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Simulation of AV Hysteresis Pacing Using An Integrated Dual Chamber Heart And Pacer Model

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Abstract—**Long term right ventricular apical pacing has been known to have adverse effects in cardiac function. The AV hysteresis (AVH) is a feature existing in many dual-chamber cardiac pacemakers that aims to minimize the right ventricular pacing, but its clinical efficacy remains inconclusive due to conflicting evidence from different studies. We have recently developed a novel integrated dual-chamber heart and pacer (IDHP) model, which can simulate various interactions between intrinsic heart activity and extrinsic cardiac pacing. In this study, we use the IDHP model to simulate various atrio-ventricular (AV) conduction pathologies, and to investigate the effects of an AVH algorithm on reducing right ventricular pacing. Our results show that the efficacy of AVH is dependent on the underlying cardiac conditions. While it can preserve intrinsic conduction during minor or moderate first degree AV block, its efficacy is reduced at higher degree AV block conditions. This pilot study further supports using the IDHP model to design and evaluate more advanced pacemaker algorithms for therapeutic interventions.**

I. Introduction

DUAL chamber cardiac pacemaker is the most common type of pacemaker implanted worldwide [1]. By sensing and analyzing electrical signals in both the right atrium (RA) and the right ventricle (RV), pacing pulses are delivered to one or both chambers as needed while attempting to maintain the atrio-ventricular (AV) synchrony.

On the other hand, growing evidence has emerged recently that long-term apical right ventricular pacing (RVP) is associated with increasing risk of developing congestive heart failure (CHF) and atrial fibrillation (AF) [2]-[4]. In particular, the percentage of right ventricular pacing has been shown to correlate with the adverse outcomes in patients with compromised left ventricular function [5]. Hence, one intuitive solution is to equip pacemakers with new features that can minimize right ventricular pacing. One typical approach is to automatic switch between atrial based pacing (e.g. AAI mode) and ventricular based pacing (e.g. DDD mode) [6,7]. Another representative strategy is to extend pacemaker AV delay (AVD) through hysteresis to promote intrinsic AV conduction (e.g., Biotronik's I-Opt ™, Medtronic's Search AV+™, St. Jude Medicals' Ventricular Intrinsic Preference™, Boston Scientific's AV Search Hysteresis™).

Despite about a decade's clinical experience, the benefits and limitations of pacemaker AV hyteresis (AVH) feature remain inconclusive due to conflicting evidence from different studies. Whereas some groups found AVH could substantially reduce RVP [8,9], others reported only limited success [10] and questioned its efficacy [11]. The underlying reasons for the apparent discrepancy are likely multifaceted, including but are not limited to, differences in study design, heterogeneity of patient etiology, differences in AVH algorithms and parameter settings, etc.

One way to control these confounding factors is by means of computer simulation, which nevertheless has been difficult due to highly complex interactions between intrinsic heart rhythm and extrinsic cardiac pacing. Recently, we have developed an integrated dual-chamber heart and pacer (IDHP) model [12,13], which was an extension and enhancement of a previous open-source AF-VP model [14,15]. The IDHP model provides an abstract yet realistic representation of the native cardiac electrical conduction system and its interactions with external dual-chamber cardiac pacing. Therefore, it provides a new simulation platform where it is possible to bench test advanced pacemaker algorithms in the presence of different types of cardiac rhythms. In this pilot study, we use the IDHP model to investigate the RVP suppression effect of a specific AVH algorithm in different AV conduction abnormalities.

II. Methods

A. IDHP Model

Detailed implementation of the IDHP model has been described elsewhere [12,13]. In brief, the model consists of 8 modular components as shown in Figure 1: (1) atrial source, (2) atrial conductor, (3) AV junction (AVJ), (4) ventricle conductor, (5) ventricle source, (6) atrial lead, (7) ventricle lead, and (8) pacer.

Through bidirectional connections between different modular pairs, the intrinsic heart rhythm generator, the cardiac conduction pathway, and the implantable pacemaker are integrated into a closed loop system. The antegrade branch of the loop starts from the atrial source output, or from atrial pace (AP) delivered by the pacer via the atrial lead. The resulting atrial depolarization passes through the atrial conductor before invading the AVJ, where the signals

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are processed, then further propagate through the ventricle conductor, until reaching the ventricle source and being sensed by the pacer via the ventricle lead. On the other hand, the retrograde branch of the loop starts from the ventricle source output, or from ventricular pace (VP) delivered by the pacer via the ventricle lead. The resulting ventricular depolarization passes through the ventricle conductor before penetrating the AVJ, where it is delayed before further invading the atrial conductor, until reaching the atrial source and being sensed by the pacer via the atrial lead. Evidently, multi-level interactions may occur between these two opposite electrical conduction branches.

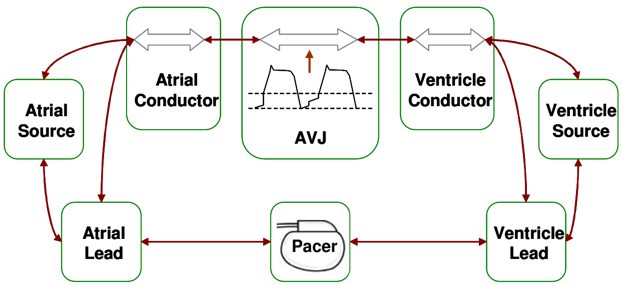

Fig. 1. Schematic diagram of the IDHP model.

B. *AVH Algorithm*

Biotronik's AVH feature combines standard hysteresis with repetitive and scan enhancements to reduce unnecessary RVP. Specifically,

- Scan AVH regularly searches for intrinsic AV conduction. After a programmable number of ventricular paces (set to 180 in this simulation) using the standard AVD, the pacer will extend to a longer AVD for a few cycles (set to 5 in this simulation) to scan for intrinsic AV conduction. If a ventricular sense (VS) is detected during the scan, then AVH is initiated by retaining the long AVD. Otherwise, the pacer will resume the standard AVD, and will retry scan AVH later after the programmed number of VPs.
- Repetitive AVH encourages intrinsic AV conduction to return quickly during intermittent AV block (AVB). If one VP occurs at long AVD, the pacer will continue operate (repetition) at long AVD for a number of cycles (set to 5 in this simulation). If a VS is detected during these cycles, the pacer will maintain the long AVD. Otherwise, the pacer will switch to standard AVD at the end of AV repetition period.

In this simulation, the standard AVD is set to 250ms after an AP or 220ms after an atrial sense (AS), and the long AVD for AVH is set to 400ms.

C. *Simulation Protocol*

By changing AVJ parameters [12]-[15], seven basic model conditions are created as summarized in Table I, where NM represents normal AV conduction; 1A, 1B, 1C simulate progressively severe 1st degree AVB; 2A and 2B respectively simulate the Mobitz I and Mobitz II 2nd degree AVB at increasing sinus rate; and 3D represents the 3rd degree AVB. Other IDHP model parameters are respectively set to similar values as being described in [12].

TABLE I
BASIC CONDITIONS SIMULATED BY THE IDHP MODEL

Basic Condition	Sinus Rate	Antegrade AV Conduction Range	Minimum AV refractory period
NM	80bpm	70ms – 200ms	100ms
1A	80bpm	200ms -350ms	100ms
1B	80bpm	250ms - 400ms	100ms
1C	80bpm	300ms – 450ms	100ms
2A	120bpm	350ms – 600ms	100ms
2B	120bpm	200ms – 350ms	450ms
3D	80bpm	>10s	100ms

These 7 basic conditions are further mixed to yield 20 test cases as summarized in Table II.

TABLE II
TEST CASES USED IN THE SIMULATION

Case	Mix of Basic Conditions	Case	Mix of Basic Conditions
1	1A	11	2A-2B-2A
2	1B	12	2B-2A-2B
3	1C	13	NM-1C-NM
4	2A	14	1C-NM-1C
5	2B	15	NM-2A-NM
6	3D	16	2A-NM-2A
7	1A-1B-1C	17	NM-1A-1B-1A-NM
8	1C-1B-1A	18	NM-1B-2A-1B-NM
9	1A-2A-1A	19	1B-1A-NM-1A-1B
10	2A-1A-2A	20	2A-1B-NM-1B-2A

Using the IDHP model, each run of each test case simulates 600s. Test cases 1-5 represent constant conditions in various degrees of AVB. Test cases 7-16 represent various combinations of 3 basic conditions, each lasting 200s. Test cases 17-20 exemplify more complex transitions between 5 basic conditions, each lasting 120s.

By feeding different random seeds to the IDHP model, each test case is run 10 times while pacer operates in standard DDD mode, and then is repeated for 10 times while activating the AVH feature. The percentage of VP (VP%) averaged over 10 runs is compared between AVH OFF and AVH ON. Student t-test is used for statistical analysis and p=0.05 is chosen for the level of significance.

III. RESULTS

As an example, Figure 2 shows a segment of model-generated event markers while simulating test case 8 in standard DDD mode. Since the standard AVD (220ms after AS) is shorter than the intrinsic AV conduction time (condition 1B during 200-400s), each AS detected by the pacer is tracked by a committed VP at the end of AVD.

In contrast, Figure 3 shows a segment of simulated event markers for test case 8 while AVH is enabled. Because the pacer has delivered 180 consecutive VPs (note: the 1st scan

AVH did not find AV conduction due to condition 1C during 0-200s), it started a scan AVH by extending the AVD. Since a VS is uncovered, the long AVD is retained to promote the intrinsic AV conduction.

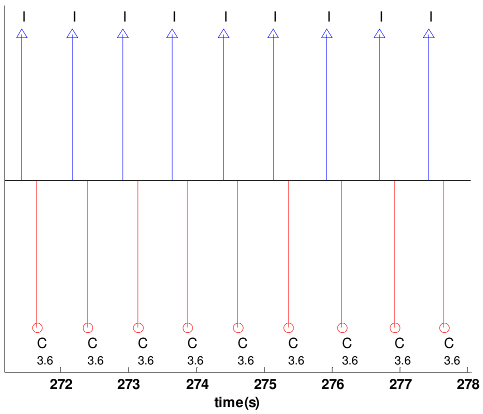

Fig. 2. A segment of simulated event markers for test case 8 while pacer operates in standard DDD mode. I – intrinsic AS, C – captured VP at 3.6V.

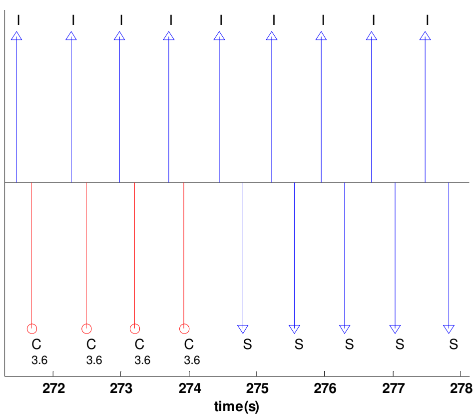

Fig. 3. A segment of simulated event markers for test case 8 while AVH is enabled. I – intrinsic AS, C – captured VP at 3.6V, S – conducted VS.

In another example, Figure 4 shows a segment of model-generated event markers for test case 15 while the pacer operates in standard DDD mode. Because the model condition changes from NM to 2A (Mobitz I 2nd degree AVB) at 200s, the rhythm transits from AS-VS to AS-VP.

In contrast, Figure 5 shows a segment of simulated event markers for the same test case while AVH is ON. Similarly, persistent AS-VS rhythm could not be maintained after 200s. However, although VPs are delivered due to intermittent AVB (note: condition 2A simulates mixed 3:2 and 4:3 Wenckebach behavior with progressively lengthening of AV conduction), many intrinsic AV conductions are preserved by the repetitive AVH.

Figure 6 compared the percentage of VP when pacer respectively operates in standard DDD and AVH for all test cases evaluated in this study. Of 20 test cases examined in this study, only 4 test cases show no difference in VP% between standard DDD and AVH. Specifically, AVH could not reduce VP either when intrinsic AV conduction is too long (100% VP for test case 3 of severe 1st degree AVB, and test case 6 of the 3rd degree AVB), or when severe AVB is mixed with normal AV conductions (100% VP in condition 1C but no VP in NM condition for test cases 13 and 14). In other 16 test cases, AVH significantly reduces VP% compared to standard DDD ($p<1e-6$ for all except for test case 5 where $p<0.05$). Also note that NM conduction does not guarantee VS (e.g., test cases 15, 16, 18, 20), mainly due to presence of retrograde atrial activations (data now shown).

Overall, in all 20 test cases evaluated in this study, standard DDD mode results in 88.1±18.2% VP, whereas enabling AVH significantly reduces VP% to 49.2±29.5%.

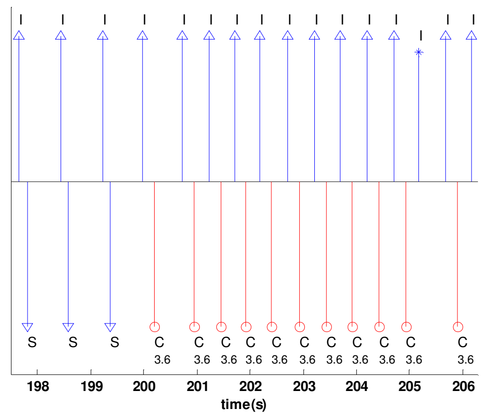

Fig. 4. A segment of simulated event markers for test case 15 while pacer operates in standard DDD mode. I – intrinsic AS (Δ normal AS, * AS in refractory window), C – captured VP at 3.6V, S – conducted VS.

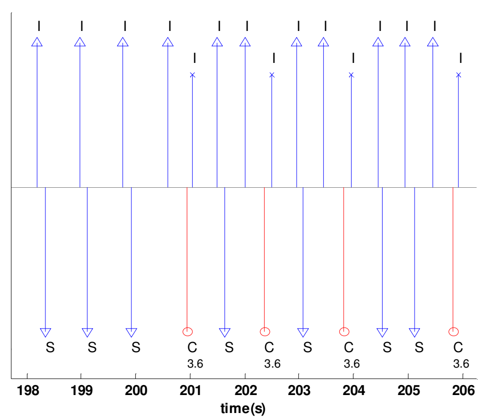

Fig. 5. A segment of simulated event markers for test case 15 while AVH is enabled. I – intrinsic AS (Δ normal AS, x undetected AS in blanking window), C – captured VP at 3.6V, S – conducted VS.

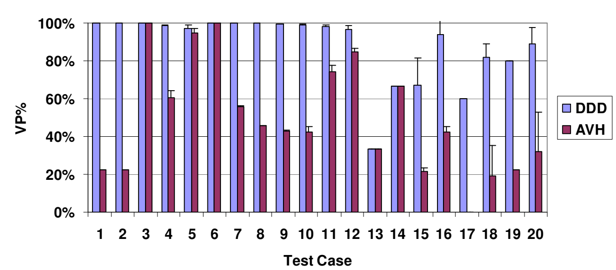

Fig. 6. Comparison of the percentage of VP for all test cases when pacer respectively operates in standard DDD and AVH.

IV. DISCUSSION

Using a recently developed IDHP model, this work represents the first simulation study that investigates the efficacy of a specific AVH algorithm in reducing RVP in the context of different AV conduction pathologies.

Although this study is by no means an exhaustive test of AVH in different heart rate and rhythm conditions, the results, which are consistent with previous clinical findings [10,16], have shown that the efficacy of AVH feature is dependent on the underlying cardiac conditions: whereas it is highly effective to preserve intrinsic AV conduction during minor or moderate 1st degree AVB, its efficacy is reduced as higher degree AVB develops. For the 2nd degree AVB, AVH seems more effective for Mobitz I than Mobitz II to promote the intrinsic AV conduction (see Fig. 6, test cases 4 vs. 5, and 11 vs. 12), yet the underlying mechanism and whether or not this could be generalized remain to be clarified in a more comprehensive analysis.

The role of AVH in reducing RVP has been controversial due to conflicting results from previous clinical studies [8-11]. In light of this simulation study, the efficacy of AVH could be greatly impacted by patient' disease characteristics, temporal variation of cardiac conditions, variance in AVH algorithms and pacemaker parameter settings, among other factors. Therefore, in order to fully reveal the advantages and limitations of the AVH feature, more rigorous study design is required to control these potential confounding factors. From this perspective, the IDHP model provides a preferred platform to design and evaluate more advanced pacemaker algorithms for minimizing RVP.

Finally, one caveat that must be borne in mind is that not all RVP are unnecessary. While it is true that too frequent RVP is associated with adverse effects in cardiac function [2]-[4], unconditional elimination of RVP could be just as detrimental [17], due to potential AV decoupling/uncoupling [18], increased risk of retrograde conduction and pacemaker mediated tachycardia [19], compromised ventricular support due to nonphysiologic AV intervals [20,21], and so on. Therefore, design of RVP suppression algorithm must strike a balance between promoting intrinsic AV conduction and maintaining the AV synchrony.

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