# Evaluation of the Chronotropic Function of a Closed-Loop Rate-Responsive Dual Chamber Pacemaker Driven by Contractility

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**Summary**

*A promising concept in rate adaptive pacemaker therapy aims at adjusting the heart rate of chronotropically incompetent patients in accordance to the myocardial contractility. The pacemaker system INOS² CLS (Biotronik) monitors the inotropic state of the patient via intracardiac impedance measurement to integrate the system into the baroreceptor reflex. This study was designed to compare the rate modulation of the device to the physiological sinus rate of healthy subjects focussing on two different aspects: acute responsiveness during daily life exercise and rate variations due to circadian influences. During stairs up and down climbing, walking, hyperventilation and leg flexion, the correlation between sinus rhythm and pacemaker rate modulation showed excellent values between 95 and 99%. Moreover, the 24 h trends of the pacemaker patients showed circadian variation, which was not statistically different from that of the healthy control population.*

**Key Words**

Chronotropic incompetence, rate responsive pacemaker, closed loop, physical exercise, circadian variation

## Introduction

Rate-adaptive dual chamber pacemakers are largely used for chronotropic incompetence symptom therapy in sinus node disease or high grade AV block. From a lot of different sensors evaluated between 1980 and 1990, the activity sensor (accelerometer) and two physiologic sensors (ventilation and QT) are currently the most widespread concepts for heart rate modulation. Some devices offer dual sensor functionality by combination of one physiologic sensor with an accelerometer to improve speed of response, specificity, sensitivity and proportionality to load. The increased complexity of these systems requires additional automaticity [1].

A different pacemaker concept aims at using a cardiac parameter for the restoration of an adequate heart rate response. It is well known that the heart rate as well as ventricular contractility are modulated during exercice adaptation of cardiac output. The contractility as a rate responsive signal in a pacemaker is currently used by two different approaches. The first method is based on the detection of right ventricular endocardial acceleration using a special designed lead, which is equipped with a microaccelerometer at the tip of the ventricular unipolar pacing lead [2]. The other approach measures beat-to-beat right ventricle impedance variations via standard unipolar or bipolar pacing leads implanted in the right ventricular apex. The input signal derived from the intracardiac impedance is modulated by baroreceptor activity. Thus, the heart rate is permanently adjusted in a way of closed loop adjustment [3-5].

This study was designed to assess the chronotropic function of a dual chamber pacemaker using right ventricular impedance signal as a sensor (INOS² CLS). The rate modulation of the device was compared to the normal sinus rate adaptation focussing on two different aspects: acute responsiveness during daily life exercise and rate variations due to circadian influences [6-8].

| | INOS / SINUS rate Manual mode | |
|---|---|---|
| | Correlation | Absolute difference |
| Walking | 99 % | < 0.05 |
| Squating | 99 % | < 0.01 |
| Upstairs / Downstairs | 95 % | < 0.05 |
| Hyperventilation | 94 % | < 0.05 |
| Bicycle | 99 % | < 0.05 |
| Treadmill | 92 % | < 0.05 |

*Table 1. Comparison of INOS CLS behaviour with normal sinus node stimulation during daily life tests.*

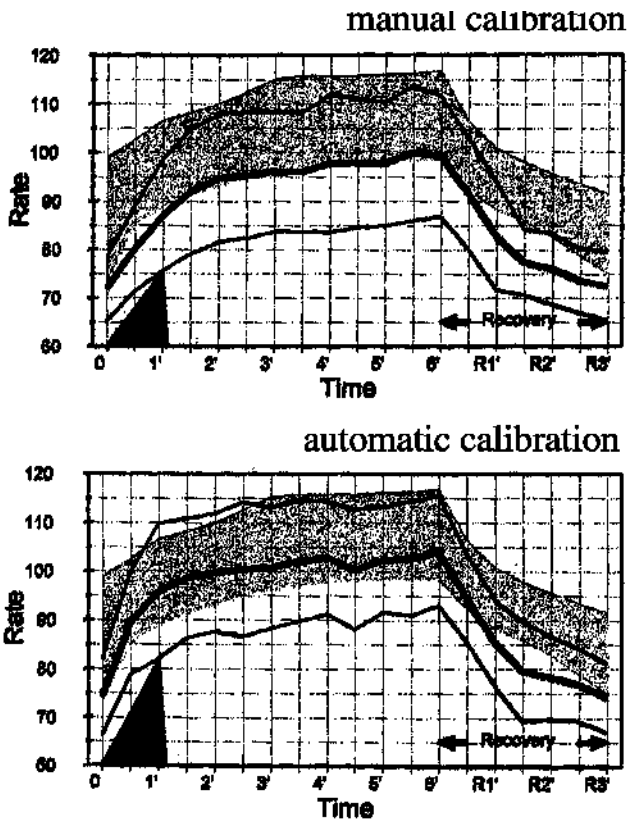


*Figure 1. INOS CLS behaviour during daily life tests. Example of walking test (2 steps/s).*

## I - ACUTE CHRONOTROPIC FUNCTION DURING DAILY LIFE EXERCISES

### Population

Thirty patients implanted with INOS² CLS (BIOTRONIK) were divided in two groups : GROUP MANUAL (19 patients, 13 male, 6 female, mean age 69 ± 12 years ; sensor mode : manual calibration) and GROUP AUTO (11 patients, 8 male, 3 female, mean age 64 ± 9 years ; sensor mode : automatic calibration). All patients are pacemaker dependent during rest and exercise due to their chronotropic incompetence. In addition, 18 patients are suffering from various degree of AV block. The basic and upper sensor rate of the pacemaker were programmed to 65 bpm and 120 bpm in all patients.

### Methods

The patients performed five daily life tests in randomized order separated each other by 3 minutes of recovery in sitting position :

- walking 2 feet/second for 6 minutes,
- upstairs: 90 steps, one step/second
- downstairs: 90 steps, one step/second
- hyperventilation with arm moving for 2 minutes
- leg flexion with squating for 30 seconds.

Additionally, the patients performed a symptom limited Bruce protocol and a bicycle exercise at 30 and 60 watt for 3 minutes each.
INOS² CLS rate modulation was compared with the sinus node rate obtained from a sex and age matched control group of 18 subjects without apparent heart disease. In both groups, the heart rate was obtained every 30 seconds. The heart rate trends were compared by use of the Willcox test and the correlation coefficient was calculated.

### Results

(Table 1, Figure 1)

### Conclusion

The correlation between sinus rhythm and INOS² CLS rate modulation showed excellent values between 95 and 99% independently of the method used for sensor calibration. The hypochronotropic shift of the INOS rate trends may be due to programming the basic and

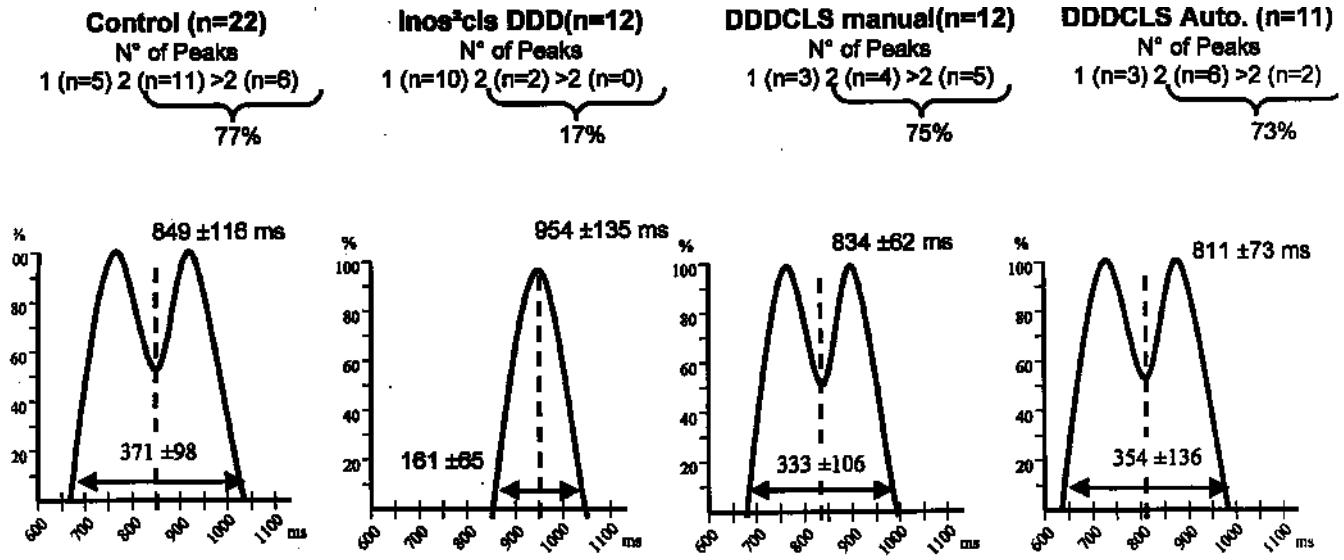


*Figure 2. Histograms of RR intervals from 24 h Holter data in circadian rate modulation with INOS CLS. All histograms, except DDD stimulation, showing multiple peak structures due to different mean heart rates during daytime and night-time.*

upper sensor rate with too low values. Rising the rate trends by 10 bpm provides perfect concordance between INOS rate response and normal sinus node.

## II - CIRCADIAN RATE MODULATION

### Population

Thirty three patients with INOS² CLS (27 male, 6 female, mean age 67 ± 9 years) were separated in 3 groups. Ten patients were programmed to DDD mode while rate response was activated in the others: 12 with MANUAL and 11 with AUTOMATIC sensor calibration.

### Methods

Twenty-four hour Holter trends were obtained in all patients and in the control group (C group) containing 22 normal age, sex and drugs matched subjects. Rate histogram, maximal daily mean hourly rate, minimum nocturnal mean hourly rate and mean hourly rate during daytime (ten consecutive hours) and night (5 consecutive hours) were analyzed and compared.

### Results

The results are presented in Table 2 and Figure 2.
With AUTOMATIC but never MANUAL mode, intermittent rate increases were observed during night-time

| | | Histogram figure 1 | | | Mean hourly rate | |
|---|---|---|---|---|---|---|
| | | percentage with n≥2 peaks | Mean cycle (ms) | D90 (ms) | Max day (bpm) | Min night (bpm) |
| C | n=22 | 77 % | 849 ± 116 | 371 ± 98 | 90 ± 8.03 | 62 ± 6.08 |
| MAN | n=12 | 75 % | 834 ± 62 ° | 333 ± 106 ° | 84 ± 5.06 ° | 65 ± 5 * |
| AUTO | n=11 | 73 % | 811 ± 73 ° | 354 ± 136 ° | 86 ± 4.2 ° | 67 ± 5 * |
| DDD | n=12 | 17 % | 954 ± 135 * | 161 ± 65 * | non relevant | non relevant |

*Table 2. 24 h Holter data in circadian rate modulation with INOS CLS. D90 : duration of the histogram including 90% of RR intervals ; °: non significant ; * : $p < 0.05$.*

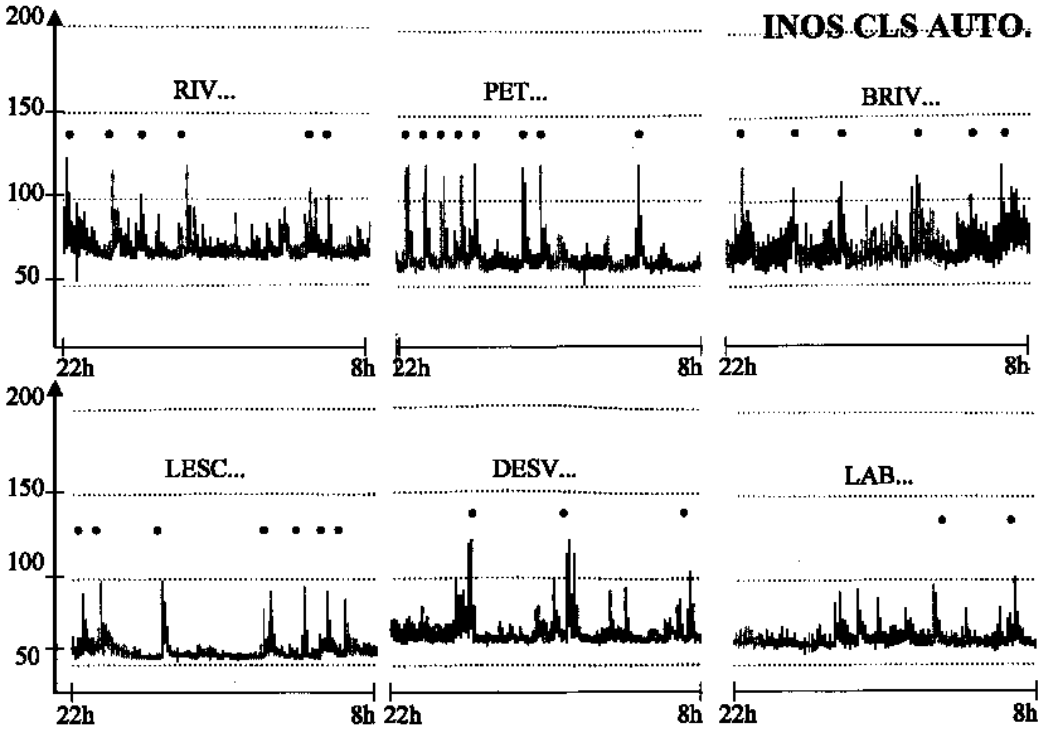


*Figure 3. 6 patients paced by INOS CLS with intermittent rate increase during night-time.*

(9) in 6 patients inducing palpitations in 2, due to body rotation in bed.

A Finapress study of these patients clearly demonstrates that intermittent acceleration of the rate during night-time are related to body rotation in the bed. The rotation is associated with sharp intermittent blood decrease inducing rate acceleration. These data illustrate the role of baroreceptors in rate modulation of INOS (Figures 3 and 4).

Correlation between mean hourly rate curves during day and night are 82% in MANUAL mode and 87% in AUTOMATIC mode, not statistically different from normal control subjects.

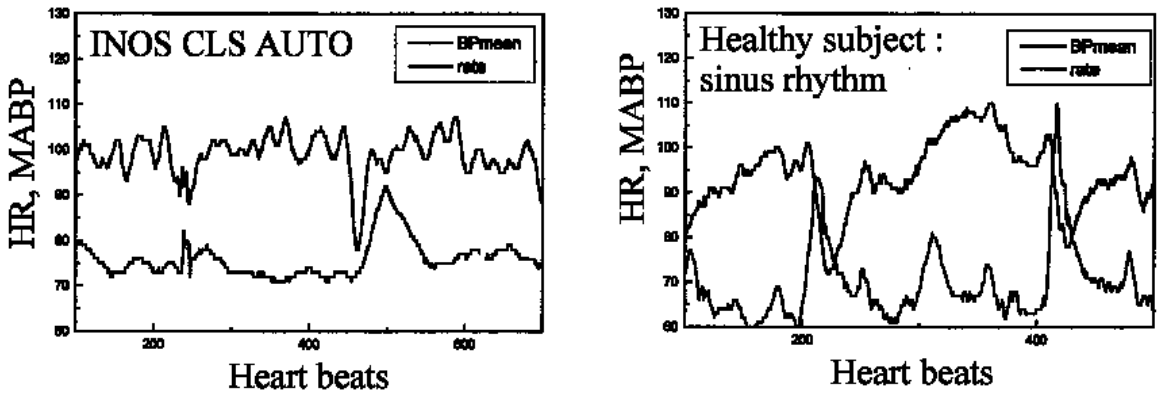


*Figure 4. Finapress assessment of the effects on blood pressure and heart rate due to body rotation in bed. Left: INOS CLS - Right: healthy subject in normal sinus rhythm.*

## Conclusion

Despite some study limitations, INOS provide significant circadian hear rate variations with a flat curve due to night-time heart rate increase. AUTOMATIC is more sensitive than MANUAL and the two possibilities to program the INOS² CLS should be preserved.

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