation. Most bi-ventricular configurations show a high PEA1 value with a relatively short EA1 duration. These results are in accordance with the expected physiological response to CRT and with our previous results based on computational models [10], suggesting that the best configurations should be on the upper-left part of the plane, where almost all BiV stimulations are located. However, further validation is required in order to select the set of EGM and EA features that should be used for intraoperative CRT optimization.

CONCLUSIONS

This work presented preliminary results showing the feasibility of feature extraction form intracardiac signals during the implant of a CRT system. A bivariate analysis of the extracted EA features (PEA1 and EA1 duration) seems to provide useful information about the modifications on the mechanical and hemodynamic conditions provoked by different CRT pacing configurations. If confirmed, this approach may be the first to provide a CRT optimization method that can be applied during the intra-operative and chronic phases. However, these results have to be confirmed with a larger patient population. Also, a validation phase with respect to a gold standard, such as the LV dP/dt, is necessary in order to derive a new marker for intraoperative CRT optimization, based on intracardiac signals.

References:

- 1 . Dickstein K , Vardas P , Auricchio A , Daubert J , Linde C , McMurray J , Ponikowski P , Priori S , Sutton R , van Veldhuisen D . 2010 focused update of esc guidelines on device therapy in heart failure . Europace . 12 : (11) 1526 - 1536 2010 ;
- 2 . Durand LG , Pibarot P . Digital signal processing of the phonocardiogram: review of the most recent advancements . Crit Rev Biomed Eng . 23 : (3–4) 163 - 219 1995 ;
- 3 . Gill D , Gavrieli N , Intrator N . Detection and identification of heart sounds using homomorphic envelogram and self-organizing probabilistic model . Proc Computers in Cardiology . Sept 25–28 2005 ; 957 - 960
- 4 . Marcus FI , Sorrell V , Zanetti J , Bosnos M , Baweja G , Perlick D , Ott P , Indik J , He DS , Gear K . Accelerometer-derived time intervals during various pacing modes in patients with biventricular pacemakers: comparison with normals . Pacing Clin Electrophysiol . 30 : (12) 1476 - 1481 Dec 2007 ;
- 5 . Giorgis L , Hernández A , Amblard A , Senhadji L , Cazeau S , Jauvert G , Donal E . Analysis of cardiac micro-acceleration signals for the estimation of systolic and diastolic time intervals in cardiac resynchronization therapy . Proc Computers in Cardiology . 2008 ; 393 - 396
- 6 . Zuber M , Toggweiler S , Quinn-Tate L , Brown L , Amkieh A , Erne P . A comparison of acoustic cardiography and echocardiography for optimizing pacemaker settings in cardiac resynchronization therapy . PACE . 31 : (7) 802 - 811 Jul 2008 ;
- 7 . Donal E , Giorgis L , Cazeau S , Leclercq C , Senhadji L , Amblard A , Jauvert G , Burban M , Hernández A , Mabo P . Endocardial acceleration (sonr) vs. ultrasound-derived time intervals in recipients of cardiac resynchronization therapy systems . Europace . 13 : (3) 402 - 408 Mar 2011 ;
- 8 . Giorgis L , Frogerais P , Amblard A , Donal E , Mabo P , Senhadji L , Hernández AI . Optimal algorithm switching for the estimation of systole period from cardiac microacceleration signals (sonr) . IEEE Transactions on Biomedical Engineering . 59 : (11) 3009 - 3015 2012 ;
- 9 . Plicchi G , Marcelli E , Parlapiano M , Bombardini T . Pea i and pea ii based implantable haemodynamic monitor: pre clinical studies in sheep . Europace . 4 : (1) 49 - 54 Jan 2002 ;
- 10 . Koon K , Thebault C , Le Rolle V , Donal E , Hernández A . Atrioventricular delay optimization in cardiac resynchronization therapy assessed by a computer model . Computing in Cardiology, 2010 . IEEE ; 2010 ; 333 - 336

Fig. 1

Mean EGM signals (upper panel) and intracardiac EA signal for configuration P18 under atrial pacing only (a) and BiV stimulation (b).

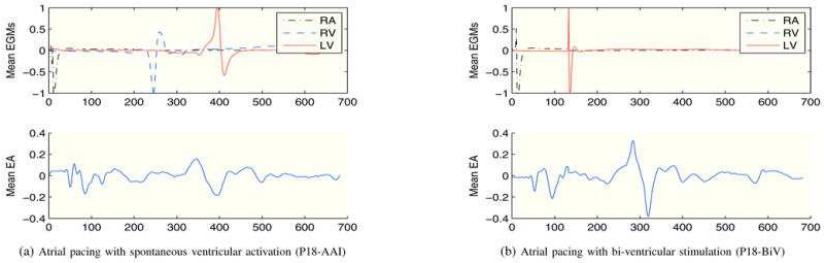

Fig. 2

Mean EA signals for all configurations tested during bi-ventricular pacing. Detection instants of the beginning and end of the EA1 component are marked with a circle. Line colors code the configurations with the same AVD and RV stimulation site.

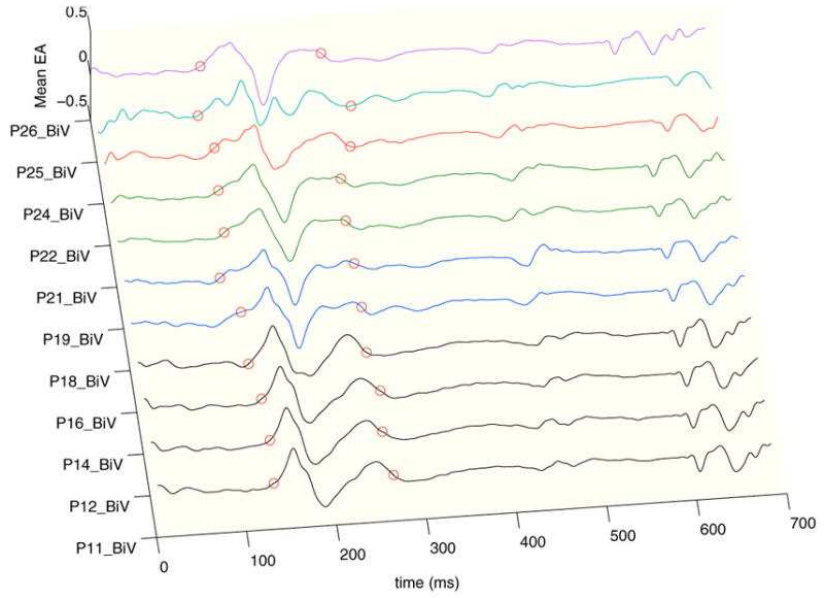

Fig. 3

Boxplots representing the intra-configuration variability for variables PEA1 and EA1 duration, and for configurations P11–P16 for spontaneous rhythm and RV, LV and BiV pacing.

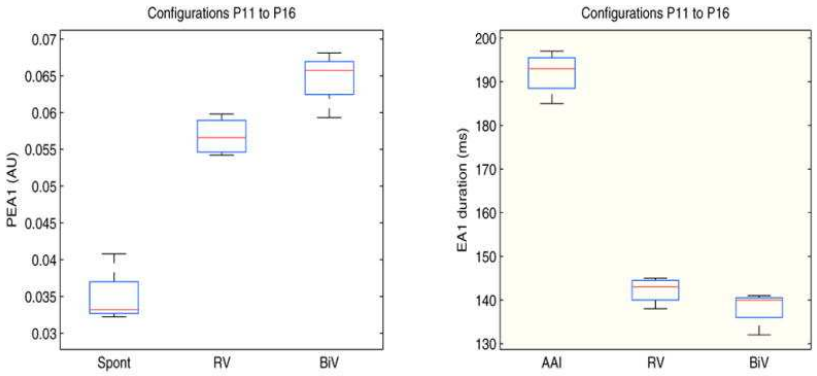

Fig. 4

Scatter plot showing the values of PEA1 vs. EA1 duration for all pacing configurations. Circles represent AAI configurations, and squares and triangles represent RV and BiV pacing, respectively. The same color coding as in figure 2 is used: P11–P16: black, P18–P19: blue, P20–P22: green, P24: red, P25: cyan and P26: magenta. Ellipses represent the intra-configuration variability of one standard deviation, using values from table I.

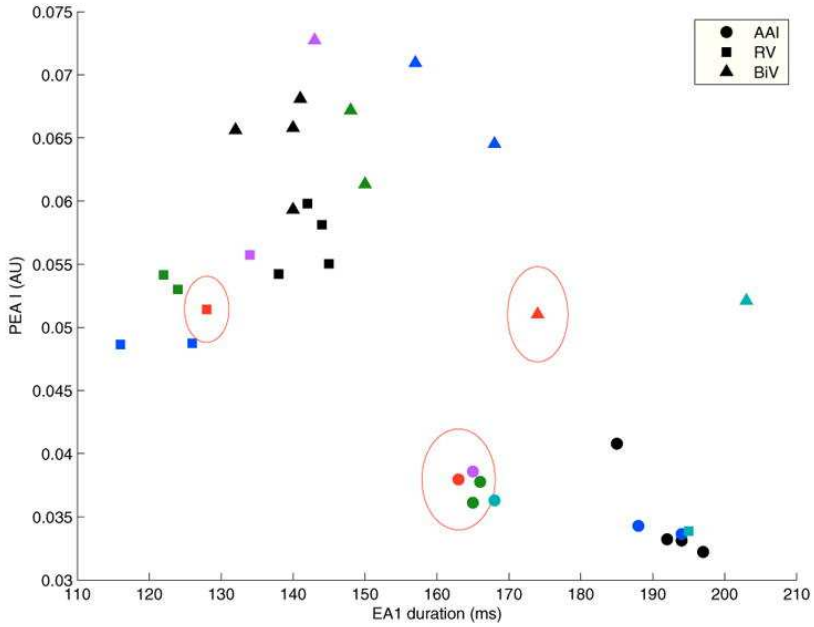

TABLE I

Median and standard deviation for PEA1 and EA1 duration calculated from configurations P11–P16 as a function of the pacing mode.

	AAI	RV	BiV
PEA1	0.332 ± 0.04	0.566 ± 0.02	0.657 ± 0.03
EA1d	193 ± 5.1	143 ± 3.1	140 ± 4.2