

Cardiac Resynchronization Guided by Ultra-High-Frequency ECG Maps

P. Jurak¹, M. Matejkova², J. Halamek¹, F. Plesinger¹, I. Viscor¹, V. Vondra¹, J. Lipoldova², M. Novak², R. Smisek¹, P. Leinveber²

¹The Czech Academy of Sciences, Institute of Scientific Instruments, Brno, CZ

²International Clinical Research Center, St. Anne's University Hospital, Brno, CZ

Abstract

Here we present a technique based on 14-lead ultra-high-frequency electrocardiogram (UHF-ECG, 5 kHz) able to measure the immediate effect of cardiac resynchronization therapy (CRT) settings on electrical ventricular dyssynchrony.

Resting UHF-ECGs were sequentially recorded during different CRT settings: CRT OFF, CRT ON, VV delays 0, -20, -40 ms, and SMART sensing (Boston Scientific) in 33 patients. Electrical depolarization maps were computed from signal-averaged UHF-ECGs in frequency band 150-1000Hz. The horizontal axis of each map indicates time, and the vertical axis indicates the activation location (VI-V8 lead). The red areas show the location-time of the maximal volume of simultaneously depolarized myocardial cells.

The optimal CRT setting is characterized by narrow and vertical activation pattern. Optimal CRT setting selected by a physician from electrical depolarization maps corresponded to minimal mechanical intraventricular delay obtained from echocardiography in 61% of patients, in 27% of patients the difference was within 10 ms interval.

UHF-ECG depolarization maps represent a useful tool for selection and setting of optimal cardiac resynchronization therapy.

1. Introduction

Cardiac resynchronization therapy (CRT) aims to eliminate ventricular dyssynchrony. However, approximately 30 percent of patients are still not appropriately treated. New stimulation technologies allow successful CRT even in patients who do not meet general criteria [1], but on the other hand, patients who meet these criteria may not respond positively. CRT treatment requires a comprehensive approach. Not only CRT responsibility predicting, but simultaneous technology

selection and CRT parameters settings and optimization.

It is inaccurate to select the patient for CRT treatment according to established electrocardiographic (ECG) parameters. If the patient has a QRSD of less than 150 ms, does not have a clear LBBB morphology, or has not a large QRS area [2], it is not a guarantee that he will respond positively. These parameters define the lower probability of positive response tested on a selected group of patients with the used technology. This probability may not be the same for another patient group and different pacing technology and criteria. Thus, the extensive studies provide results, which do not advise the physician how to resynchronize a particular patient individually. Limited sensitivity and specificity of ECG parameters require large trials and years for verification. This critically slows down the implementation of new stimulation techniques.

Here we present a new electrocardiographic method based on 14-lead ultra-high-frequency ECG (UHF-ECG) able to measure the immediate effect of CRT settings on electrical ventricular resynchronization.

2. Methods

2.1. Data recording

A 14-lead ECG was collected at 5 kHz with a dynamic range of 26 bits and a 2kHz passband (VDI monitor, ISI, Cardion, FNUSA Brno, CZ), Figure 1. Measurements were taken at the International Clinical Research Center at St. Anne's University Hospital, Brno, Czech Republic.

Resting 1-3 minute UHF-ECGs were sequentially recorded during different Biventricular CRT settings: baseline (CRT OFF), CRT ON ventriculo-ventricular (VV) delay 0, -20, -40 ms, and SMART sensing (Boston Scientific) in 33 patients (23 men and 10 women, age 65.0±10.1).

All subjects gave their informed consent to the investigation. The study was approved by the Ethics Committee of St. Anne's University Hospital, Brno.



Figure 1. 14-lead ECG VDI (Ventricular Dyssynchrony Imaging) monitor for real-time monitoring of depolarization pattern. The VDI monitor can provide the first results within 20 seconds. Installation in St. Anne's University Hospital, Brno, Czech Republic, 2019.

2.1. Processing

Electrical depolarization maps (Figure 2B) were computed from signal-averaged UHF-ECGs in frequency band 150-1000Hz. The horizontal axis of each map indicates time, and the vertical axis indicates the activation location (V1-V8 leads). The red areas show the location-time of the maximal volume of simultaneously depolarized myocardial cells. The optimal CRT setting is characterized by narrow and vertical activation pattern. Narrowing means faster depolarization conduction, and straight vertical pattern means the elimination of ventricular dyssynchrony. The electrical dyssynchrony (e-DYS) was estimated as the time delay between the first and last activation, Figure 2B.

Arrows in the Figure 2B indicate slow conduction region close to V2 and V3 leads. In this area, the depolarization getting the high delay.

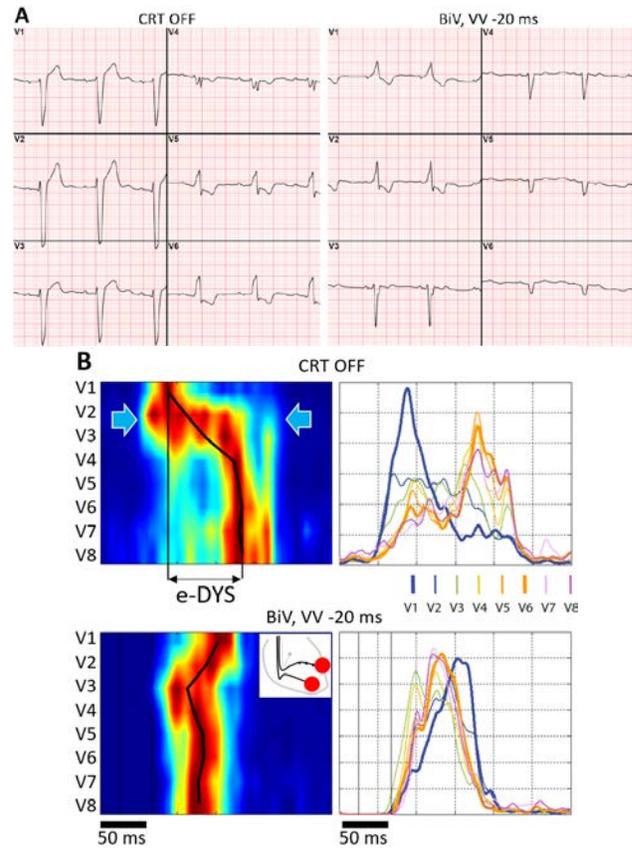


Figure 2. Determination of resynchronization effect by electrical depolarization maps; during CRT OFF and CRT ON (biventricular stimulation). Left bundle branch block (LBBB) patient.

A – precordial leads V1-V6, B - left panel: electrical depolarization maps, right panel: depolarization distribution in V1-V8 leads.

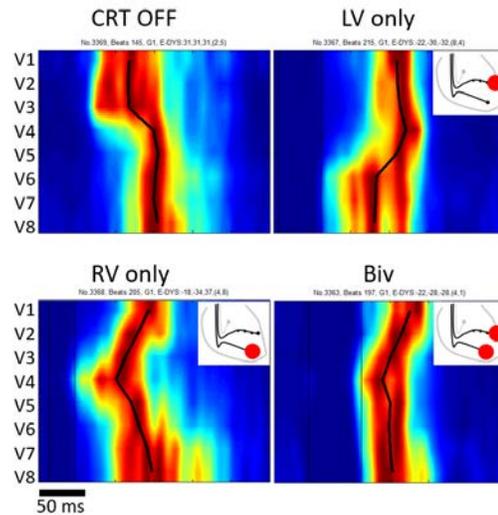


Figure 3. Electrical depolarization maps, LBBB patient

1 - CRT OFF, 2 - left ventricle pacing, 3 – right ventricle pacing, 4 – biventricular pacing.

Figure 2 shows the elimination of dyssynchrony in biventricular stimulation. Dyssynchrony reduction is identifiable from the depolarization maps better than from a conventional ECG.

Figure 3 shows the examples, how the depolarization maps change with different pacing site: stimulation in the right ventricular apex (RV only), coronary sinus (LV only) and finally biventricular pacing (Biv). It is evident that not only dyssynchrony but the whole depolarization activation pattern is important to assess.

Figure 4 shows different VV delays 0, -20, -40 ms. In this case, dyssynchrony gradually decreases from 65 ms (OFF) to 28, 15, and 11 ms. The optimal setting is VV=-40 ms.

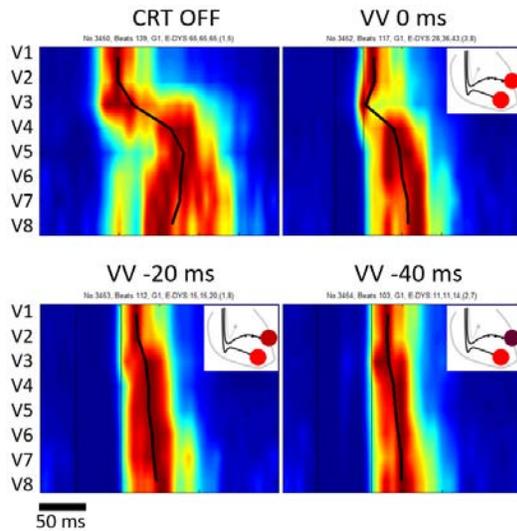


Figure 4. Electrical depolarization maps during different left ventricle pre-excitation (ventriculo-ventricular VV delay). VV=-40 ms was chosen as the optimal setting.

4. Results

The optimal CRT setting was selected by a physician from electrical activation maps for different VV delays. The mechanical intraventricular delay obtained from echocardiography was measured in all patients during CRT OFF, previously selected optimal CRT (assessed by UHF-ECG) and SMART CRT. The mechanical intraventricular delays were compared with electrical dyssynchrony. In 61% of patients, minimal mechanical intraventricular delay corresponded to optimal VV delay setting. In 27% of patients, the positive or negative effect of stimulation cannot be conclusively assessed. In these patients, the e-DYS difference between optimal and

SMART setting was lower than 10 ms interval. In 12% of patients, the minimal mechanical intraventricular delay corresponds to the SMART setting, Figure 5.



Figure 5. The UHF-ECG optimization is the best solution in 61% of patients. Only in 12% of patients, the SMART CRT setting is beneficial. In 27% of the patients, the resynchronization effect is unclear, and it was not possible to reliably assess the positive or negative settings.

5. Discussion

This contribution aims to introduce a new technique for measuring the properties of ventricular depolarization propagation. The UHF-ECG method was first introduced in [3], and clinical benefit was tested on large MADIT-CRT database [4]. Recently the study [5] compared ventricular dyssynchrony with other ECG parameters.

A significant improvement in positive outcome can be expected when it is possible to interactively assess the immediate effect of resynchronization at the time of the pacemaker implementation. Such use could allow selection of resynchronization technology (biventricular, His bundle pacing) and adjustment of pacing sites and thresholds.

The 12-lead ECG is the primary source of information to optimize pacing settings during implantation and to optimize CRT parameters during the follow-up period. The main criterion is QRS morphology and duration. However, assessing small changes in these parameters during implantation is complicated and inaccurate. It leads to the fact that the pacemaker implantation and post-implantation setting may not be optimal.

Electrical depolarization maps provide deterministic information about depolarization properties during pacing without human intervention. Both graphical representation and numerical values indicate the changes of ventricular electrical dyssynchrony during different setting of CRT. Therefore, UHF-ECG provides information that is essential for making decisions about CRT settings.

To partially confirm these assumptions, an example of the utilization of UHF-ECG methodology during optimization of post-implantation CRT settings is introduced. In a relatively small set of patients, it has been shown that UHF-ECG allows optimization of VV

delays to achieve better resynchronization results than the recommended SMART solution. More information on this study can be found at [6].

Jurak, F. Plesinger, A. Nagy, M. Novak, "Optimized CRT stimulation based on high frequency QRS analysis," *Computing in Cardiology*, 2019.

6. Conclusion

UHF-ECG electrical depolarization maps provide deterministic and straight-forward insight into the ventricular depolarization activation pattern. Simultaneous comparison of multiple maps for different CRT settings can be useful for selection of optimal pacemaker configuration.

Acknowledgments

The research was supported by the Czech Science Foundation, project GA17-13830S, by the Ministry of Education, Youth and Sports of the Czech Republic (project LO1212 and LQ1605) and by the Czech Academy of Sciences (project RVO:68081731).

Address for correspondence:

Pavel Jurak
Institute of Scientific Instruments of the CAS
Kralovopolska 147, 612 64 Brno
Czech Republic
jurak@isibrno.cz

References

- [1] M. Brignole et al., "Guidelines on cardiac pacing and cardiac resynchronization therapy," *Acta Cardiol.* vol. 69, no. 1, pp. 52-53, 2014, doi:10.2143/AC.69.1.3011345 .
- [2] UC. Nguyễn, S. Claridge, K. Vernoooy, EB. Engels, R. Razavi, CA. Rinaldi et al., "Relationship between vectorcardiographic QRSarea, myocardial scar quantification, and response to cardiac resynchronization therapy," *J Electrocardiol.* vol. 51, pp. 457-63, 2018 doi:10.1016/j.jelectrocard.2018.01.009
- [3] Jurak P, Halamek J, Meluzin J, F. Plesinger, T. Postranecka, J. Lipoldova, M. Novak, V. Vondral, I. Viscor, L. Soukup, P. Klimes, P. Vesely, J. Sumbera, K. Zeman, RS. Asirvatham, J. Tri, SJ. Asirvatham, P. Leinveber, "Ventricular dyssynchrony assessment using ultra-high frequency ECG technique," *J Interv Card Electrophysiol.* vol. 49, no. 3, pp. 245-254, 2017, doi:10.1007/s10840-017-0268-0
- [4] F. Plesinger, P. Jurak, J. Halamek, P. Nejedly, P. Leinveber, I. Viscor, V. Vondra, S. McNitt, B. Polonsky, AJ. Moss, W. Zareba, JP Couderc, "Ventricular Electrical Delay Measured From Body Surface ECGs Is Associated With Cardiac Resynchronization Therapy Response in Left Bundle Branch Block Patients From the MADIT-CRT Trial (Multicenter Automatic Defibrillator Implantation-Cardiac Resynchronization Therapy)," *Circ Arrhythmia Electrophysiol.* vol. 11, no. 5, 2018 doi:10.1161/circep.117.005719
- [5] J. Halamek, P. Leinveber, I. Viscor, R. Smisek, F. Plesinger, V. Vondra, P. Jurak, "The relationship between ECG predictors of cardiac resynchronization therapy benefit," *PLoS One.* vol. 14, no. 5, pp. 1-10, 2019, doi:10.1371/journal.pone.0217097
- [6] M. Matejkova, J. Lipoldova, P. Leinveber, J. Halamek, P.