Closed Loop Stimulation vs. Conventional DDDR Pacing: Benefits of Hemodynamic Pacing

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Summary

The goal of this ongoing clinical study is to evaluate the improvements in hemodynamic profile and patients' quality of life when a previously implanted DDDR pacemaker is selectively replaced by an INOS² CLS pacemaker, the rate modulation algorithm which is based on the principle of Closed Loop Stimulation. In 7 patients, aged 56 - 87 years, all with chronotropic incompetence and advanced AV block, a DDDR pacemaker was replaced by an INOS² CLS device. One week before and one month after the pacemaker replacement, patients underwent an ambulatory test sequence including: exercise test, mental stress, drug test (isoproterenol) and quality-of-life questionnaire. During ambulatory tests, both heart rate and arterial blood pressure were monitored. The heart rate modulation was satisfactory in all DDDR pacemakers during exercise testing. Minute-ventilation (1) and activity-based (6) pacemakers did not respond to mental stress or to drug infusion. During tests in which rate modulation did not occur, the patients' systolic arterial blood pressure reached critical values. In all patients, the CLS device responded to every test properly modulating the heart rate and keeping the systolic arterial blood pressure within physiological ranges. All but one patient experienced a substantial improvement in quality of life after replacement. In conclusion, Closed Loop Stimulation induced a pacing rate modulation which was always physiological and hemodynamically adequate in all test conditions, and improved patient quality of life.

Key Words

Closed Loop Stimulation, rate-responsive pacing, arterial blood pressure, quality of life

Introduction

In currently available dual-chamber rate responsive (DDDR) devices, the proper modulation of the heart rate (HR) depends on the nature and specificity of the signal detected by the sensor and the degree to which the artificial rate-control algorithm approximates the physiological response. Accelerometric or piezoelectric sensors give signals proportionate to body movements or skeletal muscle tremors and are specific to detect physical activity only. Other sensors can detect phenomena closely related to metabolic needs (e.g., minute ventilation and evoked QT interval) and they seem to have a more physiologic response than the previous ones. The activity-sensor response is quite fast but often limited and inappropriate to the patient's real needs; while "physiologic" sensors respond slowly but are purported to have a more appropriate response to perfusion demand [1].

Both types of devices suffer a major limitation. They usually operate in open-loop control or, in the best case represented by the evoked Q-T sensor, in closed-loop control with positive feedback. This simply means that the device is unable to verify if the actual paced rate is proper for the contingent metabolic needs and respects the general physiopathologic status of the patient, or, to the contrary, if it induces side effects (such as improper increase in arterial blood pressure) that are not well tolerated and sometimes dangerous. In other terms, they are unable to verify if the cardiac output induced by an artificial rate variation is hemodynamically correct or not [2].

The pacemaker (PM) model INOS[2] CLS (Biotronik, Germany) operates in a closed control loop with negative feedback from the cardiovascular system. Measuring the impedance variations caused by changes in the myocardium-blood ratio in the volume near the ventricular apex during systole, this pacemaker detects the variations in myocardial contractility in the right ventricle, and modulates the heart rate according to these variations [2-11]. Since this type of signal does not require a specific sensor or a dedicated lead to be detected, the INOS[2] CLS can be used as replacement device for DDDR PMs that have reached the end of life or that fail for other device-related reasons.

The goal of this ongoing clinical study is to evaluate the response of the Closed Loop Stimulation compared to a conventional DDDR pacemaker in terms of hemodynamic performance and quality of life (QoL).

Materials and Methods

At present, 7 DDDR pacemaker patients, aged 56 - 87 years, all with AV block and chronotropic incompetence, have undergone PM replacement with an INOS[2] CLS in the period between telemetric discharge alarm occurrence and PM automatic function switch (ERI). One week before and one month (3 - 5 weeks) after replacement, they underwent a series of stress tests including: physical (treadmill - 6 min. walking, modified Bruce protocol) and mental (color words - 2 steps) stress and, when possible, administration of positive inotropic drugs (isoproterenol at standard dosage).

HR, systolic (SABP) and diastolic (DABP) arterial blood pressure (ABP) were monitored during all tests but mental. Before the tests, the patients filled in a QoL questionnaire (Karolinska Institute, modified).

Table 1 reports the replaced DDDR PM models.

Patient	DDDR model	Type of sensor
1	Intermedics MARATHON DR	activity
2	Medtronic THERA DR	muscle tremors
3	Telectronics META DDDR	minute ventilation
4	Intermedics MARATHON DR	activity
5	Intermedics RELAY	activity
6	Medtronic THERA DR	muscle tremors
7	Biotronik DROMOS DR	activity

Table 1. DDDR pacemaker (PM) models replaced by an INOS[2] CLS.

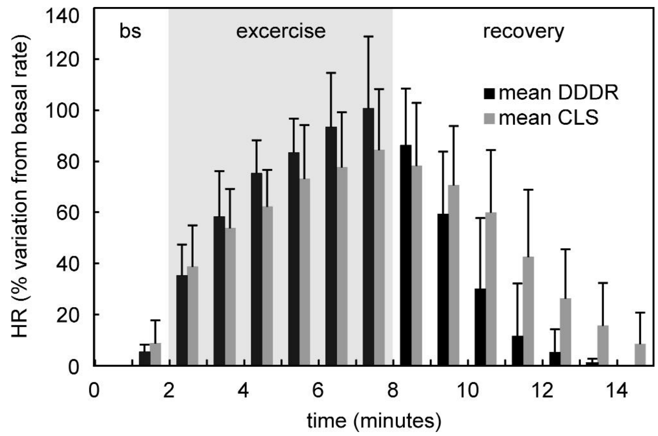

Figure 1. Heart rate (HR) trend during treadmill.

Results and Discussion

Response to Exercise

Figure 1 compares the mean trend of HR during a 6-minute treadmill test performed in DDDR and DDD-CLS pacing. During the exercise phase, the HR modulation was satisfactory for all DDDR devices tested, independent of the sensor used, but the rate reached by RR devices during the last four minutes of exercise was in average 15 to 20 % higher than that reached with CLS pacing. In contrast, during the recovery phase, RR devices reduced HR more rapidly than CLS pacemakers. In RR PMs, HR was artificially brought back to the basic value by about 5 minutes after the end of the exercise, while with INOS[2] CLS, HR followed, in that phase, a more soft decrease and was, on average, still higher than the basic rate 7 minutes after the end of the stress.

Additional and interesting information is supplied by the SABP and DABP trends recorded contemporaneous to the HR during the test (Figures 2 and 3). All mean values of SABP, measured at each minute during the test procedure, were drastically lower (up to 65 %) for CLS pacing as opposed to RR. In all patients other than Patient 5, RR pacing caused the SABP to reach levels higher than 205 mmHg, while with CLS pacing the same patients never exceeded the level of 175 mmHg at the peak of the test. The mean course of

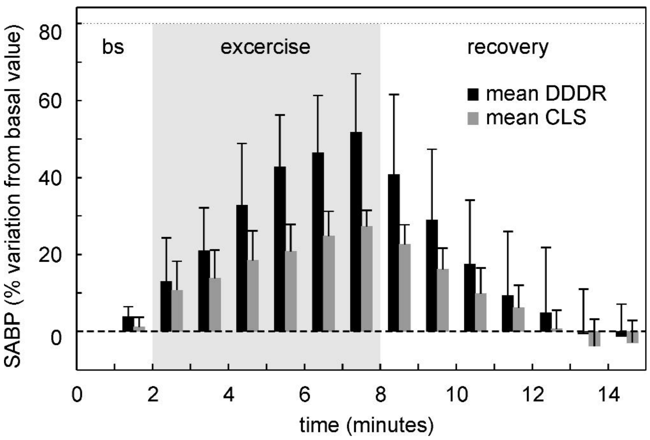

Figure 2. Systolic arterial blood pressure (ABP) trends during treadmill.

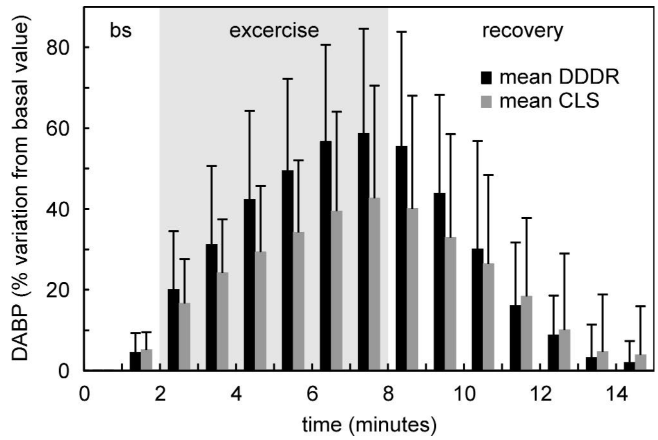

Figure 3. Diastolic ABP trends during treadmill.

DABP reflected the same behavior as before, but the maximum difference between RR and CLS pacing was smaller (no more than 43 %).

The data obtained during the exercise test allow some considerations to be made. During the last four minutes of the exercise phase, the non-physiologic rate increase in RR pacing was too fast and excessive, causing a hemodynamic unbalance, with a probable consequent sympathetic hypertonicity that increased cardiac contractility. That resulted in an immoderate increase of the ABP that overloaded the cardiovascular system.

In the same way, the rapid rate decrease during the recovery phase in RR pacing left the cardiovascular system in a condition of energetic deficit with an increase in the afterload. This forced the SABP up to high levels during the entire recovery time, and elevated the DABP during the first three minutes after the end of the stress.

This general situation presented by RR pacing may expose hypertensive patients (5/7 patients included in this study were found to be borderline basally hypertensive at the preliminary ABP recording at rest performed before the test sequence) to a potential risk of coronary failure or stroke.

CLS pacing, which is modulated by beat-to-beat variations in cardiac contractility, shows a more physiologic trend [10,11]. In accordance with baroreceptor messages that influence contractility, CLS pacing properly blends the HR-ABP ratio, maintaining a correct hemodynamic equilibrium during either exercise and recovery, exerting a protective action against immoderate peaks of pressure or rate that may lead to acute pathologic consequences in patients with impaired hemodynamics and/or damaged conductive substrate.

Response to Mental Stress

The mean trends of HR attained in the 7 patients during the mental stress test (Color Word, 2 steps), shown in Figure 4 do not require commentary.

As expected, no frequency adaptation was observed in any of the DDDR devices except for META PM (Telectronics, Pat. 3), based on minute ventilation, which only showed an 8 % rate increase from the programmed basic rate (PBR) during the greatest effort at

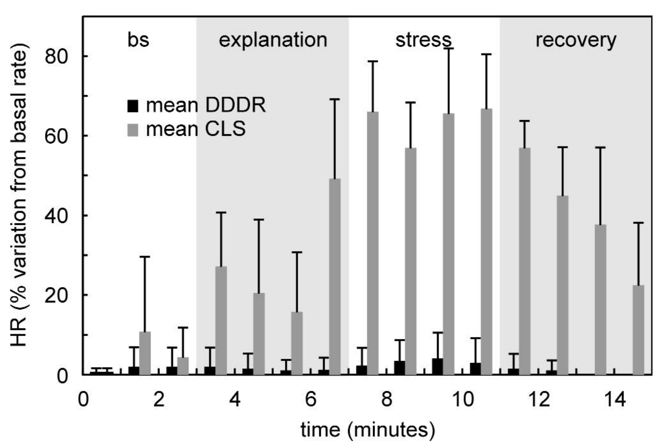

Figure 4. HR trend during mental stress. At minute 4, the physician explains the test procedure to the patient; the test starts at minute 7 and ends at minute 11.

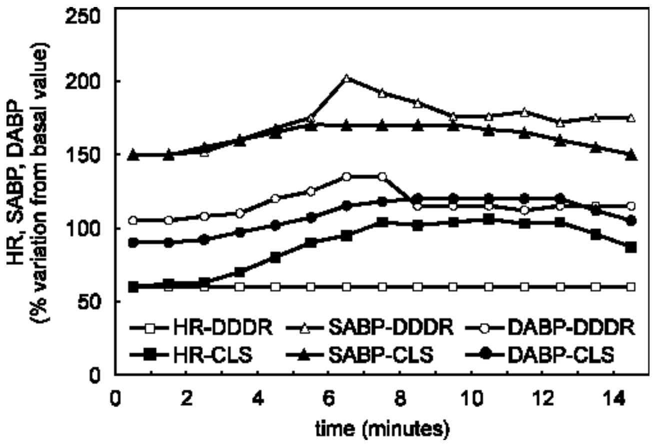

Figure 5. HR, systolic ABP (SABP) and diastolic ABP (DABP) trends during drug infusion in Pat. 1.

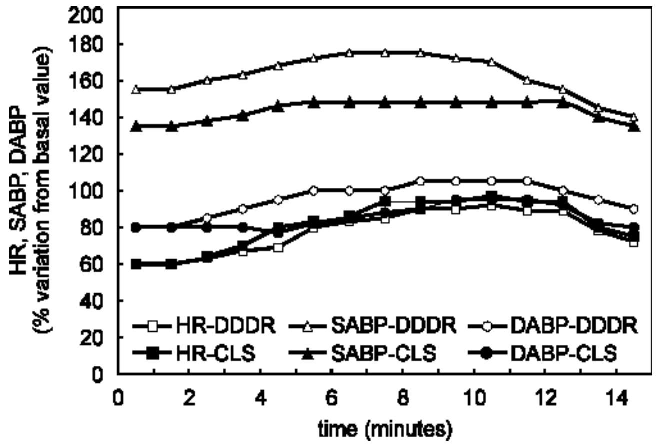

Figure 6. HR, SABP and DABP trends during drug infusion in Pat. 6.

the peak of the stress. In Patient 7 (activity based Biotronik DROMOS DR PM), an apparent and limited frequency modulation (range 3 - 18 % rate increase from PBR) was observed, but it was due to patient motion induced by a general stressed state. In order to not introduce an additional emotional effect to this patient, ABP was not measured during this test.

CLS pacing responded appropriately to unconscious metabolic demand, modulating HR not only during the test, but also in the preliminary phase (minutes 4 and 5 in Figure 4), in which the physician explained the test procedure to the patient.

Response to Drug Infusion

A test for inotropic-positive drugs (isoproterenol EV infusion at standard dosage) was performed in the two normotensive patients only (Pat. 1 and 6). In Pat. 1 (activity based Medtronic THERA DR PM), no rate adaptation was effected by the DDDR pacemaker. This caused an excessive increase of both SABP and DABP at the time of maximal contractile response to the drug. The CLS device properly modulated HR, in accordance with the ABP trend, smoothing and substantially limiting the pressure increase. The trends of HR, SABP, and DABP detected in Pat. 1 are shown in Figure 5 for both pacing modalities.

During DDDR pacing, in Pat. 6 (activity based Medtronic THERA DR PM), one minute after drug delivery, a sinus rhythm onset with VDD pacing proportional to the inotropic effect occurred. The SABP and DABP trends did not show any peak and the course was more physiologic. Six weeks after, the test was again performed in the same patient, but did not cause sinus rhythm onset.

CLS pacing, operating in DDD mode, modulated HR similarly to sinus response during the first test, but the courses of both SABP and DABP where softer and reached lower maximum values. The difference in the ABP maximum pressure values reached during the two tests may be justified by the progressive improvement of the patient hemodynamic unbalance caused by the change from an RR to a CLS pacing approach. HR, SABP and DABP trends (in both pacing modalities) detected in Pat. 6 are presented in Figure 6.

Results of QoL Questionnaire

Immediately after the two test sequences, all patients filled in a QoL questionnaire (Karolinska Institute, modified). The significance of this test has particular value in the context of this study, as the compared patient conditions are basically similar. Both times, the patient gives a subjective evaluation of his healthy and psychological status based on the same therapeutic condition, i.e., with rate responsive pacing.

The QoL questionnaire analysis shows that 6 out of 7 patients experienced a better QoL after PM replacement (see Table 2).

Conclusion

The results of this study, which are limited by the number of cases and models of DDDR pacemakers

Patient	Score DDDR	Score DDD-CLS
1	26	32
2	60	70
3	27	70
4	60	58
5	30	60
6	40	65
7	50	62
Mean	42.8	59.4

Table 2. Quality-of-life scores before and after PM replacement.

replaced, seem very interesting and promising, and the authors decided to draft a detailed clinical study protocol to extend this experience to other implant centers and achieve a significant amount of data. This will allow verification of whether the hemodynamic improvement showed by preliminary data, based primarily on activity-driven RR pacing, can also be achieved with more "physiological" artificial sensor-driven devices, including dual-sensor devices.

At present, the obtained data allow the conclusion that CLS pacing adapts the heart rate more physiologically, in better accordance with the real hemodynamic profile of the patient as compared to conventional activity-based DDDR pacing. CLS pacing respects the patient's functional metabolic needs and his or her physiopathological general status. A few weeks after switching the pacing method, a sensible patient QoL improvement can be already observed.

References

[1] Lau CP. Rate Adaptive Cardiac Pacing: Single and Dual Chamber. Futura Publishing Co., New York, USA, 1993.

[2] Schaldach M, Hutten H. Intracardiac impedance to determine sympathetic activity in rate responsive pacing. PACE. 1992; 15: 1778-1786.

[3] Pichelmaier AM, Braile D, Ebner E, et al. AND controlled closed-loop cardiac pacing. PACE. 1992; 15: 1787-1791.

[4] Schaldach M. What is Closed Loop Stimulation?. Prog Biomed Res. 1998; 2(3): 49-55.

[5] Osswald S, Gradel C, Crohn T, et al. Correlation of intracardiac impedance and right ventricular contractility during dobutamine stress test. In: Cardiac Arrhythmias. Raviele A (ed.). Springer, Milan, Italy, 1997: 87(abstract).

[6] Malinowski K. Interindividual comparison of closed loop stimulation and rate-adaptive sensor systems. Prog Biomed Res. 1996; 4(1): 56-60.

[7] Pichelmaier AM, Ebner E, Greco OT, et al. A multicenter study of a closed-loop ANS-controlled pacemaker system. PACE. 1993; 16: 1930.

[8] Woermsen J van, Kempen L van, Res JCJ, et al. ANS controlled closed-loop cardiac pacing - a multicenter study. Prog Biomed Res. 1996; 4(1): 13-16.

[9] Res JCJ, Woermsen RJ van, Malinowski K, et al. Dual chamber pacing and closed-loop regulation - clinical results. Prog Biomed Res. 1996; 4(1): 27-30.

[10] Zecchi P, Bellocci F, Ravazzi AP, et al. Clinical benefits of Closed Loop Stimulation. Preliminary results of an intensive validation study. Prog Biomed Res. 1999; 3(4): 185-189.

[11] Zecchi P, Bellocci F, Ravazzi AP, et al. Closed Loop Stimulation; A new philosophy of pacing. Prog Biomed Res. 2000; 2(5): 126-131.