Mechanical dyssynchrony indices from an electrophysiological contact mapping system predict response to CRT

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Abstract. We present a methodology to extract mechanical dyssynchrony indices from an electrophysiological (EP) contact mapping system that was applied to a database of ten patients undergoing Cardiac Resynchronization Therapy (CRT), before and after the therapy. The mechanical dyssynchrony indices were obtained after post-processing high temporal resolution data recorded at several endocardial positions with the measuring catheter of the EP system. Velocity profiles of these catheter trajectories were analyzed to identify abnormal patterns of motion such as septal flash, whose presence is strongly related to a positive response to CRT in patients with left bundle branch block. Septal flash motion was identified in four cases, which was qualitatively validated by visual inspection of imaging data, and a strong correlation with response to CRT was observed a posteriori. Finally, the effect of biventricular pacing was clearly observable by a substantial reduction of the septal flash motion.

Key words: Electrophysiological contact mapping system, septal flash motion, left bundle branch block, cardiac resynchronization therapy

1 Introduction

Electrophysiological (EP) mapping systems are nowadays routinely used in invasive EP procedures in order to have a better understanding of cardiac arrythmias. Since their introduction in the mid $90's$ by Ben-haim et al. [1] (CARTO,

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Biosense, Cordis Webster, Marlton, NJ), the most common functionalities of these EP mapping systems are the static anatomical guidance of ablation procedures and the analysis of electrical activation patterns derived from intracardiac electrograms in both atria and ventricles.

However, mechanical information can also be extracted from contact mapping systems such as CARTO or NOGA-XP (Biologics Delivery Systems, Diamond Bar, CA), by analyzing the catheter's temporal trajectories to estimate myocardial motion, under the assumption that the catheter's spatial location is at the endocardial surface and follows the motion undergone by the corresponding heart segment. The main advantage of these motion estimates is their trivial combination with electrophysiological data since both are obtained with the same system, unlike traditional indices derived from echocardiography or Magnetic Resonance (MR) images, which require manual or complex registration [2] procedures. To the best of our knowledge, Klemm et al. [3] were the first researchers exploiting this type of data, recently studying maps of activation and longitudinal motion (so-called electromechanical mappings) corresponding to healthy and ischemic heart subjects, simultaneously acquired with a NOGA-XP system.

This straighforward combination of electrophysiological and mechanical data can also be potentially beneficial for the optimization of Cardiac Resynchronization Therapy (CRT). CRT is an innovative treatment for congestive heart failure aiming at synchronizing the left ventricle (LV) contraction. However, up to a third of the patients who are treated with CRT do not properly respond or even worsen from this very expensive therapy. Therefore, the development of new patient selection indices would lead to better success rates of CRT. For instance, a fast motion pattern called septal flash, a mechanical consequence of dyssynchronous contraction which occurs in some left bundle branch block (LBBB) patients at the isovolumic contraction (IVC) period, has been associated to a high probability of response to CRT [4].

We recently proposed [5] a methodology to identify septal flash motion from electromechanical mappings provided by an EP system, which was applied to CRT candidates at sinus rhythm, thus giving additional motion information whenever EP data is acquired. In this paper, we present some improvements on the methodology such as the use of velocity profiles, allowing us to generate quantitative mechanical dyssynchrony indices. We applied them to a database of ten patients composed of pre- and post-CRT electromechanical mappings. Furthermore, we studied the correlation between the presence of septal flash and clinical response to CRT.

2 Acquisition and clinical data

2.1 Patient population

For the present study data from 10 heart failure patients (age 66 ± 8 years) was collected, following adequate patient protection and informed consent, as well as the approval of the study by an ethics committee. All the patients were candidates for CRT, according to current recommendations based on the NYHA classification, the ejection fraction (EF) and the QRS length. Details about the characteristics of each patient are given in Table 1.

Table 1. Clinical Data. 6MWT: 6 minutes walking test (metres); B: baseline; F: 6 months follow-up; EF: ejection fraction; ESV: end-systolic volume; VVD: biventricular delay; Clin resp: clinical response; Vol resp: volume response; transp: transplanted

	Age	6MWT B/F[m]	NYHA B/F	EF (B)	ESV B/F	QRS[ms]	VVD[ms]	Clin resp	Vol resp
1	75	276/392	II/I	50.9	118/77	200	0	yes	yes
2	71	224/380	III/II	22.8	164/67	160	0	yes	yes
3	68	204/240	III/III	26.2	213/172	120	0	yes	yes
4	80	176/256	III/II	25.0	205/75	200	0	yes	yes
5	66	416/496	III/I	25.0	340/305	200	-30	yes	yes
6	58	336/496	III/I	27.0	155/175	200	-30	yes	no
7	55	416/416	II/I	24.8	193/198	120	-30	no	no
8	68	245/312	III/II	9.0	260/202	140	-30	yes	yes
9	65	308/364	III/II	26.0	138/75	120	-30	yes	yes
10	55	-/-	III/transp	15.0	174 / -	120	-30	no	no
11	75	196/322	III/II		216/201	200	0	yes	no
12	58	252/490	III/III		163/142	166	0	yes	yes
13	71	371/402	I/I		123/94	120	0	yes	yes
14	56	360/460	III/II		130/84	145	0	yes	yes
15	70	392/392	II/II		103/73	160	0	no	yes
16	56	352/490	II/I		166/95	200	-30	yes	yes
17	58	343/315	II/III		179/108	180	-30	no	-
18	78	392/392	II/II		165/158	170	0	no	no
19	56	308/322	II/I		251/254	80	-30	no	no
20	76	0/350	III/I		70/64	150	0	yes	yes

2.2 Intracardiac electrophysiological mapping acquisitions

Data collected from of these patients consisted of endocardial EP contact mapping (CARTO, Biosense, Webster). These EP maps are composed of a set of intracardiac samples that contain electrical signals (recorded at $1kHz$) and position of the catheter (recorded at $100Hz$) over $2500ms$ (around 3 heart cycles) so that intracardiac electrogram (EGM) and trajectory data can be derived. The electrical measurements consist of uni- and bipolar voltages where the unipolar peak-to-peak voltage refers to the potential difference between the catheter tip and a reference electrode, whereas the bipolar voltage is the potential difference between the 2 electrodes within the catheter (Ring-Tip).

For each patient, the average number of acquired EP points were 54.5 ± 20.5 in sinus rhythm and 31.1 ± 17.3 for optimized pacemaker settings. Analysis of the mapping data was carried out for patients in sinus rhythm and with settings of the pacemaker optimized according to echocardiography response.

Customizable settings were the atrio-ventricular delay (AVD) and the interventricular delay (VVD). Hence, the following settings of the pacemaker were tested for optimization purposes: i) simultaneous pacing (LV-RV), $VVD = 0$; ii) RV pre-excitation, $VVD = 30ms$; and iii) LV pre-excitation, $VVD = -30ms$. In all patients, the pacemaker leads were allocated in the posterolateral branch of the coronary sinus, and AVD was set to $140ms$.

2.3 Echocardiographic acquisition

A standard echo-Doppler (Vivid 7; General Electric-Vingmed, Milwaukee, Wisconsin, USA) was performed before initiating CRT and repeated at 6 months follow-up. In each scan, LV dimensions and ejection fraction were determined [6]. All the studies were digitally stored and analyzed off-line by two experienced cardiologists who were not involved in the clinical follow-up and were, therefore, unaware of each patient's clinical outcome.

2.4 Definition of response

Patients were considered as clinical responders when they were alive without heart transplantation and presented an improvement of 10% in the distance walked in the six-minute walking test at 6 month follow-up [7]. Echocardiographic response was also defined as a reduction in LV end-systolic volume $\geq 10\%$ at 6 months follow-up as compared to baseline [8].

3 Mechanical dyssynchrony indices

3.1 Septal flash motion

Dyssynchrony indices to identify CRT candidates have been an issue of debate over the last years. Some simple indices measured from echocardiographic data [9] have proven to have a poor prediction capability of CRT success. Recently, a fast motion pattern, called *septal flash*, which occurs in some LBBB patients at early systole, has been related to a high probability of response to the CRT therapy [4]. A septal flash can be explained by unbalanced forces appearing in the septum due to a conduction delay between the activation of the septum and the lateral wall. This provokes a fast succession of inward and outward motion of the septum during the (wide) QRS complex and the IVC time period. In this paper, we present a methodology to identify the presence of this septal flash from EP data, that will consequently be used to generate quantitative mechanical dyssynchrony indices.

3.2 Cardiac motion analysis

The proposed methodology for the analysis of cardiac motion from EP data can be divided in the following stages:

1. computation of the 4D displacement field;
2. temporal smoothing of the 4D displacement field;
3. estimation of the radial component of the 4D displacement field and the associated velocity profiles.

The first stage of the methodology is the estimation of the trajectory of each EP point over time, i.e. the computation of the 4D displacement field. For doing so, we made use of the spatial locations of the measuring catheter tip at consecutive timepoints, which are available every 10ms. Lessick et al. [10] analyzed catheter stability during contraction, showing an average distance of $1.33 \pm 0.61mm$ between the catheter tip and the endocardium after respiration correction (which mostly affects longitudinal deformation), which is small enough for our purposes. Moreover, it must be pointed out that the EP system provides visual signs informing when the catheter is in contact with the endocardial wall, which is when measurements are taken.

The study of the resulting displacement field can be quite challenging when mixing data from multiple heart beats. Therefore, we only considered temporal data around the trigger point ($t = 2000 \pm 200ms$), only from the last acquired heart cycle. Furthermore, we applied a temporal smoothing to the EP points based on a binomial filter using the previous and following positions in the trajectory.

The next step consisted in estimating the radial component of the 4D displacement field since the inward and outward septal displacements are mainly observed in the radial direction. For doing so, we projected the 4D displacement field onto the unit vector pointing to the centroid of the cloud of EP points, at each timepoint of the sequence. Hence, the scalar projection of a given EP point will be positive when its displacement vector points towards the centroid (inward motion, contraction), and negative when moving away from the centroid (outward motion, dilation). These scalar values can be plotted over time, deriving 1D curves with information that can be used to identify particular motion patterns for some EP points. In order to be almost independent of respiratory effects, we computed the temporal derivatives of these 1D radial displacement curves, i.e. velocity, as proposed by Klemm et al. [3]. Moreover, velocity estimates will make the comparison with tissue Doppler measurements possible.

3.3 Identification of septal flash

We analyzed the 1D velocity curves mentioned above to identify septal flash motion. For doing so, we selected the EP point with the earliest local activation time (LAT), EP_{elat}, and the one with the latest LAT, EP_{llat} since their corresponding bipolar EGMs gave us the time interval where, if present, the septal flash must occur, i.e. the IVC period. We defined this *septal flash interval* as the time between the R peaks of the EGMs of the EP_{elat} and EP_{llat}, $\pm 30ms$ in order to account for possible mechanical and electrical delays.

In a normal heart, the 1D radial velocities of septal EP points should slightly oscillate around zero during the whole heart cycle. On the other hand, septal

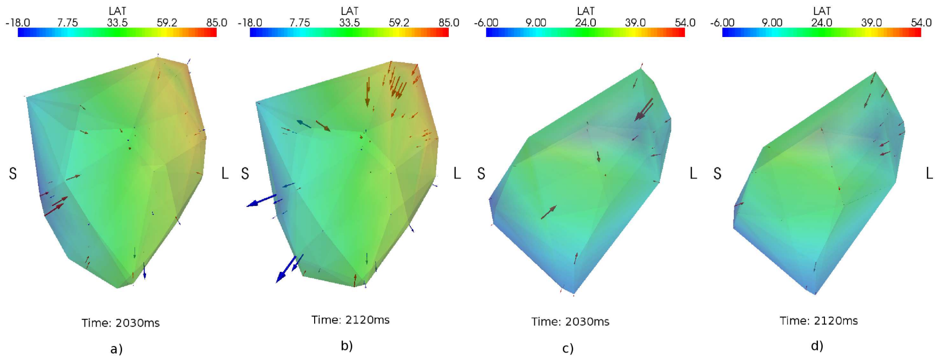

Fig. 1. Clouds of EP points, colored according to the LATs, together with displacement field (arrows) at two different timepoints within the IVC period, pre- (a) and b)) and post-CRT (c) and d)). S: septum; L: lateral wall.

flash cases will show up abnormally large positive (sudden contraction) and negative (sudden relaxation) septal velocities as well as a zero-crossing indicating a change in displacement direction (from inward to outward motion) within the septal flash interval (see shady region in Fig. 2 and Fig. 3) for septal EP points. In this paper, septal EP points were manually selected by two expert technicians from the pre- and post-CRT electromechanical mappings.

4 Results

Triangulations of the EP points and corresponding radial displacements at two different frames within the IVC period for one patient having septal flash, pre- and post-CRT, are shown in Fig. 1. From this figure, one can observe the presence of large inward and outward displacement of the septal wall, representing the fast motion pattern that corresponds to a septal flash. Biventricular pacing substantially reduced the magnitude of the septal flash motion, thus improving heart assynchrony, as demonstrated in Fig. 1.

Fig. 2 and Fig. 3 show the velocity profiles and the EGMs for patients with (four cases) and without (six cases) septal flash, respectively. It is straightforward to distinguish septal flash from not septal flash cases by visual inspection of these figures. In the cases illustrated in Fig. 2, abnormally large velocities and a zero-crossing appeared during the septal flash interval while no remarkable event developed in cases displayed in Fig. 3. The same classification of septal/no septal flash cases was obtained by visual inspection of the corresponding MRI and US data by an expert cardiologist. In addition, we measured maximum absolute inward and outward velocities as well as their range within the septal flash interval. As shown in Fig. 4, these quantitative indices, in particular the maximum velocity range, can be used for group separation purposes of septal vs. non-septal flash cases.

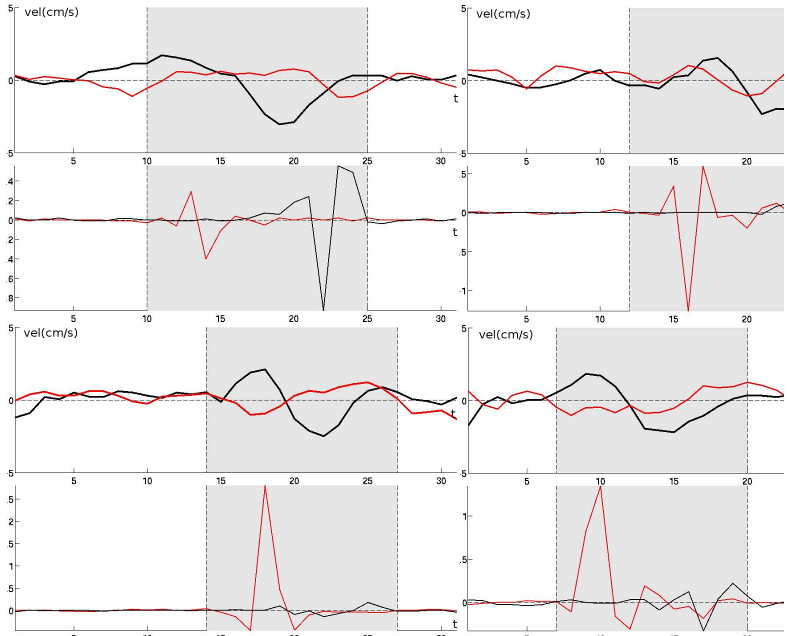

Fig. 2. Velocity profiles (top in each subplot) corresponding to pre- (black) and post-CRT (red) data, together with EGMs (bottom in each subplot) of EP_{elat} and EP_{llat} (black and red, respectively) for cases with septal flash. The dashed markers and grey area define the septal flash interval.

Finally, we analyzed a posteriori the correlation between the presence of septal flash obtained from EP data and clinical and volume response, as detailed in Table 1. All four patients in which septal flash was identified from EP data were responders, both clinical- and volume-wise. The remaining six cases included two clinical non-responders (20% of all cases; 33.3% of non septal flash cases) and three volume non-responders (30% of all cases; 50% of non septal flash cases), which is in good agreement with recent findings in the literature [4] (54% of septal flash cases, 88% of them clinically responding; 46% of non septal flash cases, 40.5% of them with a negative response, which represented 18.6% of all cases).

5 Conclusions

We have presented a methodology to generate a quantitative index to detect and quantify the presence of septal flash from EP data which fully correlated with response to CRT of LBBB patients. This mechanical information may give additional insights whenever EP data is available. Future work will be focused on quantitatively comparing these results with deformation indices provided by ultrasound imaging.

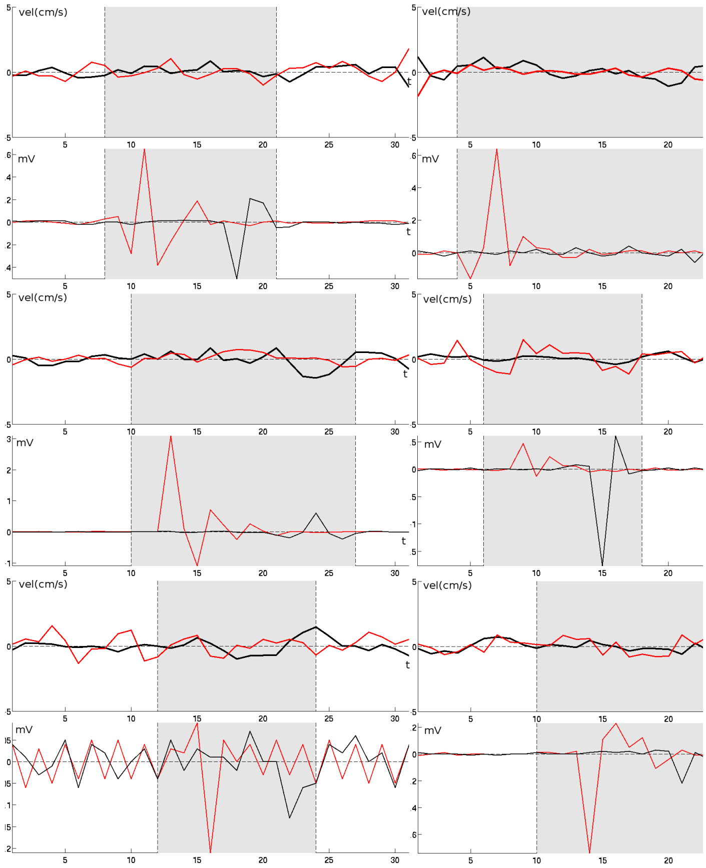

Fig. 3. Velocity profiles (top in each subplot) corresponding to pre- (black) and post-CRT (red) data, together with EGMs (bottom in each subplot) of EP_{elat} and EP_{llat} (black and red, respectively) for cases without septal flash. The dashed markers and grey area define the septal flash interval.

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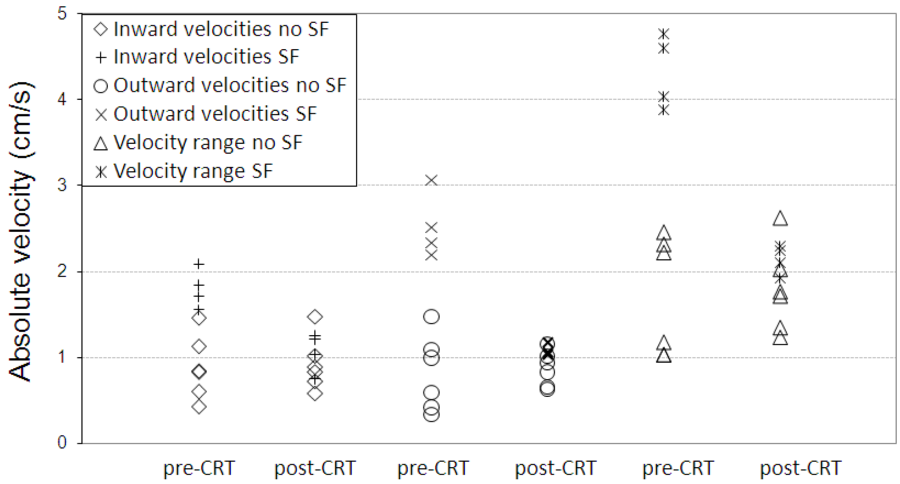

Fig. 4. Group separation of patients with and without septal flash (SF), pre- and post-CRT, according to absolute maximum radial velocities and their range.

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