



Interruption of cardiac resynchronization therapy triggered by the automatic right-ventricular pacing threshold test

S. Serge Barold ^{a,*}, Andreas Kucher ^b

^a Department of Medicine, University of Rochester School of Medicine and Dentistry, Rochester, NY, United States of America

^b BIOTRONIK, Berlin, Germany

ARTICLE INFO

Keywords:

Cardiac pacing
Cardiac resynchronization therapy
Automatic pacing threshold test
Desynchronization
Left ventricular sensing
Left ventricular pacing

ABSTRACT

We report on three patients with heart failure and left bundle branch block who received a BIOTRONIK implantable defibrillator with resynchronization therapy which manifested loss of resynchronization only at a specific time of the night. Desynchronization was sudden and repeatedly initiated by the daily automatic right ventricular pacing threshold test. Loss of resynchronization occurred after switching back from the temporary test mode to the permanent biventricular pacing mode due to the reactivation of the left ventricular (LV) control of the timing cycles. LV sensed events prevented the emission of an LV paced event by virtue of a realigned LV upper rate interval, thus inhibiting LV pacing.

© 2019 Published by Elsevier Inc.

Introduction

Some cardiac resynchronization therapy (CRT) devices combined with a defibrillation function (CRT-D) are capable of left ventricular (LV) sensing [1]. LV sensing is used to prevent stimulation into the vulnerable phase of the left ventricle, through a programmable LV upper rate interval (LVURI). Under special circumstances, a desynchronizing event at pacing rates still far below the programmed maximum sensor-driven rate or upper tracking rate can interrupt resynchronization therapy and initiate a self-perpetuating desynchronization process. Such desynchronization sequences are characterized by inhibition of the LV pacing output which becomes locked into a displaced LVURI consequent to the repeated occurrence of LV sensed events conducted from right ventricular (RV) paced events (1). Desynchronization occurs only when the heart rate interval becomes shorter than the critical desynchronization interval, which is equal to $(IVC + LVURI)$ where IVC is the interventricular conduction interval (RV to LV). This report documents three cases of sudden desynchronization initiated by the automatic RV pacing threshold test (RV-PTT) of BIOTRONIK CRT devices, when performed in VVI mode (RV pacing) in the absence of LV pacing when LV sensing is preserved. Desynchronization was induced when the device switched back to its permanent biventricular VVIR mode, whereupon the reactivation of the LVURI as a controlling timing cycle was responsible for inhibition of the LV pacing output.

Recording of ventricular electrograms

The current BIOTRONIK CRT-D generation (Intica, Ilivia and Inlexa) [2–4] use trigger events for electrogram (EGM) recordings, including the detection of CRT pacing interruption [5,6]. A “CRT pacing interrupt” is identified if the detection criterion based on a ‘20-out of-48’-counter is fulfilled. The algorithm checks the rhythm within a sliding window of 48 RV cycles [both RV paced events (RVp) and RV sensed events (RVs), but no premature ventricular complexes], whether at least 20 LV paced events (LVp) events are inhibited because of the detection within the LV upper rate interval [1,5,6]. The recorded episodes of “CRT pacing interrupt” show the history prior to the interrupt detection, therefore the restoration of resynchronization is not documented. The maximum duration of these EGM recordings can be up to 30 s, depending on compression capability.

Case reports

Three patients presenting with refractory heart failure and left bundle branch block received a BIOTRONIK Intica 7 HF-T QP device (BIOTRONIK, Berlin, Germany) for CRT. No atrial lead was implanted in two patients (case 1 & 2) because of chronic atrial fibrillation and the atrial channel was deactivated. Barring the lower rate (70 ppm for Case 1 and 60 ppm for Case 2), the parameters were identical in cases 1 and 2: biventricular VVIR with maximum sensor rate 120 ppm, LV T-wave protection = on, LV maximum trigger rate 130 ppm (equivalent to the LV upper rate with LVURI = 460 ms), and the interventricular VV delay 0 ms. An atrial lead was implanted in the third patient and the device was programmed with the following parameters: biventricular DDDR 60, adaptive AV delay 150–110 ms, upper tracking rate

* Corresponding author.
E-mail address: ssbarold@aol.com (S.S. Barold).

130 ppm, LV upper rate 150 ppm, and VV delay 0 ms. Home monitoring was activated in all three cases. The detection algorithm identified several episodes of CRT interruption triggered at about 1 a.m. in all 3 patients at the time when the automatic RV pacing threshold test was scheduled (Figs. 1–3).

Basic function of the automatic pacing threshold test

The test amplitude steps down until a pulse is ineffective, followed by a backup pulse. A = ineffective test pulse (at a pulse width of 0.4 ms). B = backup pulse with a pulse amplitude 0.6 V higher than the ineffective test pulse and a pulse width of 1 ms. In the two VVIR cases (Figs. 1 & 2), the overdrive stimulation during RV-PPT is 10 ppm faster than the intrinsic rate. The overdrive pacing rate during the test remains unchanged until the end of the test. A backup pulse (B) is delivered with a coupling interval of 100 ms following an ineffective test pulse (A). The rate is measured from a backup pulse (B) to the subsequent test pulse (A). Thus, the backup pulse always restarts the prevailing overdrive pacing interval. The 2-out-of-3 algorithm is applied. When two of three test pulses are ineffective, the test is terminated. A pacing threshold test always ends with two double stimulation pulses. In the case of two consecutive test pulses below the pacing threshold, the pacing interval lengthens during the test period the basic interval plus 100 ms, due to the coupling interval of the backup pulse. After switching back to the permanent pacing mode, annotated in the tracing as a vertical line labeled VVIR, the sensor-driven interval may be shorter than it was prior to the start of the pacing threshold test. In the DDDR case (Fig. 3), the ventricular overdrive stimulation ensures that by shortening the AV delay to 15 ms after an atrial sensed (As) event, and 50 ms after an atrial paced (Ap) events.

Although the test pulses can generate effective stimulated QRS complexes in the FF-EGM, in the presence of frequent ventricular premature complexes, either the phase of the signal quality check may fail or the threshold search can be prematurely aborted. A premature abort can occur if the algorithm cannot distinguish between pacing artifacts and truly evoked signal responses.

Interpretation of recordings

Fig. 1 (Case 1). Triggering of desynchronization during automatic right ventricular pacing threshold test (in the VVI mode) in a biventricular VVIR device. The marker channels are shown on top (RV = right ventricle; LV = left ventricle). The lower part of the recording shows the far-field electrogram (FF), RV electrogram (RV), and the LV

electrogram (LV). IVC = interventricular conduction delay (RVp-LVs = 180 ms), LVURI = left ventricular upper rate interval = 460 ms. The tracings show part of the EGM recording of a CRT pacing interruption. The double stimulation pulses demonstrate the end of the automatic RV-PTT (performed in VVI exclusively in the RV). Since LV pacing was suppressed, the interventricular conduction delay was predominant. Resynchronization was not restored after a return to the permanent pacing parameters (VVIR).

The vertical grey line marks the mode switch from the pacing threshold test (VVI RV) back to the permanent biventricular VVIR mode. The oblique arrow represents the interventricular conduction delay (IVC) of 180 ms from a RV paced event to a LV sensed event. The overdrive pacing rate was 102.5 ppm (585 ms). In the case of two consecutive test pulses below the pacing threshold the pacing interval lengthened to 679 ms, due to the coupling interval of the backup pulse which restarted the pacing interval. After switching back to the permanent pacing mode, the current sensor-driven interval shortened to 617 ms. LV paced (LV) vents are still inhibited because the LVURI = 460 ms had not yet timed out. LVp inhibition continues to cause conduction from the RV paced event (RVp) to a LV sensed (LVs) event. The critical desynchronization rate was $60,000 / (180 + 460) = 93.7$ ppm. Desynchronization occurred because the sensor-driven rate was 97 ppm (617 ms) after the test, which was faster than the desynchronization rate. Desynchronization persisted at below the maximum sensor-driven pacing rate. The bold numbers show the incremental steps of the counter on the way to fulfill the 20-out-of-48 detection algorithm. RVp = RV paced event, LVs = LV sensed event, LVURI = LV upper rate interval, PTT = pacing threshold test.

Fig. 2 (Case 2), panel A. Initiation of desynchronization at the termination of the right ventricular pacing threshold testing when the pacing mode switches back to biventricular VVIR mode. LV pacing is suppressed during the RV pacing threshold test (VVI mode). Then, the device switches back to the permanent VVIR mode (annotated by the vertical line marked "Perm VVIR"). The oblique arrow represents the interventricular conduction delay (IVC) of 250 ms from a RV paced event to a LV sensed event. The overdrive pacing rate was 100 ppm during the test. Two of three test pulses were ineffective and the test was terminated. Two consecutive test pulses below the pacing threshold lengthened the pacing interval to 700 ms, according to the altered pacing cycles. Although the pacing rate is unchanged during the PTT, the sensor-driven rate has increased from 90 to 94 ppm (640 ms) during this time and will be directly applied when the PTT is finished. LVp events are still inhibited because the LV upper rate interval (LVURI = 460 ms) has not yet timed out. The critical desynchronization rate was

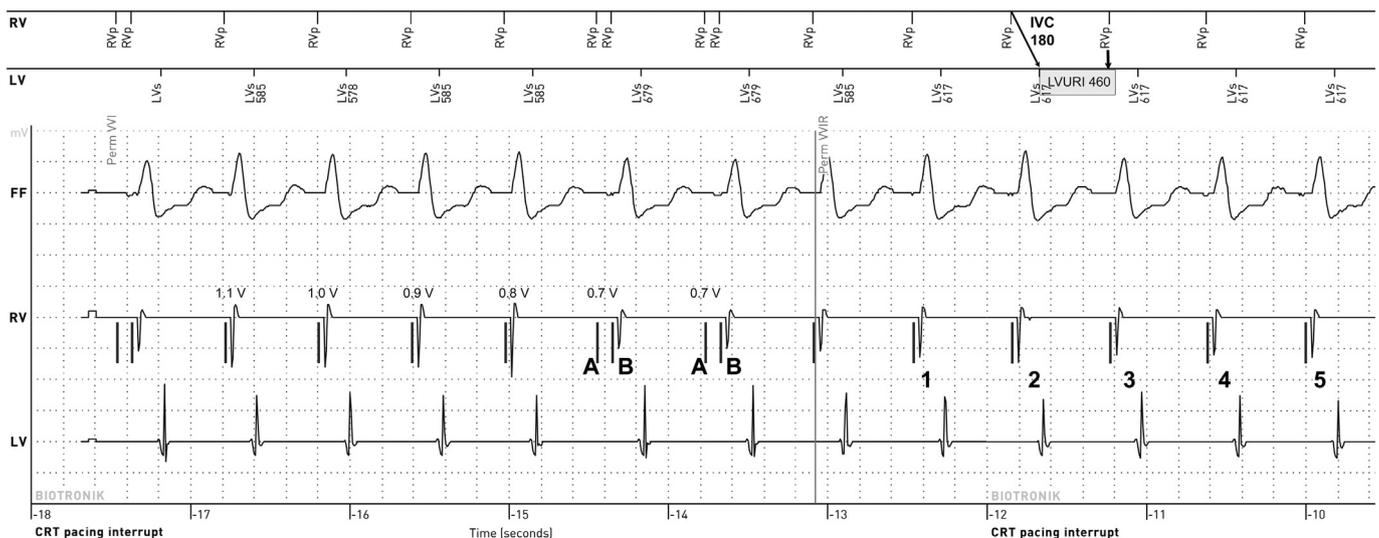


Fig. 1 (Case 1). Permanent VVIR pacing mode. Triggering of desynchronization during automatic right ventricular pacing threshold test. See text for details.

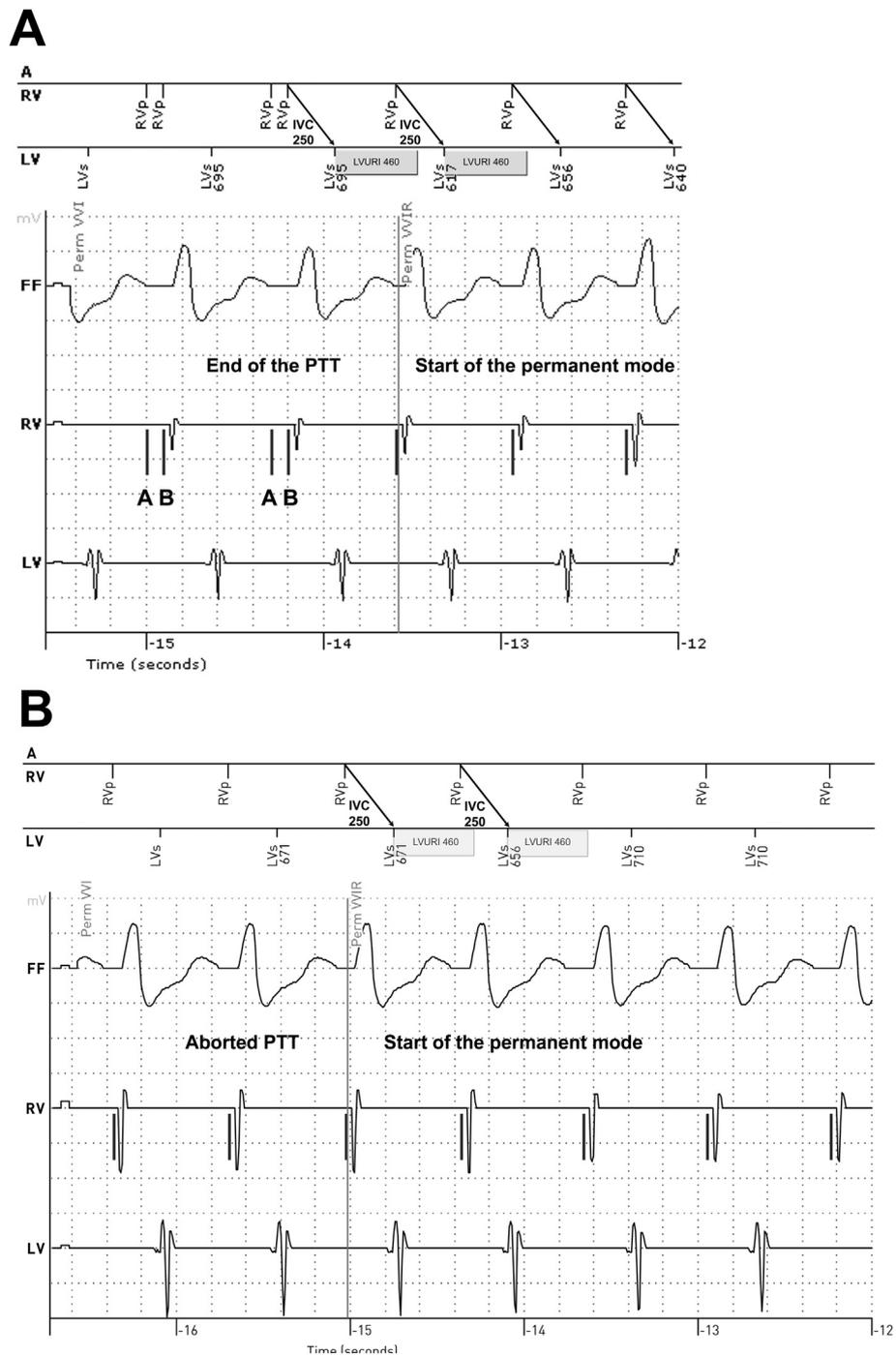


Fig. 2 (Case 2). Permanent VVIR pacing mode. Panel A. Initiation of desynchronization at the termination of the right ventricular pacing threshold. Panel B. Initiation of desynchronization after an aborted pacing threshold test. See text for details.

$60,000/(250 + 460) = 84.5$ ppm. Desynchronization occurred because the sensor-driven rate was 94 ppm (640 ms) after the test, which is faster than the critical desynchronization rate. Abbreviations as in Fig. 1.

Fig. 2 (Case 2), panel B. Initiation of desynchronization after an aborted pacing threshold test if the signal quality criteria are not fulfilled yet the device switches prematurely back to the permanent biventricular VVIR mode. Incomplete automatic pacing threshold test showing that the last two displayed test pulses (A) are not followed by backup pulses. The annotated vertical line with the mode switch indicated the threshold test was over. The pacing rate during the RV-PPT was 90 ppm (670 ms). The sensor-driven rate has increased from 80 to 84 ppm (710 ms) in the background rate and is directly used after

termination of the PTT. This emerging rate is very close to the critical desynchronization rate. The RVP events and the end of the LVURI timing bars were almost simultaneous (at 710 ms and a critical desynchronization interval of 710 ms), making LVp events suppressed on a borderline basis. A further slight decrease of the rate would immediately restore resynchronization. Abbreviations as in Fig. 1.

Fig. 3 (Case 3). Recording at the termination of the automatic RV pacing threshold test in DDDR device. There is no vertical line indicating a mode change because the RV-PTT is also performed in DDDR without mode switching, but a shortened AV-delay of 50 ms is used. During the automatic RV-PTT, LV pacing is suppressed. The termination of the RV-PTT can be identified exclusively by the switch back to the

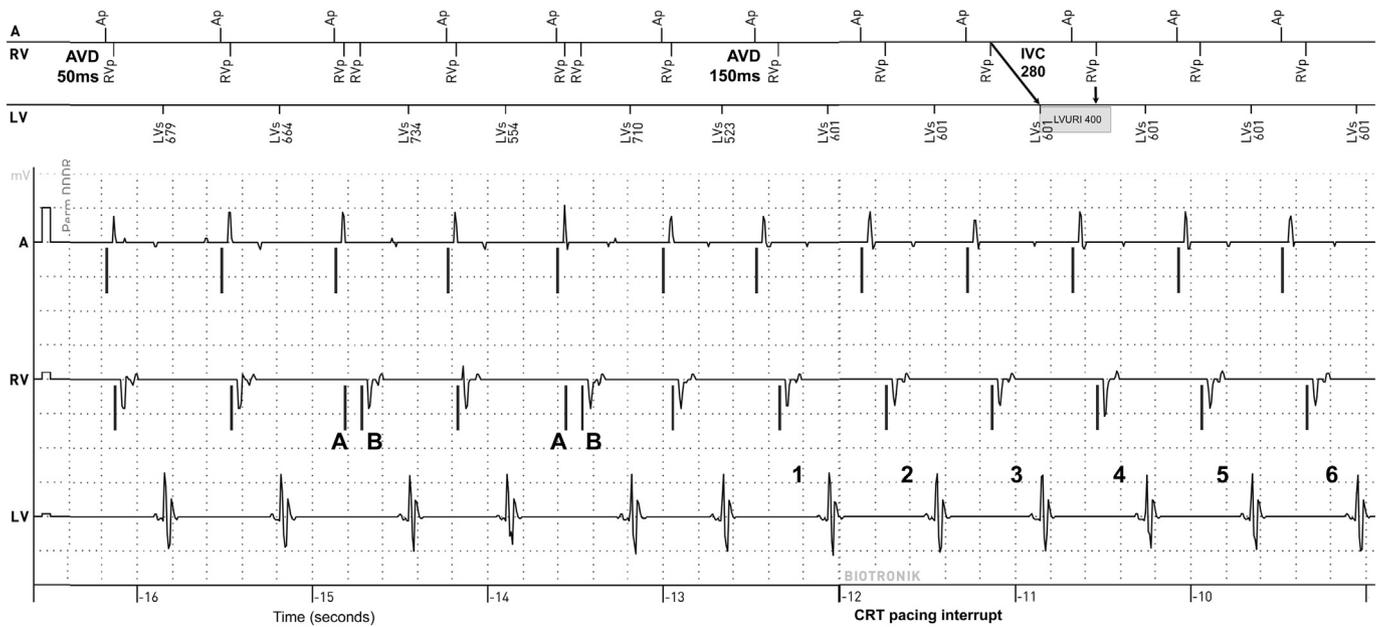


Fig. 3 (Case 3). Permanent DDDR pacing mode. Recording at the termination of the automatic RV pacing threshold test. See text for details.

programmed AV delay of 150 ms, and the 2-out of-3 confirmation algorithm characterized by the two back-up pulses. Since the sensor-driven atrial pacing rate was faster (100 ppm) than the critical desynchronization rate $[60,000/(280 + 400) = 88 \text{ ppm}]$, resynchronization cannot be restored directly after the termination of the RV-PTT. The marker channels are shown on top (A = atrium, RV = right ventricle; LV = left ventricle). The lower part of the recording shows the atrial electrogram (A), RV electrogram (RV), and the LV electrogram (LV). IVC = 280 ms, LVURI = 400 ms. Abbreviations as in Fig. 1.

Discussion

Event-triggered EGM recordings as in BIOTRONIK CRT-D devices are important to discover possible mechanisms of desynchronization and to find reprogramming options to restore resynchronization. Such recordings permit the diagnosis of desynchronization precipitated by an atrial premature complex [5], and by the automatic sensing test [6]. This type of desynchronization as in our 3 cases is related to the inhibition of LV pacing (LVp) scheduled to occur within a realigned LVURI secondary to displaced LV sensed events. Desynchronization occurs at increased pacing rates, but is still below the maximum sensor-driven rate in VVIR or DDDR mode, or the maximum tracking rate in DDD mode. Desynchronization can typically occur if two conditions are fulfilled simultaneously. First, the heart rate has to exceed the critical desynchronization rate. The desynchronization interval must be shorter than $(IVC + LVURI)$ if the V-V interval = 0, where IVC = interventricular interval. The IVC delay is determined by the separation of the LV lead from the RV lead. The only programmable parameter which has an effect on the critical desynchronization rate is the LVURI. Second, a disruptive single desynchronizing event must occur to precipitate the process. Such a trigger can be a physiological event such as an atrial, a right- or a left-ventricular premature complex, or another event capable of realigning the LV timing cycles including the LVURI.

Temporary suppression of LV pacing

Temporary suppression of LV pacing as in automatic test algorithms, including the present cases, can also realign LV timing cycles and precipitate CRT interruption [6]. In the described cases, the suppression of LV pacing (but not sensing) during the RV-PTT enabled active interventricular conduction (RVp to LVs). The same interventricular conduction

delay set the stage for desynchronization whenever the emerging sensor-driven rate after test completion was faster than the critical desynchronization rate. An RV-PTT will not lead to desynchronization if the sensor-driven rate at the end of the RV-PTT is below the critical desynchronization rate. The episode charts in our patients showed many CRT interruptions, but there were also days without desynchronization. On these days, the sensor-driven pacing rates were apparently below the critical desynchronization rate at night time when the RV-PTTs were performed. Desynchronization can persist for an unpredictably long time provided the rhythm remains faster than the critical desynchronization rate even though the heart rate is still far below the maximum sensor-driven rate or maximum tracking rate. Programming a shorter LVURI should reduce the incidence probability of a desynchronization. If shortening the LVURI is insufficient, the RV pacing threshold function can be turned off. There would be no need to turn off LV sensing or the LV T-wave protective function.

Left ventricular sensing and event recording

The event-triggered EGM recordings in the devices used in patients have enabled insight of possible trigger mechanisms for CRT pacing interruptions. These trigger mechanisms might also occur in older ICD generations, as the LV timing rules have been identical since the CRT-D generation of Lumax 340 HF-T (1). The evaluation and the programming options are comparable in older devices.

Desynchronization by RV-PTT. Probability of occurrence

Since desynchronization triggered by the automatic RV-PTT can only occur if the heart rate (either driven by the R-mode or by an intrinsic heart rate) is faster than the critical desynchronization rate, the incidence is usually rare, because the test will be done only once per night (close to the programmed Home Monitoring transmission time), when the patient is asleep. Changing the time of the Home Monitoring transmission might be helpful if the resting time of the patient occurs later.

So far it desynchronization is rarely reported during the automatic RV-PTT in DDDR mode. This may be related to the larger relative difference of at least 20 ppm between the default RV upper rate (130 ppm) and the default LV upper rate (150 ppm) in the DDDR mode. As opposed to a difference of only 10 ppm between the 'maximum sensor rate' of

120 ppm and the default upper LV rate at 130 ppm using VVIR mode, which makes VVIR more susceptible to desynchronization. It is therefore recommended for a biventricular VVIR mode to reprogram the upper LV rate higher, which should result in a larger relative difference of at least 20 or 30 ppm.

Conclusion

Temporary suppression of LV pacing in CRT-D devices during the automatic test algorithm can realign LV timing cycles and precipitate CRT interruption. The changes during the test procedure set the stage for a CRT interrupt upon restoration of the permanent biventricular pacing mode. The CRT interrupt can be eliminated or diminished by using a fast LV upper rate. In refractory cases, the RV threshold test can be programmed off.

References

- [1] Barold SS, Kucher A. Understanding the timing cycles of a cardiac resynchronization device designed with left ventricular sensing. *Pacing Clin Electrophysiol* 2014;37:1324–37.
- [2] Function manual Intica 5/7, revision: a (2016-08-09) 422209. Berlin, Germany: BIOTRONIK SE & Co. KG; 2016.
- [3] Function manual Ilivia 7, revision: a (2016-08-09) 422207. Berlin, Germany: BIOTRONIK SE & Co. KG; 2016.
- [4] Function manual Inlexa 3/7, revision: a (2016-08-09) 422211. Berlin, Germany: BIOTRONIK SE & Co. KG; 2016.
- [5] Barold SS, Kucher A. Interruption of cardiac resynchronization therapy by atrial premature complexes. *J Electrocardiol* 2018;51:247–51.
- [6] Barold SS, Kucher A. Desynchronization by cardiac resynchronization device related to automatic sensing test. *Pacing Clin Electrophysiol* 2017;40:1164–6.