Cardiac Pacing with Heart Rate Variation in Closed Loop Systems: Long-term Evaluation

J.C.S. ANDRADE[1], V.S. ANDRADE[1]; P.C. AZAMBUJA[2], G.V. BARBOSA[3]; R.P.T FALLEIRO[2],
L.S. FRAGOMENI[3], J. JAZBIK[4], N.J.M. MOTTA[5], A.A. TOMAS[6]
[1]Universidade Federal de Sao Paulo, São Paulo, SP;
[2]Hospital São Vicente de Paulo, Passo Fundo, RS;
[3]Hospital de Clínicas de Porto Alegre, Porto Alegre, RS;
[4]Hospital Universitário Pedro Ernesto, Rio de Janeiro, RJ;
[5]Hospital Santa Isabel, Blumenau, SC;
[6]Casa de Saúde São José, Uberaba, MG;
all Brazil

Summary

The need to treat bradycardia with a rate-adaptive dual chamber DDDR-pacemakers has instigated the search for an ideal system. As the myocardial contractility is one of the basic mechanisms reflecting autonomic heart regulation, it is a very suitable parameter for analysis by a pacemaker system. By continuously monitoring myocardial contraction dynamics, Closed Loop Stimulation (CLS) therapy is capable of producing heart rates corresponding to physiologic needs. Three years ago, we investigated a group of patients implanted with CLS pacemakers suffering from sinus node disease and complete heart block. From 38 patients enrolled in the initial study in 1997, 30 patients (18 male, mean age 61 years, range 17 – 87) participated in the recent re-evaluation study. With the patients engaged in daily activities and clinical exercise tests, heart rate trends were evaluated using 24h-Holter ECG recordings and pacemaker diagnostic data. Chronic atrial and ventricular pacing and sensing thresholds were assessed and compared with the intraoperative and post-operative data. High-energy consumption was observed in two patients, and the pacing rates were suboptimal in other two patients, probably due to the limitations of the manual initialization of the system. In the remaining patients, the CLS systems functioned at the same level and produced very similar rates to that recorded at the 30-day follow-up after pacemaker implantation. This multicenter clinical study is first to prove long-term stability of the CLS systems.

Key Words

Binodal disease, Closed Loop Stimulation (CLS), long-term stability

Introduction

Although the first generation of single chamber pacemakers alleviated symptoms and reduced mortality caused by advanced atrio-ventricular (AV) block, there was no ability to adapt to a patient's metabolic demands and substantially improve their impaired exercise capacity. Subsequently, the physiological role of atrioventricular synchronization and heart rate modulation were thoroughly investigated and the corresponding improvements in the pacemaker design were made. Although the first reports on the clinical use of "physiologic" AV synchronous pacemakers appeared in 1963 [1], their widespread use did not occur until mid-1980's, when pacemaker circuitry technology, pacemaker lead design, and operative techniques advanced sufficiently to solve all major problems initially associated with the design and implantation of complex dual-chamber devices (DDD) [2-4].

Nevertheless, DDD pacemakers with no artificial sensors of metabolic demands could not ensure appropriate cardiac output in response to physical or mental stress in chronotropically incompetent patients. During cardiovascular stress, increased body movement

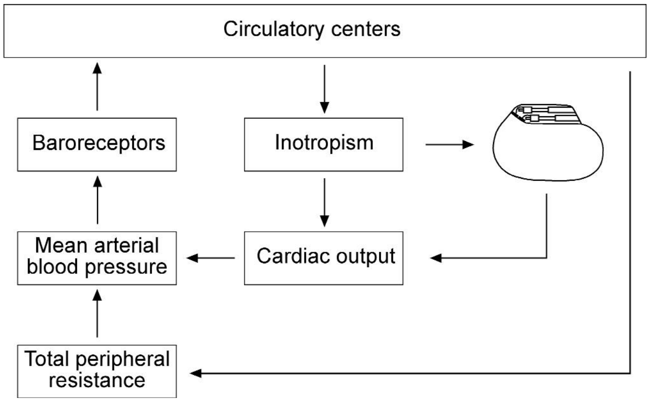

Figure 1. The concept of Closed Loop Stimulation involves an integration of the pacemaker into the natural control loop of the cardiovascular system by monitoring myocardial contractility.

(activity) can be sensed with the aid of a piezo-electric crystal or an accelerometer sensor, and a number of physiological parameters change: respiratory frequency, blood pH, temperature, systolic volume, intraventricular pressure, QT interval, blood oxygen saturation, heart contractility, etc. By monitoring one or more of these parameters, rate-responsive pacemakers adapt the heart rate and, more or less, meet current metabolic demands.

An optimal rate-responsive system should sense a cardiac parameter reflecting the influence of all circulatory regulation centers. Myocardial contractility is believed to be this most suitable parameter for this purpose. The concept of Closed Loop Stimulation (CLS) is developed to integrate the pacemaker system (Inos pacemaker family Biotronik, Germany) into the natural cardiovascular control loop. These pacemakers monitor the inotropic state (Figure 1) via intracardiac impedance measurements [5-11]. It has been shown that CLS generates adequate pacing rates during physical and mental stress, and provides physiological circadian rate variation [12-15]. However, this was studied within a multicenter study in patients with binodal disease followed for up to 30 days after implantation of an Inos DR pacemaker [16-18]. There has been a lack of data on the long-term performance of the modern CLS concept. The majority of patients from our previous study were thus reevaluated three years after pacemaker implantation to analyze chronic heart rate modulation and compare it to the previous findings.

	Pacing threshold (V)		Amplitude (mV)	
	Atrium	Ventricle	P-wave	R-wave
Intraoperative measurement (n = 38)	0.82 ± 0.45	0.55 ± 0.43	2.37 ± 1.49	10.6 ± 4.92
30-days follow-up (n = 38)	1.44 ± 0.68	1.18 ± 0.71	2.81 ± 1.79	6.3 ± 1.36
3-years follow-up (n = 30)	1.10 ± 0.58	1.00 ± 0.4	2.67 ± 1.37	6.36 ± 2.58

Table 1. Acute and chronic sensing and pacing thresholds in the studied patients.

Materials and Methods

In the initial Brazilian multicenter study, Inos DR pacemakers were implanted in 38 patients (21 male/17 female; mean age 57 years, range 13 – 83) suffering from binodal disease [16-18]. These devices had to be initialized manually. The heart rate trends were analyzed 30 days after pacemaker implantation during routine daily activities and stair climbing. For this purpose, 24h-Holter ECG recordings and heart rate trends stored in the pacemaker memory were used. After 3 years, 30 patients (18 male/12 female; mean age 61 years, range 17 – 87 years) from the initial group were analyzed under similar conditions. Additionally, chronic pacing and sensing thresholds in the atrium and ventricle were compared to the acute values and to the measurements conducted 30 days after implantation.

Results

In two patients high stimulation frequency required pacemaker reprogramming. In two other instances, the pacemakers were explanted 33 and 38 months after implantation due to pacemaker battery depletion. We observed almost a doubling of the pacing threshold after 30 days due to the electrode-tissue maturation processes. After three years atrial and ventricular threshold values were lower than those obtained after 30 days and by about 30 % higher than the acute values (Table 1). Sensed P- and R-wave amplitudes after three years were comparable to the intraoperatively measured values and to that determined at the 30-day follow-up. The very similar findings after 30 days and after three years demonstrate a high capture stability of

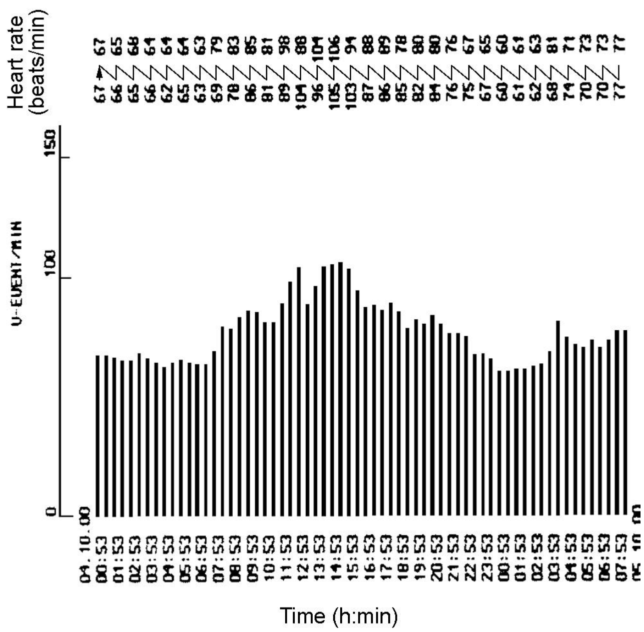

Figure 2. Ventricular rate trend over 32 hours in a patient with binodal disease treated by Closed Loop Stimulation. The therapy offers a physiological circadian variation of the pacing rate.

cardiac electrical activity in the face of the maturation of the lead-heart interface.

The pacing rate analysis showed a physiological circadian variation (Figure 2). A statistically significant difference between daily (6:01 – 21:59) and nightly (22:00 – 6:00) heart rates was seen, as well as during the physical exercise (Figure 3). The results from the previous study (Figure 3a) are maintained in the current study.

Discussion

The heart, as the central response organ of the cardiovascular system, responds almost immediately to the requests of the central nervous system. This results in chronotropic (cardiac frequency) and inotropic (myocardial contractility) changes. Although both mechanisms are important for cardiac activity, chronotropy is more pronounced during exercise [19]. Consequently, adequate frequency modulation is of major importance in reestablishing the patients' exercise tolerance.

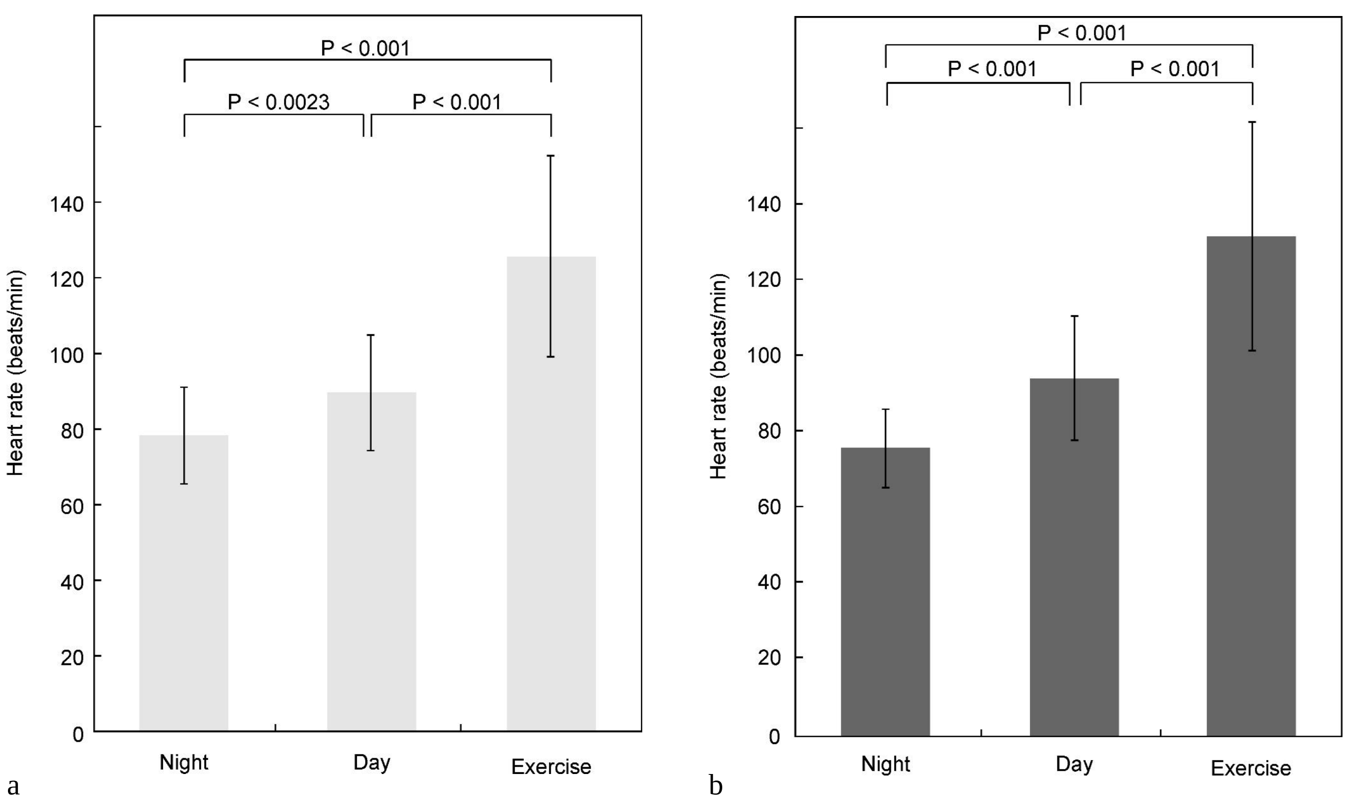

Figure 3. Mean heart rates in 30 patients at 30 days (a) and three years (b) after implantation of an Inos DR pacemaker (Biotronik, Germany).

In this study, we have shown that the rate behavior of CLS systems is stable for a long time, ensuring adequate pacing rates for increased metabolic needs. Moreover, the physiologic circadian heart rate variation was preserved after three years without any special programming. High battery consumption in two patients was apparently caused by high pacing thresholds following encapsulation of the electrode. The initialization problems observed in two patients, resulting in too fast pacing rates, can be explained by the manual procedure used during the pacemaker initialization. It is expected that distinct pathological changes in cardiac contractility, for instance due to myocardial infarction, will influence the system. The latest generation of $Inos^2$ CLS and $Inos^{2+}$ CLS pacemakers incorporate automatic initialization and continuous self-adjustment function to adapt the system to a defined dynamic frequency range.

Conclusion

The aim of this study was to evaluate the long-term stability of Closed Loop Stimulation. The results of the clinical stress test and 24-hour heart rate recordings indicated that CLS systems offered stable rate regulation over several years, which was adapted to the patient's current needs. Although manual initialization was necessary in the studied pacemaker model, the appropriate pacing rates were achieved in > 90 % of the participating patients without the need for additional parameter optimization. These results are not surprising knowing that any inappropriate initialization that might occur should be compensated for by the integration of the pacemaker into the natural cardiovascular control loop. The automatic initialization and continuous evaluation of the pacing rates in the latest generation of CLS systems should contribute to further optimization of pacemaker performance and simplification of pacemaker programming and follow-up.

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Contact

José Carlos S. Andrade, MD, PhD
Universidade Federal de Sao Paulo
Rua Borges Lagoa, 783 – 5º andar
São Paulo/SP
Brazil
Telephone: 011 557390
Fax: 011 55730303