

## AV-Delay Optimization According to the Right Ventricular Intracardiac Impedance

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### Summary

*An optimal atrioventricular (AV) delay allows end-diastolic filling completion before ventricular contraction in pacemaker patients. The optimal AV-delay assessment by means of non-invasive hemodynamic measurements is feasible, but time and resource consuming. The goal of this preliminary study is to show that optimal AV-delay assessment is feasible by means of right ventricular intracardiac impedance (RVI) variations measured by an Inos<sup>2</sup> CLS pacemaker. In 12 pacemaker patients, optimal AV delay was calculated using the Ritter's formula. During an echocardiographic examination, the pacemaker measured RVI at a range of AV delays. The measurements were transmitted via telemetry and stored in a laptop for post-processing. The value for  $(d(RVI)/dt)^2$  was calculated at each AV delay. Assuming that RVI is proportional to the blood volume surrounding the tip electrode of the ventricular lead, this parameter represents the myocardial contractility. In all patients, the peak of the  $(d(RVI)/dt)^2$  curve was at its maximum when the optimal AV delay determined by echo measurements was programmed. As clinically expected, this meant that the heart contractility was maximal when optimal AV delay was programmed. Right ventricular intracardiac impedance seems to be a valid tool for optimal AV-delay assessment. Such an algorithm implemented in a pacemaker would significantly improve patient hemodynamics and reduce follow-up time.*

### Key Words

Dual-chamber pacemaker, AV delay, intracardiac impedance

### Introduction

Since its advent in 1969, the dual-chamber pacing has been regarded as "physiologic pacing." This concept later evolved into "true physiologic pacing", when sensors for rate-adaptive pacing were added to dual-chamber devices to improve hemodynamic performance in chronotropically incompetent patients. The next step along the path of progress in physiologic pacing is optimization of atrioventricular (AV) synchrony in patients with impaired dromotropic response. In a normal heart, cardiac output (CO) is regulated by several physiologic factors, among them the AV delay.

Optimization of the CO in DDD patients requires that atrial and ventricular contractions are appropriately timed. An optimal AV delay (OAVD) allows completion of the end-diastolic filling flow prior to ventricular contraction, thus providing the longest diastolic filling time. A long programmed AV delay would produce a mitral pre-systolic insufficiency, thus decreasing the ventricular filling. A short programmed AV delay would produce an early interruption of the active ventricular filling. Modern dual-chamber pacemakers provide a wide range of programmable AV intervals, fixed

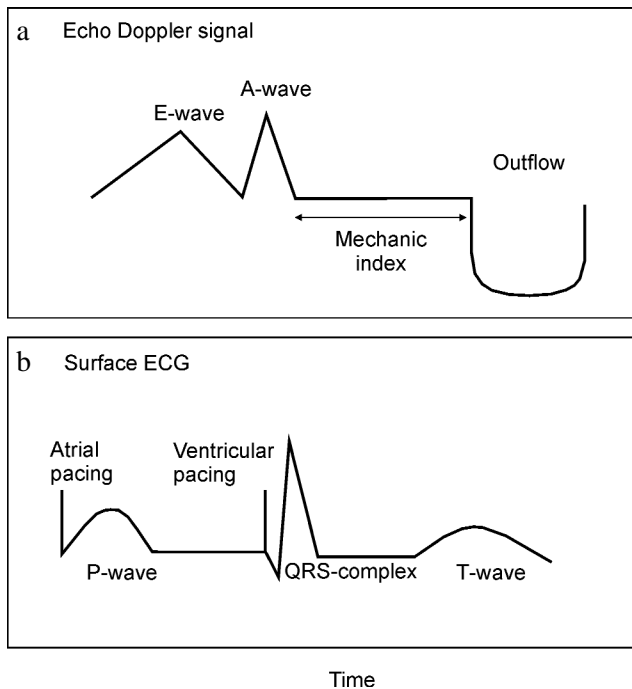


Figure 1. Optimal atrioventricular delay (OAVD) according to the Ritter's formula [16] is:  $OAVD = (LAVD - SAVD) - (MI SAVD - MI LAVD) + SAVD$ . Here, MI is the mechanic index, SAVD is the shortest atrioventricular delay tested, and LAVD is the longest atrioventricular delay tested.

or modulated as a function of the spontaneous or sensor driven atrial rate. The contribution of a proper AV delay is significant and varies from 13 % to 40 % of the CO, thus providing a hemodynamic improvement in both normal and diseased hearts [1-12].

AV delay optimization has been investigated in several studies [3,13-15]. All investigated methods were based on hemodynamic measures performed with echocardiographic or other time- and resource-consuming CO measurement techniques. Ritter et al. [16] proposed a simple method based on Doppler echocardiography of transmitral flow. According to this method, OAVD is calculated after measuring the time shift of the mitral valve closure caused by reprogramming from a long to a short AV delay (Figure 1). Kinderman et al. [17] demonstrated that the OAVD evaluated by Ritter's formula predicts the AV delay producing maximum stroke volume in the majority of patients.

The Inos<sup>2</sup> CLS pacemaker (Biotronik, Germany) determines the right ventricular intracardiac impedance (RVI) by measuring the induced voltage following injection of the sub-threshold constant-current pulses

between the case and the right ventricular tip electrodes. Since the RVI is proportional to the blood amount within a small volume around the right ventricular tip [18,19], the first RVI derivative is proportional to blood amount changes in the same volume. AV-delay optimization aims to maximize the stroke volume through an AV resynchronization that induces the best myocardial contractility, which is a measure of the ventricle's contraction power. Since power is energy over time and energy is proportional to the square of velocity (here we are interested in the kinetic energy), it seems correct to hypothesize that contractility is proportional to the squared derivative of the RVI. The aim of this study was to compare the OAVD calculated with Ritter's method to that assessed using the RVI signal recording.

## Materials and Methods

Twelve Inos<sup>2</sup> CLS patients with a mean age of  $59 \pm 10$  years (eight men, four women) were enrolled in the study. Eight patients had AV block and four sick sinus syndrome. All patients had a normal left ventricular ejection fraction. During Echo Doppler evaluation at the 1-month follow-up, a manual AV-delay scanning (100, 120, 150, 180, and 210 ms) was performed in the DDD pacing mode. This was done at 20 beats/min above sinus rhythm to ensure 100 % atrial pacing. During the whole scanning period, the RVI was downloaded via telemetry from the pacemaker to a dedicated Holter device (Unilyzer, Biotronik). The RVI averaged curve was post-processed at each AV delay.

The OAVD was determined by Echo Doppler according to Ritter's formula and by RVI as the value with the maximum peak in the squared derivative of the averaged RVI curves within a window covering the ejection phase (90 – 140 ms).

The Pearson r-value of the correlation between OAVDs obtained by Echo Doppler and those obtained by RVI were calculated. A corresponding p-value  $< 0.05$  was considered statistically significant to take the hypothesis  $|r| > 0$ .

## Results

Mean OAVD measured by Echo Doppler and by RVI were  $166.7 \pm 21.5$  ms and  $165.0 \pm 23.9$  ms respectively. No statistical differences were observed between these values. In all patients, OAVDs obtained by Echo

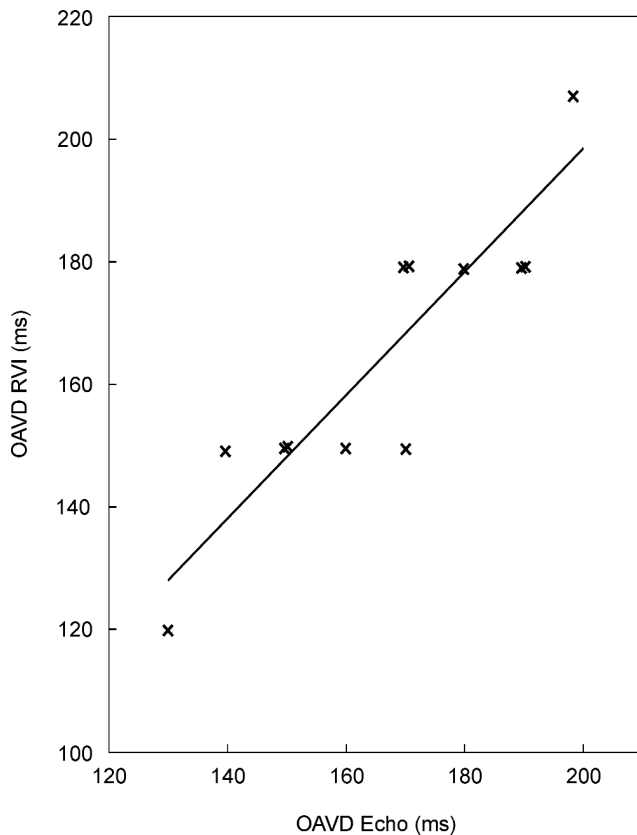


Figure 2. Correlation between optimal atrioventricular delay (OAVD) measured by means of right ventricular intracardiac impedance (RVI) and by Echo Doppler. Pearson's coefficient of correlation was  $r = 0.90$  and the corresponding  $p$ -value  $< 0.0001$ .

Doppler and by RVI showed a good correlation, as illustrated in Figure 2 ( $r = 0.90$ ,  $p$ -value  $< 0.0001$ ).

## Discussion

Most studies report that OAVD varies widely between individual patients in the range of 150 – 200 ms [20]. Optimal values shorter than 60 ms [13] and longer than 225 ms [21] have been reported as well. It has also been demonstrated that the OAVD is longer during DDD than during VDD pacing, and the difference is in the range of 30 – 50 ms [22,23]. This is a first limitation of this study since only DDD pacing was tested. Daubert et al. [24] showed that the P-R interval immediately adapts to exercise in an inversely proportional manner to the heart rate. Ritter et al. [25] investigated the benefit of an adaptive AV interval during maximal exercise using an automatic adaptive AV interval algo-

rithm. Compared with a fixed AV interval, exercise duration is enhanced using the rate-adaptive AV interval. Metha et al. [26] demonstrated that rate-adaptive AV-interval shortening is also important during sub-maximal exercise. Thus, the OAVD is not a static, but a dynamic and continually changing parameter, which at every cycle enables the atrial systole to give its maximum contribution to the stroke volume should the patient be resting or exercising. In our study, OAVD was assessed in patients at rest in the supine position only. The AVdelay variability, depending on different conditions, was not considered. This is the other limitation of this study.

Our results show that Echo Doppler and RVI evaluations lead to similar AV-delay values with a significant correlation between the OAVDs measured using the two methods when the patient is at rest and paced in the DDD mode at a fixed heart rate.

## Conclusion

An appropriate timing of the atrioventricular sequence is critical to optimize hemodynamics in patients paced in the DDD mode and may have clinically important consequences in cases of an underlying reduced left ventricular function. Echo Doppler evaluations are costly and time-consuming and are not easily feasible during exercise or daily activity. Since RVI and Echo Doppler evaluations lead to similar OAVDs with a significant correlation between the values measured by the two methods, in patients implanted with the Inos<sup>2</sup> CLS system, OAVD could be calculated directly from the device, using a cost-efficient and time-saving procedure. The Inos<sup>2</sup> CLS system could provide a valid method to ensure the required OAVD at any moment, in order to maximize atrial contribution to the stroke volume. Such an algorithm implemented in a pacemaker would improve a patient's hemodynamic performance and reduce follow-up time.

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