

# Cardiac Resynchronization Efficiency Estimation by New Ultra-High-Frequency ECG Dyssynchrony Descriptor

Tereza Reichlova<sup>1</sup>, Pavel Jurak<sup>2</sup>, Josef Halamek<sup>2</sup>, Filip Plesinger<sup>2</sup>, Jolana Lipoldova<sup>1</sup>,  
Miroslav Novak<sup>1</sup>, Pavel Leinveber<sup>1</sup>

<sup>1</sup>International Clinical Research Center, Brno, Czech Republic

<sup>2</sup>Institute of Scientific Instruments, AS, Brno, Czech Republic

## Abstract

*The biventricular implantable pacemaker (BiV) is usually recommended for heart failure patients with  $LVEF \leq 35\%$  and QRS duration  $> 120\text{ms}$ . We introduce promising marker evaluating suitability and efficiency of the Cardiac Resynchronization Therapy (CRT) recipients.*

*Data: 12-lead UHF-ECG, 25 kHz sampling, 10 minute resting measurement, 28 CRT subjects, each before BiV and with BiV on, VV delay 0. Methods: A new parameter DYS was computed as the time difference between two maxima of UHF envelopes computed from V1 and V6 leads in QRS complex in 500-1000Hz frequency band. The values of DYS and QRS width before and after BiV implantation are analysed.*

*The assumption for being responder for BiV is high value of DYS before CRT and significant DYS decrease during biventricular pacing. Subjects with no response on BiV stimulation are under the borderline of  $DYS = 30\text{ms}$  before stimulation.*

*Thus the DYS parameter can serve as a new marker for the prediction of BiV pacemaker efficiency. This information cannot be derived from standard QRS width values prior BiV implantation.*

## 1. Introduction

Cardiac resynchronization therapy (CRT) in the form of biventricular stimulation (BiV) became an integral part of the medical spectre. It would reduce the risk of death and hospitalization among patients with chronic heart failure (HF) and intraventricular conduction delays. [1,2,6]

Dyssynchrony of left ventricular contraction caused by regional delays in the electrical activation of the chamber, which reduces systolic function and increases end-systolic volume, occurs in patients with heart failure due to dilated cardiomyopathy. A weakened heart reacts to increased demands via stronger blood circulation. It causes distention of the left ventricle muscle which

cannot contract coordinately with the right ventricle. Biventricular stimulation synchronizes the activation of the intraventricular septum and left ventricular free wall and thus improves left ventricular systolic function. [1,7]

Indications for CRT device implantation are based on the guidelines [2,6] NYHA functional class III or ambulatory class IV with LV ejection fraction  $\leq 35\%$  and QRS duration  $\geq 120\text{ ms}$ .

However, using currently accepted implantation criteria, about 30% of patients may not show substantial benefit from CRT [4,5]. Therefore the ability to predict positive response to CRT is a valuable tool that may allow optimization of programming or prevention of harm from inappropriate device therapy.

The importance of differentiating responders from nonresponders prior to implantation is researched in many studies. The most often discussed parameter included in implantation guidelines is QRS duration (width). It is a powerful predictor of the effects of CRT on morbidity and mortality in patients with symptomatic HF and left ventricular systolic dysfunction who are in sinus rhythm. [9] Nevertheless there are some studies which disagree. [8] Although the condition of mechanical dyssynchrony is more prevalent in the wide QRS group, it is not uncommon in patients with narrow QRS complexes. Analyses found that the degree of LV dyssynchrony do not correlate with the duration of QRS complex. [8]

We introduce a new Ultra-High-Frequency ECG (UHF-ECG) dyssynchrony descriptor which we compare with arguable QRS width parameter. The submitted study continues the work, where UHF ECG technology was introduced. [10,12] Using this technology we can describe heart electrical inhomogeneity with time resolution of 1ms. UHF-ECG is capable of measuring very weak signals. We assume these are the depolarization phases of action potentials in heart ventricle contractive cells.

## 2. Method

### 2.1. Study group

Patients who suffer from heart failure due to idiopathic dilated cardiomyopathy (IDCM) or ischemic cardiomyopathy (ICM), suggested for CRT, were chosen for this study. 12 subjects with IDCM, 12 subjects with ICM and 4 subjects with combination of IDCM and ICM were in NYHA class II-IV, had LVEF  $\leq 35\%$ , QRS width  $\geq 110\text{ms}$  and 13 of them in addition were diagnosed with left bundle branch block (LBBB).

## 2.2. Data acquisition

To record ECG, the special data acquisition system (M&I Prague, CZ) placed in electromagnetically shielded room (Faraday cabin – FC, MR-Schutztechnik, Dieburg, Germany, 2013) was used. The system, which was fully battery-powered without electromagnetic radiation, enabled us to acquire accurate ECG data in microvolts using 25 kHz sampling rate and dynamic range of 24 bits. The digitized data transmitted via an optic cable outside the Faraday cabin were then analysed.

We collected 12-lead UHF-ECG data from 28 subjects on cardiac resynchronization therapy. Every patient went through two 10 minute resting measurements, first before implantation of BiV and again after intervention with optimized programmable parameter LV Delay set on the value 0. A new parameter of dyssynchrony (DYS) was thereafter computed as time difference between the two maxima of UHF envelopes computed from V1 and V6 leads in QRS complex in 500-1000Hz frequency band. DYS was calculated before and after implantation of the BiV pacemaker. The two values of DYS were compared with standard QRS width. [10]

Initial data preprocessing had to be implemented. It included detection of the QRS complex position in the ECG signal and correlation analysis which eliminated shape different QRS complexes such as ventricular extrasystoles. [11] Subsequently 25 kHz sampled data, which had been filtered and down-sampled to 5 kHz with a pass band of 2 kHz, were computed using Hilbert transform. Figure 1B shows an example of obtained envelopes in ultra-high frequency band (500-1000Hz), its power is approximately  $10^6$  times lower in comparison to QRS complex power depicted in the part A. In graphical interpretation of these envelopes in V1 and V6 leads we can evaluate the left ventricle dyssynchrony represented as parameter DYS.

## 3. Results

Numerical results of QRS width and DYS are shown in Table 1. As mentioned before, both were calculated before and after implantation of BiV (LV Delay = 0) pacemaker in all 28 patients.

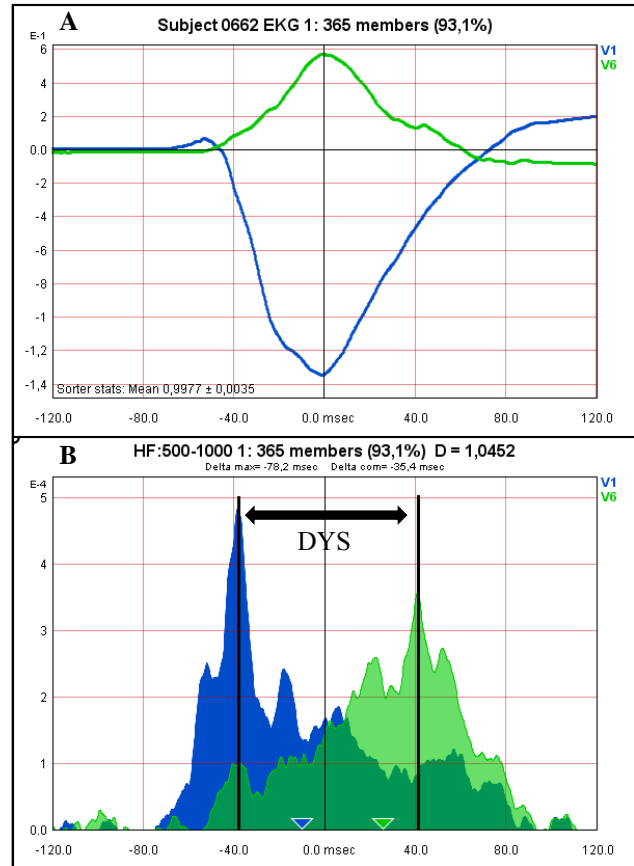


Figure 1. A: Shapes of QRS complexes in standard ECG B: Demonstration of electrical dyssynchrony by UHF envelopes in leads V1 (blue) and V6 (green).

The assumption for being responder for BiV is high value of DYS before CRT and significant DYS decrease during biventricular pacing. This index of dyssynchrony decrease (DYSindex) is defined as ratio of DYS before and after.  $\text{DYSindex} > 1$  identifies improvement in patient's condition after BiV implantation.

Subjects who do not benefit from BiV are in the lower part of the Table 1. They have no synchrony improvement of electrical activation between right (V1) and left (V6) ventricle according to  $\text{DYSindex} < 1$ . Also the values of QRS width almost did not change after implantation. They have simultaneously DYS values before stimulation  $\leq 30\text{ms}$ . Therefore this value can be considered as the lower limit for responders.

The numbers from Table 1 were plotted in the graph which we can see in Figure 2. Both measurements for each patient are linked together with a blue dotted line. Subjects under the red borderline of  $\text{DYS} = 30\text{ms}$  potentially designated as nonresponders are highlighted with a black solid line.

Table 1. DYS and QRS width differences

Patient number	DYS before [ms]	DYS after [ms]	DYS index	QRS width before [ms]	QRS width after [ms]	QRS index
1	108	52	2,08	170	155	1,10
2	102	23	4,43	190	145	1,31
3	100	45	2,22	180	160	1,13
4	88	3	29,33	170	160	1,06
5	79	9	8,78	160	150	1,07
6	70	23	3,04	170	135	1,26
7	66	12	5,50	160	125	1,28
8	66	42	1,57	155	130	1,19
9	63	12	5,25	170	120	1,42
10	62	14	4,43	135	125	1,08
11	60	27	2,22	175	115	1,52
12	58	4	14,50	170	140	1,21
13	55	26	2,12	160	145	1,10
14	54	33	1,64	170	160	1,06
15	50	24	2,08	130	115	1,13
16	46	30	1,53	162	115	1,41
17	46	17	2,71	160	135	1,19
18	42	26	1,62	160	155	1,03
19	42	9	4,67	160	130	1,23
20	37	27	1,37	145	140	1,04
21	33	21	1,57	185	120	1,54
22	23	23	1,00	120	125	0,96
23	22	22	1,00	140	150	0,93
24	17	28	0,61	160	160	1,00
25	12	14	0,86	150	145	1,03
26	10	40	0,25	185	180	1,03
27	8	11	0,73	110	110	1,00
28	0	3	0,00	115	115	1,00

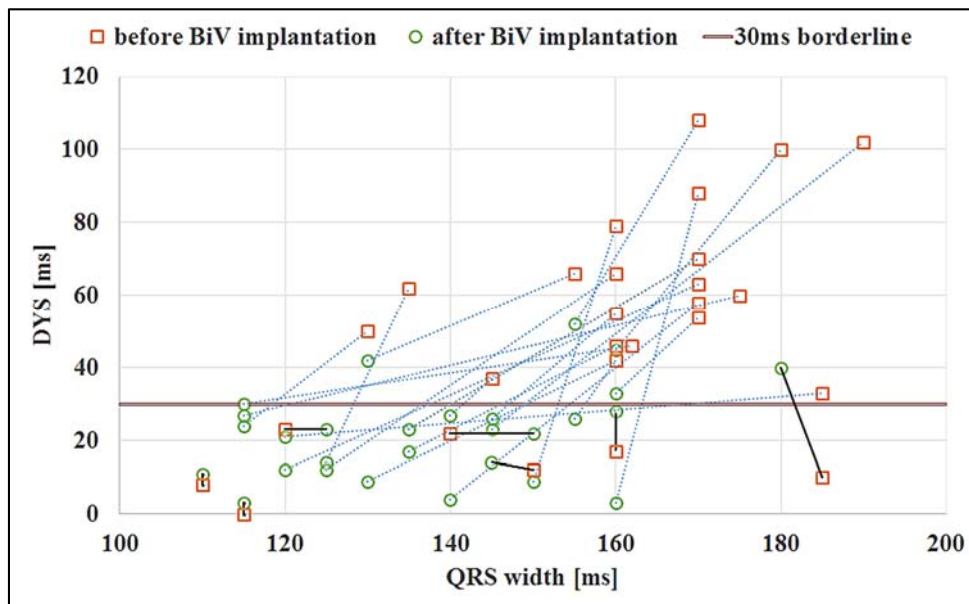


Figure 2. DYS and QRS width parameters before and after BiV implantation.

## 4. Conclusion

In the presented study, a new UHF ECG dyssynchrony descriptor for CRT efficiency estimation has been proposed. In accordance with QRS width shortening after pacemaker implantation, we divided the data from diseased subjects into two groups – responders and nonresponders. Suggested lower limit for responders is still being tested but our method is nowadays clinically used during the setting of right parameters for biventricular stimulation.

This promising marker can give us additional information about ventricle dyssynchrony which cannot be obtained from low-frequency ECG. The presented UHF ECG method which estimates CRT efficiency could avoid pointless implantation of biventricular pacemakers. The number of patients treated with CRT who do not benefit from the therapy can be reduced using this new selection criteria.

## Acknowledgements

This work was supported by MEYS CR (LO1212), its infrastructure by MEYS CR and EC (CZ.1.05/2.1.00/01.0017) and by ASCR (RVO: 68081731); European Regional Development Fund – Project FNUSA-ICRC CZ.1.05/1.1.00/02.0123.

## References

- [1] Bristow MR, et al. Cardiac-Resynchronization Therapy with or without an Implantable Defibrillator in Advanced Chronic Heart Failure. *New England Journal of Medicine* 2004; 350(21): 2140-2150.
- [2] Dickstein K, Vardas PE, Auricchio A, Daubert JC, Linde C, McMurray J, Ponikowski P, Priori SG, Sutton R, van Veldhuisen DJ; ESC Committee for Practice Guidelines. 2010 focused update of ESC guidelines on device therapy in heart failure: an update of the 2008 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure and the 2007 ESC guidelines for cardiac and resynchronization therapy developed with the special contribution of the Heart Failure Association and the European Heart Rhythm Association. *Eur Heart J* 2010; 31:2677-2687.
- [4] Coverstone E, et al. The postimplantation electrocardiogram predicts clinical response to cardiac resynchronization therapy. *Pacing Clin Electrophysiol* 2015; 38(5): 572-580.
- [5] Dupont M, et al. Differential response to cardiac resynchronization therapy and clinical outcomes according to QRS morphology and QRS duration. *J Am Coll Cardiol* 2012; 60(7): 592-598.
- [6] Brignole M, et al. 2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy: the Task Force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association (EHRA). *Eur Heart J* 2013; 34(29): 2281-2329.
- [7] Butter C, Auricchio A, Stellbrink C et al., Pacing Therapy for Chronic Heart Failure II Study Group. Effect of resynchronization therapy stimulation site on the systolic function of heart failure patients. *Circulation* 2001; 104:3026–3029
- [8] Yu C-M, Lin H, Zhang Q, Sanderson JE. High prevalence of left ventricular systolic and diastolic asynchrony in patients with congestive heart failure and normal QRS duration. *Heart*. 2003; 89(1):54-60.
- [9] Cleland JG, et al. An individual patient meta-analysis of five randomized trials assessing the effects of cardiac resynchronization therapy on morbidity and mortality in patients with symptomatic heart failure. *Eur Heart J* 2013; 34(46): 3547-3556.
- [10] Jurak P, et al. Ultra-High-Frequency ECG Measurement. *Computing in Cardiology Conference (CinC) 2013*. 783-786. ISBN: 978-1-4799-0886- 8.
- [11] Plesinger F, et al. Robust multichannel QRS detection. *Computing in Cardiology Conference (CinC) 2014*. 557-560. ISBN: 978-1-4799-4346-3.
- [12] Jurak P, et al. An additional marker of ventricular dyssynchrony. *Computing in Cardiology Conference (CinC) 2015*.

Address for correspondence.

Tereza Reichlova  
International Clinical Research Center (ICRC)  
Pekarska 53  
656 91 Brno  
Czech Republic  
E-mail address: tereza.reichlova@fnusa.cz