The Use of Autocorrelation Maps for Evaluation of Cardiac Resynchronization Therapy Outcome

Jana Svehlikova[1], Anna Pribilova[1], Michal Sasov[2], Jan Zelinka[1], Robert Hatala[2], Milan Tysler[1]

[1]Institute of Measurement Science, SAS, Bratislava, Slovakia
[2]National Institute for Cardiovascular Diseases, Bratislava, Slovakia

Cardiac resynchronization therapy (CRT) is one of the established treatment technologies for heart failure however, the parameters predicting and characterizing the success of the therapy are still searched

Body surface potential maps (BSPMs) from 128 electrodes on the torso were measured on 30 healthy subjects (control group) and three patients with implanted CRT systems. Of the three patients, one was a responder and the latter two were non-responders. BSPMs for all patients were measured during their spontaneous sinus rhythm and then during their "standard" CRT stimulation setting and "other" CRT setting. Pearson's correlation coefficient between corresponding BSPMs for each couple of time instants during the depolarization time interval was computed and depicted as an autocorrelation map (ACM). Several parameters derived from the ACMs of healthy subjects and patients with heart failure were computed and compared.

The ACM of the "standard" CRT setting of the responder was similar to the ACMs of the control group, while the ACMs of the nonresponders were different. When the "other" CRT setting was temporarily programmed, the ACMs of the nonresponders changed to be more similar to the control group.

We hypothesize that ACMs can be used as an additional tool for the evaluation of the depolarization dynamics of the heart and evaluation of the CRT outcome.

1. Introduction

Some failing hearts are characterized by a prolonged duration of QRS complex in ECG signal and electrical and mechanical dyssynchrony of the left and right ventricles [1]. The dyssynchrony leads to a decrease in the ejection function of the heart. CRT aims to improve the synchrony of an activation propagation wavefront using the implanted device with few electrodes providing a supporting stimulation of selected areas of the heart muscle. Despite large progress in such a treatment, there are still more than 30% of patients who do not benefit from CRT [1]. Therefore, several methods and parameters are suggested to evaluate and design a proper patient-specific chronology of stimulation during the CRT. The CRT is usually evaluated from the 12-leads ECG [2], [3], but some parameters were introduced also using multiple-leads measurements [4], [5]. The differences in the autocorrelation maps (ACMs) computed from the body surface maps (BSPMs) for groups with normal and abnormal ECG during depolarization and repolarization were shown in [6]. The first parameters to evaluate such differences in the ACMs were suggested in [7]. In [8], it was shown that contrary to integral BSPMs, the ACMs are not sensitive to the heart position and orientation.

In this study, some parameters of ACMs for subjects with normal ECG and patients with CRT are studied, and their possibility of being an indicator of CRT quality is investigated.

2. Material and Method

Body surface potentials were measured on 30 subjects with a normal ECG and three patients with heart failure with CRT. Each person included in this study subscribed to the informed consent with the measurement.

The measurements were performed by the ProCardio multichannel measuring system [9] developed in our laboratory. The ECG signals were recorded from 128 disposable electrodes placed regularly in 16 vertical strips with 8 electrodes on the torso. Another three electrodes were placed in the limb-leads positions. The active grounding electrode was placed on the right leg (driven right leg – DRL). The recorded ECG signal was measured with respect to the reference electrode (common mode sense – CMS) positioned on the torso, hence together 133 electrodes were used for the measurement.

The signals were recorded with a sampling frequency of 1 kHz. The duration of each measurement was about five minutes. The measured signal was processed using the high-pass filter for baseline drift removal and a 50 Hz filter for elimination of the power noise. Then, the heartbeats were identified in the lead II using the Pan-Tompkins method for identification of the R-peak. The representative ECG signal was estimated by averaging the identified heart

 ISSN: 2325-887X DOI: 10.22489/CinC.2022.269

cycles. The beginning and end of the QRS interval were defined manually on the averaged signal.

The body surface mapping of each of the three patients with the CRT was performed during the regular follow-up of their CRT system in the Department of Arrhythmology, NICD. The measurements were realized for their spontaneous rhythm and a CRT with two different settings.

It is known that failing hearts have impaired dynamics of activation. In this study, we suggested evaluating the dynamics of activation propagation by ACM computed for QRS time interval representing a period of ventricular depolarization.

Let's have BSPMs measured in N time instants $t_1 \ldots t_N$ during the QRS interval. The BSPM was considered as a vector with a size of 128x1. We computed the Pearson's correlation coefficient (PCC) between two BSPMs for each possible couple of time instants from the QRS interval, which resulted in a matrix with NxN values of PCC. The matrix is symmetrical since

$$PCC(BSPMs(ti,tj)) = PCC(BSPMs(tj,ti)) \qquad (1)$$

The computed values of the ACM were depicted in colour as the squared map. Then, we studied several parameters of ACMs characterizing the depolarization of healthy and failing hearts and selected a few of them to distinguish between the two heart conditions.

Considering the values of ACM for subjects with normal ECG as a distribution of samples, we studied four parameters of the ACM values in each ACM in this study: mean, standard deviation, skewness and kurtosis. The latter three are the moment-based characteristics of the distribution. While standard deviation characterizes the variation of the values, skewness characterizes the symmetry of a distribution, its positive value means that the majority is on the left, outliers are on the right, and its negative value means the opposite. Kurtosis characterizes a distribution's tail-heaviness, so whether the values are concentrated around the average value of the distribution or the values are farther from the average value.

3. Results

BSPMs with 128 electrodes were measured on thirty volunteers with a normal 12-leads ECG to create a reference group. There were three women and 27 men in the group. The mean age was 36.8 ± 12.8 years (from 12 to 63), and their mean QRS duration was 107 ± 10 ms (from 90 to 127).

The same BSPMs were measured on three patients with chronic heart failure and treated by CRT. The first patient (P101) was a 70-year-old man with a sinus rhythm and left bundle branch block (LBBB). He was considered a good responder to CRT. The second patient (P102) was a 71 years old man with sinus rhythm, complete right bundle branch block (RBBB) and left anterior hemiblock (LAH). This patient did not respond positively to his CRT treatment and was considered a nonresponder. The third patient (P108) was 68 years old man with sinus rhythm and LBBB. He also did not respond satisfactorily to his CRT treatment and was considered a nonresponder. For each patient, the BSPM measurements were performed under three stimulation protocols: during their spontaneous heart activity (spont), during their "standard" setting of CRT (standCRT = long-term setting), and during the "other" setting of CRT (otherCRT) suggested by the physician in the time of the examination.

Duration of depolarization (QRSd) as the basic indicator of the failing heart is summarized for each patient and each pacing mode in Table 1.

Table 1. Duration of QRS complex for the patients and different stimulation settings.

QRSd [ms]	spont	stand CRT	otherCRT
P101 (LBBB)	163	135	140
P102 (RBBB+LAH)	160	152	134
P108 (LBBB)	150	155	155

Visual examination of computed ACMs for 30 volunteers revealed a repeated pattern of PCC values in the ACM as illustrated in Fig.1.

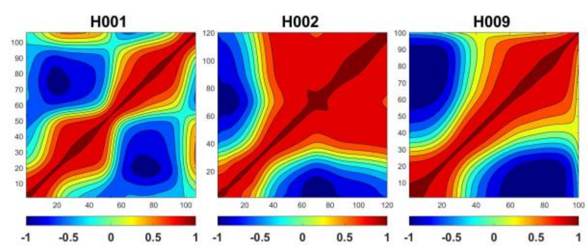

Figure 1. Examples of ACMs of three selected healthy volunteers.

However, the ACM values for spontaneous heart activity for patients with LBBB were significantly different as it is shown in Fig.2.

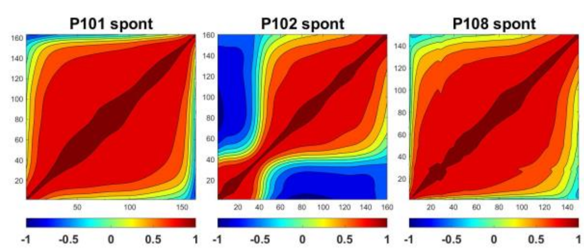

Figure 2. ACMs of spontaneous ventricular activation from the three patients with CRT

The distribution of the mean values of the ACMs for healthy volunteers and the mean values of ACMs for the three patients is illustrated in Figure 3.

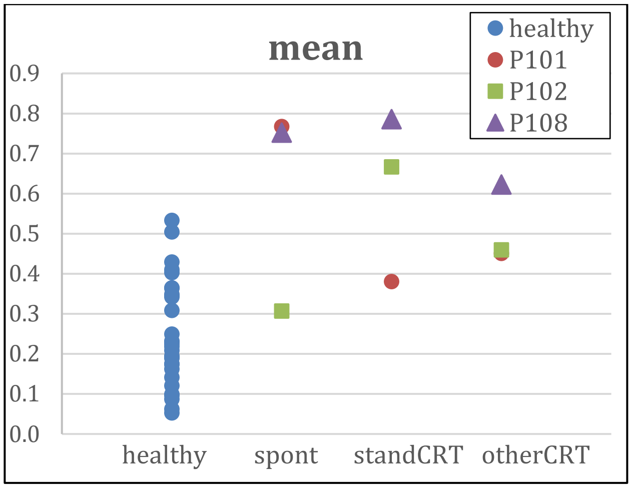

Figure 3. The mean value in ACMs from 30 healthy volunteers and the value of the such parameter for each patient and his three stimulation modes.

To compare the ACMs for healthy and failing hearts we compared the above-mentioned specific parameters of the patients' ACMs with an average value of these parameters for the control group. The average values of the parameters of the control group and respective individual parameters for patients are summarized in Table 2. The smallest differences in parameters for each patient from the control group are highlighted in bold.

Table 2. Average values of ACM parameters for the healthy volunteers and each patient for three pacing protocols.

ACM values	mean	std	skewness	kurtosis
control	0.25	0.64	-0.37	1.73
P101 spont	0.77	0.31	-1.86	6.23
P101 standCRT	**0.38**	**0.54**	**-0.37**	**1.62**
P101 otherCRT	0.45	0.45	-0.20	1.49
P102 spont	**0.31**	**0.66**	**-0.49**	**1.58**
P102 standCRT	0.67	0.36	-1.19	3.64
P102 otherCRT	0.46	0.53	-0.94	2.70
P108 spont	0.75	0.28	-1.40	4.24
P108 standCRT	0.79	0.24	-2.30	10.14
P108 otherCRT	**0.65**	**0.32**	**-0.59**	**2.15**

For the responder P101, the differences decreased for his "standard" CRT setting while for nonresponders (P102 and 108) the differences from the control group did not decrease for their "standard" CRT setting. It is apparent also in Figure 4, that the ACM of the responder with a "standard" CRT setting is similar to the ACMs of the control group. ACMs of the nonresponders with "standard" CRT settings are different from ACMs of the control group.

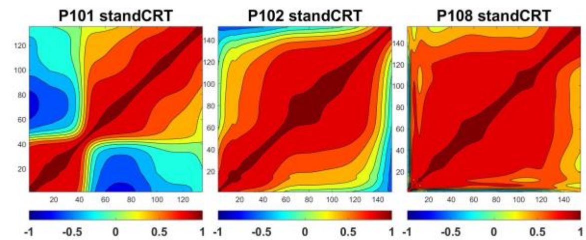

Figure 4. ACMs from the three patients when the CRT was set to their "standard" CRT setting.

4. Discussion

In this study, the ACMs computed from BSPMs in QRS time interval are introduced as a possible new indicator of dynamics of depolarization. Four parameters of ACMs were studied for healthy and failing hearts.

The results imply that for the responder (P101) the differences between his ACM parameters and the ACM parameters of the control group decreased in comparison to his spontaneous activity when the CRT was set to his "standard" mode (Table 2 bold row for P101). His ACM became similar to the ACMs of the control group. Considering the "other" CRT mode suggested by the physician during the BSPM measurement, for the responder the differences from the control group increased.

For the nonresponder with the same diagnosis of LBBB (P108), the differences did not decrease during his "standard" CRT setting and the ACM remained similar to that for spontaneous heart activity. However, for the "other" CRT setting the differences decreased. For the nonresponder with RBBB (P102), his ACM from spontaneous depolarization was very similar to the ACMs of the control group so his standard CRT setting increased the differences from the control group. When the nonresponders were paced by the "other" CRT setting the differences from the control group were smaller than the differences for their "standard" CRT setting, see Fig 5. Therefore, we can hypothesise that the use of ACM parameters can lead to better CRT settings for these patients.

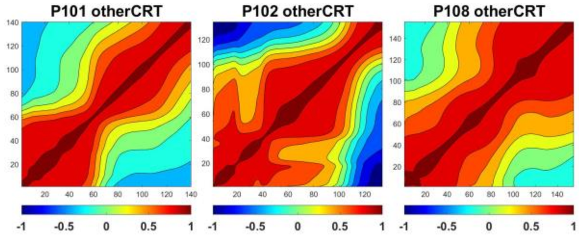

Figure 5. ACMs from the three patients when the CRT was set to the "other" CRT setting suggested by a physician during the measurement.

The ACM for the nonresponder with RBBB was similar to the ACMs of the control group. Such a situation can be an indicator of a bad prognosis for CRT treatment. Thus, his ACMs for two CRT settings were not better than the ACM for spontaneous heart rhythm, only QRS duration was shortened from 160 to 152 or 134 ms respectively.

5. Conclusion

In this pilot study, it was shown that the depolarization dynamics of the ventricles can be characterized by the ACM depicting all mutual correlations computed between the instantaneous BSPMs during the QRS time interval. The distribution of PCC values in ACM was characterized by its mean and three moment-based measures: standard deviation, skewness and kurtosis. The comparison of these parameters for individual patients revealed their potential to be an additional criterion for CRT setting.

This hypothesis should be validated on a larger number of patients and compared with up-to-date diagnostic criteria.

Acknowledgements

This work was supported by the research grant 2/0125/19 from the VEGA Grant Agency in Slovakia, the grant APVV-19-0531 from the Slovak Research and Development Agency, and COST CA19137.

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Address for correspondence:

Jana Svehlikova
Institute of Measurement Science,
Slovak Academy of Sciences
Dubravska cesta 9,
84104 Bratislava, Slovakia
jana.svehlikova@savba.sk