Adaptive Cardiac Resynchronization Therapy Device: A Simulation Report

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ROM, R., ET AL.: Adaptive Cardiac Resynchronization Therapy Device: A Simulation Report. *We report the results of a simulation of an adaptive cardiac resynchronization therapy (CRT) device performing biventricular pacing in which the atrioventricular (AV) delay and interventricular (VV) interval parameters are changed dynamically in response to data provided by the simulated IEGMs and simulated hemodynamic sensors. A learning module, an artificial neural network, performs the adaptive part of the algorithm supervised by an algorithmic deterministic module, internally or externally from the implanted CRT or CRT-D. The simulated cardiac output obtained with the adaptive CRT device is considerably higher (30%) especially with higher heart rates than in the nonadaptive CRT mode and is likely to be translated into improvement in quality of life of patients with congestive heart failure. (PACE 2005; 28:1168–1173)*

cardiac resynchronization therapy*, *neural network

Introduction

Cardiac Resynchronization Therapy (CRT) is currently an established therapy for patients with congestive systolic heart failure and intraventricular electrical or mechanical conduction delays. It is based on synchronized pacing of the atrium and the two ventricles.[1] The resynchronization task demands exact timing of the cardiac chambers so that the overall stroke volume is maximized for any given heart rate (HR). Optimal timing of activation of the atrium and the right and left ventricles is one of the key factors in determination of the cardiac output. The timing parameters that are programmable in a CRT device that determines the pacing intervals are the atrioventricular (AV) delay and interventricular (VV) interval. Clearly, optimizing resynchronization is patient dependent as well as time and activity dependent. Intuitively, the best combination of pacing time intervals that restores optimal synchrony will change considerably during normal daily activities. CRT devices must be individually optimized, "fine-tuned" to provide optimal benefits. In addition to being time consuming and expensive, echo-guided AV and VV interval programming is limited to a static, sedentary activities. The impact of HR, body position, medications, and many other variables on these programmable variable is unknown. Determining these programmable variables should ideally be automatic and adaptive to the patient's activities.

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The next generation of CRT devices should have online adaptive capabilities determined by hemodynamic performance.

There are no clinical trial data to date systematically assessing the effect of optimized versus nonoptimized programming of CRT devices. However, the difficulty and importance of optimal programming of CRT devices is often noted.[3,4,5]

Optimization of a CRT device by continuous hemodynamic monitoring using the Medtronic Chronicle™ device has recently been reported.[3] In this case report, the authors demonstrated that continuous hemodynamic monitoring provided useful information for optimization of the AV delay. This article takes this to the next level by using a simulation where both the AV delay and the VV interval are changed dynamically by a simulated adaptive CRT device according to hemodynamic sensors.

Hence, the hypothesis of the adaptive CRT device presented here is that dynamic optimization of the AV delay and VV interval according to feedback from hemodynamic sensors, and managed by a combined controller and neural network processor, may significantly improve heart failure patients' quality of life and general well-being.

Methods

We use a closed simulation environment that simulates the intrinsic cardiac electrical and hemodynamic behaviors and an adaptive CRT pacemaker. The simulated adaptive CRT pacemaker is designed to process the simulated heart module electrical and hemodynamic inputs and to deliver optimized CRT pacing to the simulated heart. The goal of the simulated systems is to demonstrate the importance of dynamically

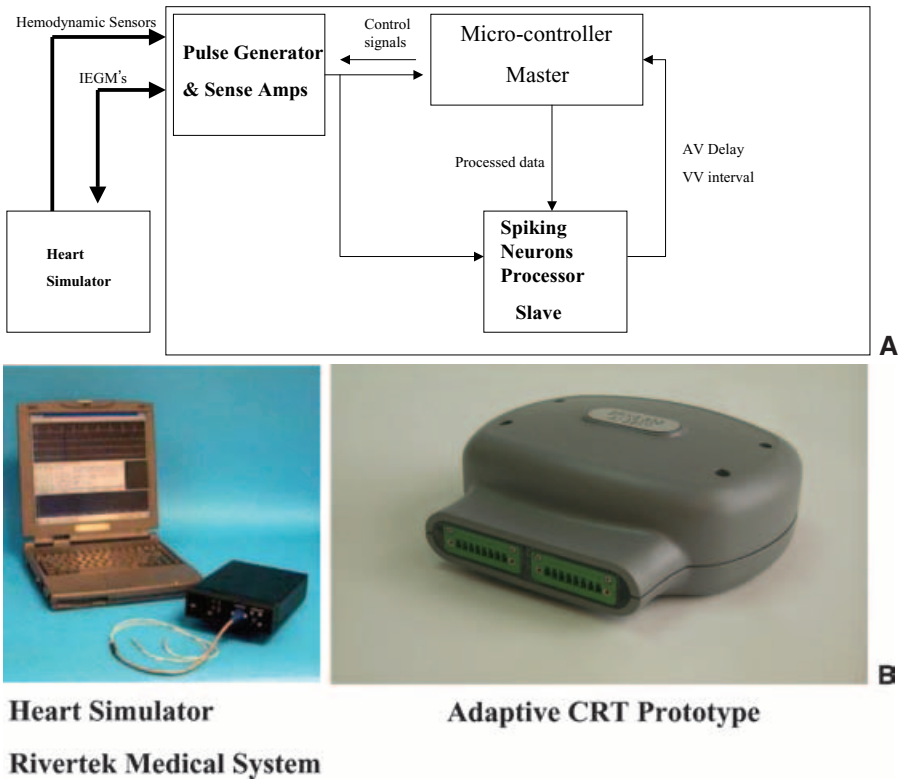

Figure 1. *A: The adaptive CRT device simulation setup in a block diagram. B: The electronic laboratory prototype development setup. A heart simulator of Rivertek Medical Systems (RSIM 2000) is paced by the adaptive CRT device prototype.*

changing the AV delay and VV intervals according to hemodynamic sensors in order to achieve optimal hemodynamic performance. The simulation modules were implemented both as a software simulator and by a hardware simulator in order to test the spiking neuron co-processor performance with an FPGA (field programmable gate array) chip. A detailed technical description of the adaptive CRT device neural network processor was previously published by the authors of this article.[7,8]

Figure 1A shows the adaptive CRT device simulation setup in a block diagram. A heart module that responds to pacing according to its state, and transmits right atrial, right ventricular, and left ventricular electrograms (IEGMs) and right and left ventricular impedance outputs representing stroke volumes to the adaptive CRT pacemaker module. The adaptive CRT module is built from a microcontroller, pulse generator module, and a spiking neural network co-processor. The spiking neural network co-processor is the learning module that processes the IEGMs and hemodynamic (impedance) sensors' data and generates online, beat-to-beat prediction to the microcontroller for the hemodynamically optimal AV delay and VV intervals. The microcontroller is the master of the electrical system and manages the pulse generator module and acts also as a teacher that trains the neural network processor online.

Figure 1B shows the electronic laboratory prototype development setup. A heart simulator of Rivertek Medical systems (RSIM 2000) is paced by an adaptive CRT device prototype implemented on an Altera FPGA, Stratix 80, with additional analog components for the interface with the Rivertek Heart simulator.

Figure 2 demonstrates the simulated ventricular impedance waveform that is generated at the heart simulator. The simulated waveform depends on the HR and on the timing of the ventricular event, measured from the right atrial event. The ventricular event in this simulation is the evoked response topacing delivered by the pulse generator and managed by the microcontroller. The impedance waveform is used to evaluate beat-by-beat hemodynamic performance via the simulated stroke volume from the adaptive CRT device. The impedance waveform follows the hemodynamic of the ventricle. When the ventricle is maximally filled with blood at the end of diastole (EDV) the impedance value is minimal. After the ventricle ejects the blood at the end of systole (ESV) the impedance value is maximal. The difference between the amplitudes of the simulated EDV and ESV represents the simulated stroke volume. When the atrial event is sensed the impedance waveform begins to decrease and when the ventricular event is sensed the impedance waveform begins to increase. During

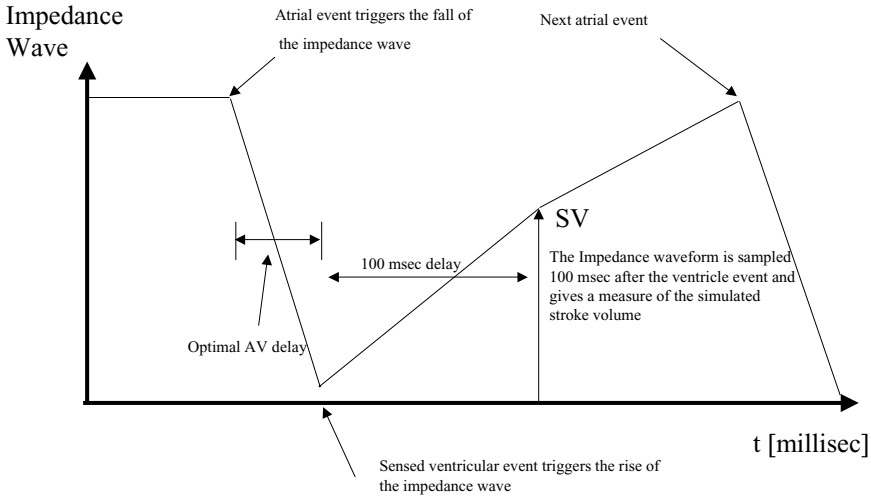

Figure 2. *Demonstrates the simulated ventricular impedance wave form that is generated at the heart simulator.*

the simulation, the impedance waveform changes beat by beat according to atrial and ventricular event timing. The maximal simulated stroke volume is achieved when the time difference between the sensed atrial and ventricular events is equal to the pre-defined optimal AV delay of the simulated heart.

Simulation Results

Figure 3 shows the simulated cardiac output during an exercise scenario. The HR was changed using Rivertek Medical systems' programming scenario user interface, from 65 beats/min (BPM) to 125 BPM at steps of 20 BPM; six simulation cycles are shown in Figure 3 and the last simulation cycle is shown with a blue rectangle. The entire simulation period was slightly more then 2 hours. During the simulation, the heart simulator pace delay parameter for the right ventricle was kept constant (5 ms) and the pace delay parameter for the left ventricle was programmed such that it was "rate-adaptive." At a heart rate of 65 BPM the left ventricle pace delay was 65 m; at 85 BPM, it was 55 ms; at 105, it was 45 ms; and at 125 BPM, it was 35 ms. The left ventricular pace delay was used to mimic a patient with left bundle branch block (LBBB) where the conductance to the left ventricle is slow relative to the right ventricular conductance.

Figure 4 shows a comparison of the simulated cardiac output during a simulation cycle with dynamic optimization of the AV delay and VV interval performed by the adaptive CRT device versus a CRT device optimized at rest (65 BPM) and subsequently pacing the heart with a constant intervals. Dynamic optimization of the AV delay and VV interval produces 30% higher simulated

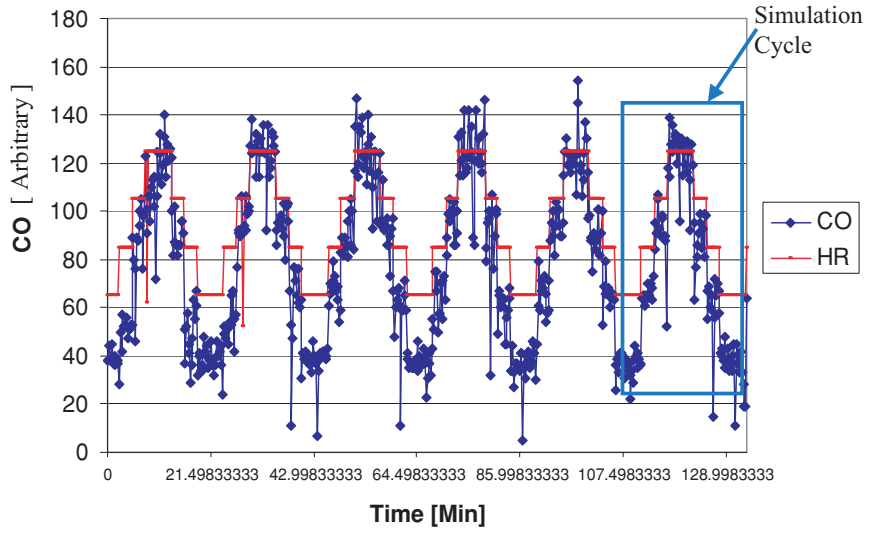

Figure 3. *The simulated cardiac output during an exercise scenario.*

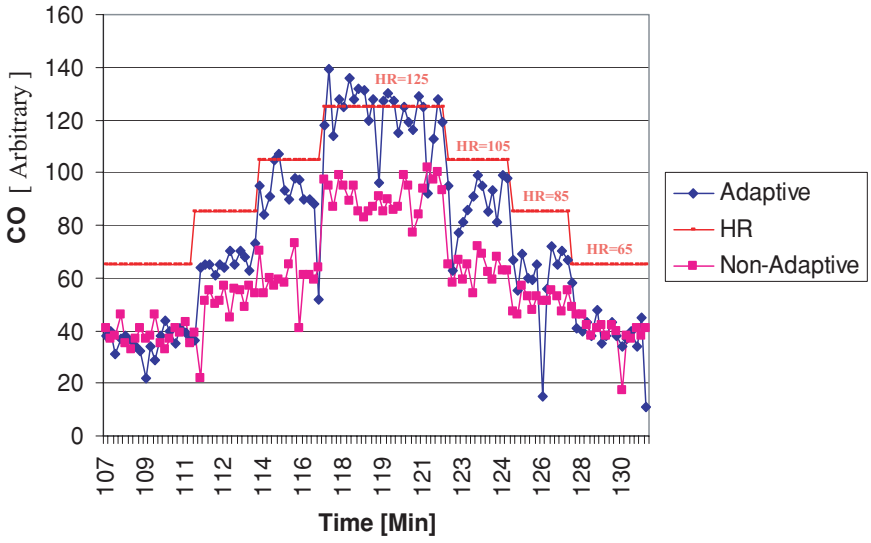

Figure 4. *A comparison of the simulated cardiac output with dynamic optimization of the AV delay and VV interval vs. nonadaptive CRT pacing.*

cardiac output on average during a simulation cycle. The benefit of the dynamic optimization is more significant at higher heart rates where the AV delay and VV intervals are at their most difference from resting values.

Figure 5 shows the dynamic optimization of the AV delay and VV intervals performed by the adaptive CRT device. The AV delay was 130 ms at 65 BPM and was reduced gradually to 50 ms at 125 BPM. The VV interval was −60 ms at 65 BPM and reduced gradually to −20 ms at 125 BPM. This simulation demonstrates the potential benefits expected with dynamic optimization according to hemodynamic sensors in a closed loop system and clinical advantages over available CRT devices.

Figure 6 shows a comparison of the simulated stroke volumes of a responder to CRT and a nonresponder to CRT as a function of time. In the adaptive CRT mode, the AV delay and VV interval are changed dynamically according to the information obtained from the hemodynamic sensors. When the patient is a responder to CRT, the device will change the pacing intervals in order to achieve a higher stroke volume as shown in Figure 6 (pink rectangles). When the patient is a nonresponder, the stroke volume will not improve and remain unchanged (blue triangles). When a patient is identified that does not respond to hemodynamically derived automatic adjustment of pacing intervals, the clinician might need to consider other options including lead repositioning.

Discussion

The simulation results presented here demonstrate the potential of the adaptive CRT device with

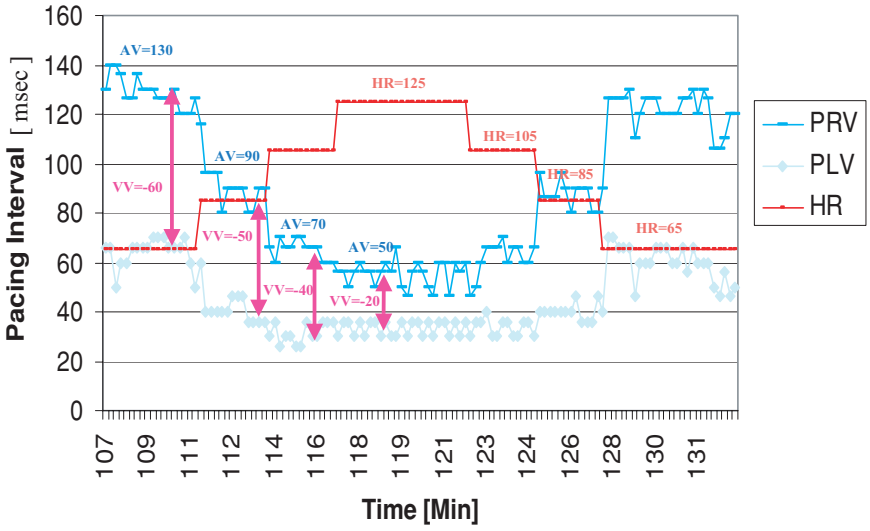

Figure 5. *The dynamic optimization of the AV delay and VV intervals performed by the adaptive CRT device.*

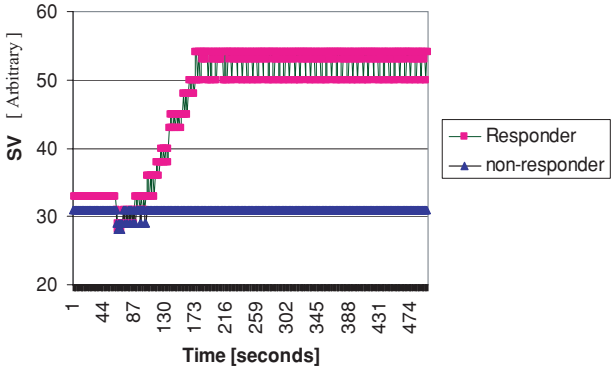

Figure 6. *A comparison of the simulated stroke volumes of a responder to CRT and a nonresponder to CRT.*

dynamic optimization of AV and VV intervals for improving cardiac output beyond the current nonadaptive CRT devices.

The improvement in the simulated cardiac output shown in Figure 4, as a result of online optimization of the AV delay and VV interval according to simulated hemodynamic sensors, is the primary result demonstrated in this study. Hemodynamics are influenced by many variables, activity being one of the most significant. The model reported suggests that an online adaptive therapeutic device that stimulates the heart and auto adapts in response to the hemodynamic variation can improve hemodynamic performance considerably and deliver optimal and consistent CRT. Performance at higher heart rates is especially important in CHF patients, who tend to be tachycardic even at low exercise levels. The present simulation report demonstrates the potential improvement of cardiac output with adaptive CRT device at higher heart rates. This may therefore translate to an improvement in exercise capability and quality of life of CHF patients with a future adaptive CRT device.

The adaptive CRT device working in a closed loop with hemodynamic sensors will enable a clinician to optimize pacing intervals and to select a better lead position using a responder to the CRT online diagram shown in Figure 6. Using this diagram the clinician might be able to convert a "nonresponder" into a "responder" and a "responder" into a "better responder."[4]

The adaptive CRT device is expected to simplify and hence to shorten the time required by the clinician during a patient's follow-up. Since the device has built-in autoprogrammability capabilities the clinicians will primarily need to review stored histograms and verify the appropriateness of automatic features.

Dynamic optimization of the AV interval in response to hemodynamic sensors will also be beneficial to patients with a dual chamber pacemaker, since it is well known that phsyiologically the AV delay is rate-dependent. Since dynamic optimization enables more physiologic pacing, it is expected to be beneficial to all future pacemakers and defibrillators after clinical benefit is proven.

The adaptive CRT device shown in the block diagram in Figure 1, adds a "spiking neuron network co-processor" to the existing microcontroller. This architecture has the advantage of the combined deterministic algorithmic module (the microcontroller) and a learning module, the spiking neuron network. The microcontroller master trains "online" the learning module that is responsible for adjusting to the patient's intrinsic hemodynamics. The adaptive CRT device architecture shown in Figure 1 enables minimal changes to the existing CRT device microcontroller code that will ease the integration and regulatory efforts.

CRT device management and more specifically the management of the AV delay and VV intervals are especially suitable for neural network processing given the marked interindivudal and intraindividual variation in these parameters. Neural network are able to process the hemodynamic sensors biological signals using pattern recognition techniques and to perform a feedback control task dynamically and online.[5] Neural networks are a different paradigm for computing. They are based on parallel architecture with simple processing elements and a high degree of interconnection. Neural networks are known to have advantages over standard algorithmic processing in performing tasks such as adaptive control and pattern recognition.[5] Spiking neural networks architectures are a unique form of neural networks that are inspired by the biological nervous system.[6] The adaptive CRT device described here is based on a novel spiking neural network architecture and learning rule developed specifically for adaptive CRT devices and for closed loop therapeutic medical devices more generally.[7,8]

A primary and novel feature of the spiking neural network architecture, used here for the adaptive CRT device, is the combination of a spiking neural network architecture with the Hebbian learning rule to perform an *online feedback control* task combined with a *pattern recognition* task implemented to the hemodynamic sensor signal. The second important feature of the spiking neuron network is its ability to perform both tasks with *extremely low power dissipation* or current drain. Low power dissipation is a crucial point for implanted pacemakers and defibrillators devices that need to operate 5–7 years with a battery power source only.

In the next phase of investigations the adaptive CRT device will be tested in an acute animal experiment with implanted pressure sensors

in the right and left ventricles and with sono crystals implanted in the left ventricular wall. Later, in planned chronic animal experiment investigations and clinical studies the ideal hemodynamic sensor will be defined. Whether the ideal sensor is indeed stroke volume as derived from intracardiac impedances as used in the in vitro model described,[9] intraventricular pressure sensing as performed with the Medtronic Chronicle™ device,[3] or wall motion sensing as performed with SORIN peak endocardial accelerometer (PEA™) sensor is yet to be determined.

Whereas the greatest potential use of the neural network processor is when integrated into an implanted cardiac rhythm device with continuous interval adaptation, a similar external adaptive CRT device can be developed. In the external adaptive CRT device, the spiking neuron network learning module will be utilized externally to the implanted CRT device that will telemetrically receive the IEGMs and hemodynamic sensors' data and transmit back the optimal AV and VV intervals to the implanted device. The external device will be used to optimize an implanted CRT device, to identify responders to CRT and may reduce the time and cost of the follow-up procedure for CRT patients.

Conclusion

The present simulation model suggests that an online adaptive CRT device based on a neural network—learning module has the potential to solve major weaknesses of the current CRT devices. The adaptive CRT device with feedback control from a hemodynamic sensor can provide a solution for the need for auto-programmability and auto-adjustment capabilities in a CRT device.[4]

In addition, an external adaptive CRT device is expected to significantly simplify the follow-up procedure, to optimize pacing intervals and to select a better lead position and hence to identify and improve response to CRT, and subsequently reduce costs. In vivo data are needed to prove the clinical benefits expected from the adaptive CRT device.

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