ANS Controlled Closed-Loop Cardiac Pacing-A Multicenter Study

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Summary

Single- and dual-chamber pacemaker systems (BIOTRONIK Neos-PEP, BIOTRONIK Diplos-PEP) providing ANS-controlled rate-adaptation were implanted in 240 patients in 16 clinical centers worldwide. Clinical exercise protocols, Holter monitoring, and psychological stress tests were performed over a mean total follow-up time of 2.6 ± 1.3 years. In a subset of patients additional investigations aimed at provoking variations of the sympathetic tone were performed to confirm physiological rate-adaptation for various types of hemodynamic challenges. The results confirm that physiological rate-adaptation can be achieved using the ANS closed-loop concept.

Introduction

For patients with chronotropic incompetence, the most attractive concept providing rate-adaptive cardiac pacing is the physiological restoration of a closed-loop chronotropic control.[1] In the healthy patient, the autonomic nervous system (ANS) adjusts the cardiac output (CO) to meet hemodynamic and metabolic requirements.

Even in the presence of chronotropic insufficiency the ANS controls the performance of the heart through myocardial contractility. The ANS pacemaker system evaluates this effector-level ANS-signal to establish a physiological closed-loop system which supplies the body with the demand for CO requested by the ANS to maintain an adequate mean arterial blood pressure (MABP).

The local motion of the ventricular walls near the stimulating electrode was used as a sensor for changes in myocardial contractility. The mechanical contraction is mapped to the time course of the unipolar intracardiac impedance measured between the stimulating electrode and the pacemaker housing. Since sympathetic influence changes this contraction pattern (increase in peak tension, steeper rise in tension of contractile elements of the myocardium), the impedance signal inherently contains ANS-information.[4]

Thus, in the ANS-controlled pacemaker, the electrode serves three functions:

a) as an actuator for stimulation,
b) as a sensor to detect the intracardiac evoked potentials for control of the pacemaker, and
c) to detect the sympathetic tone by intra-cardiac impedance measurements.[3]

This method has the clinical advantage that the pacing electrode itself serves as a sensor. Therefore, no additional device is required for that purpose.

Methods

ANS-controlled pacemakers have been implanted in 240 patients in 16 clinical centers worldwide. The average age of these patients was 62 ± 7 years (64% male). 178 were single-chamber pacemakers (BIOTRONIK Neos-PEP) and 62 were dual-chamber versions (BIOTRONIK Diplos-PEP).

Before implantation, 80% of patients had an indication for a rate-adaptive stimulation mode due to chronotropic insufficiency, 20% of patients had adequate intrinsic sinus activity. The patients were examined regularly over a maximum period of 47 (Neos-PEP) and 37 (Diplos-PEP) months, respectively, with a mean follow-up interval of 3.9 ± 5.4 months.

Clinical exercise protocols, Holter monitoring, and psychological stress tests were performed with a mean total follow-up time of 2.6 ± 1.3 years.[2] Additional interventional studies aimed at provoking variations of the sympathetic tone were performed to confirm physiological rate-adaptation for various types of hemodynamic challenges.

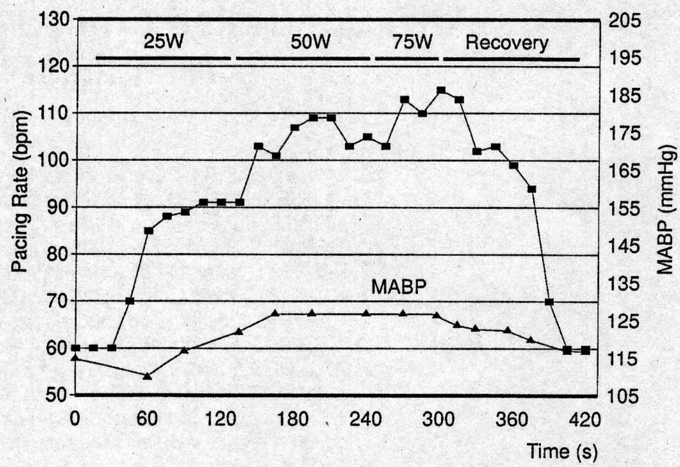

Figure 1. *ANS-controlled DDDR-pacing during bicycle ergometry.*

Results and Discussion

The evaluation of successful rate-adaptive performance was based on an analysis of 24h HR-trend data (stored within the pacemaker memory) and HR response to a standardized exercise protocol as described below. Successful rate-adaptive pacing was achieved in 93% of the single-chamber systems and in 96% of the dual-chamber systems. Of those patients in whom rate-adaptive pacing failed, the majority had progressive Chagas disease or pronounced coronary heart disease and, therefore, a high degree of regional (non-transmural) scar tissue and regional disturbance of ANS-control.

Exercise Examinations

The exercise examinations were performed according to a standardized protocol using bicycle ergometry and a stepwise increase of the exercise load. Criteria for the evaluation of the exercise tests are:

a) resting pacing rate close to the (patient specific) basic stimulation rate (BSR),
b) response time to a stepwise increase in exercise level of less than 30 seconds,
c) correlation between the pacing rate and the exercise level,
d) maintenance of a appropriate MABP, and
e) decrease of the pacing rate within 6 minutes after the end of exercise,
f) longer decay time than attack time.

Figure 1 shows a typical HR response during bicycle ergometry, while figure 2 shows the HR response during an ambulatory challenge.

One observes a graded exercise response of the pacemaker system, and a typical time course of the pacing rate through exercise and recovery. MABP remained nearly constant during the entire period, with a slight increase at the beginning of exercise. Decay and attack times are not determined by any programmable parameter, but reflect the time constants of sympathetic activity. Most notable is the significant HR increase during stair climbing, reflecting increased metabolic demand (Figure 2). In contrast, the HR response to descending stairs is comparatively moderate.

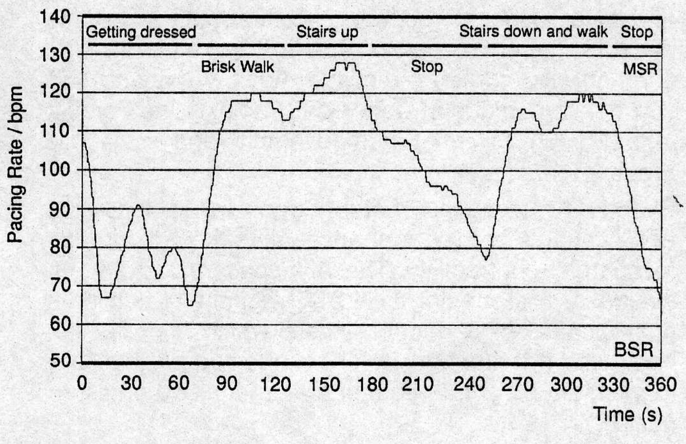

Figure 2. *ANS-controlled DDDR-pacing during ambulatory challenge.*

24h HR-Trends

The 24h HR-trends and diaries were evaluated according to the following criteria:

a) the time correlation between the pacing rate and daily activity,
b) the proportionality between the pacing rate and the exercise level, and
c) the diurnal characteristics of the mean pacing rate.

Figure 3 is an example of 24h HR-trend data that clearly shows the correlation between the patient's daily activity and the pacing rate.

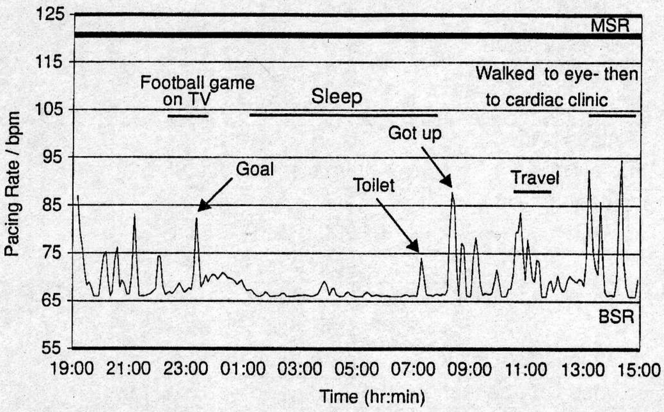

***Figure 3.** 24h Trend of the heart rate for ANS-controlled DDDR-pacing.*

Psychological Stress Evaluation

The ANS-controlled pacing system is acutely sensitive to all changes in sympathetic tone. Therefore, not only changes induced by exercise, but also by psychological conditions such as anxiety, excitement, and mental stress, should affect the sensor. The response of the ANS pacemaker system to psychological stress was investigated by using color-word conflict tasks (CWT). Psychological exercise also resulted in an increase in the pacing rate (Figure 4).

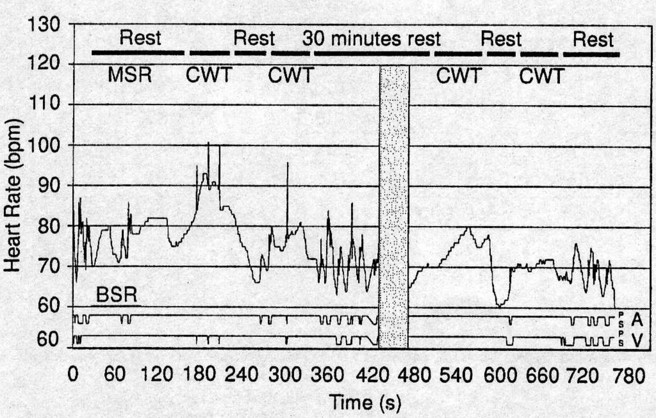

***Figure 4.** ANS-controlled DDDR-pacing during several successive psychological stress tests (color-word conflict task).*

Despite the absence of variations in pre- and afterload, a pronounced frequency response occurs due to sympathetic changes in contractility. Furthermore, a "training effect" appears, expressed as a reduced heart rate increase over multiple CWT exercises.

NYHA Classification

Therapeutical improvements in clinical status are clearly demonstrated by a decrease in the NYHA classification index. In the case of first implants, the mean NYHA index improved from 2.3 to 1.6. Even if the ANS pacemaker system replaced an existing system, the NYHA index improved from 2.6 to 1.7 (Figure 5).

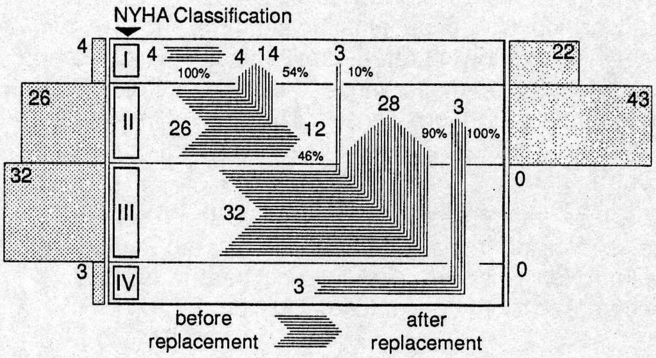

***Figure 5.** Change of NYHA-classification after replacement implant of an ANS-controlled pacing system.*

Conclusions

A new concept for a rate-adaptive pacemaker system has been presented. The system monitors sympathetic tone by assessing changes in myocardial contractile state from the unipolar intracardiac impedance measurement. The results obtained during an extended clinical study demonstrate the unique features of the ANS-controlled pacing system concept. The transition of the paced HR at the beginning of exercise, as well as during recovery, shows typical, physiological response times and the HR increase is proportional to the exercise load. The ANS-controlled rate-adaptation also works during emotional and mental stress.

In conclusion, the ANS-controlled pacing system provides a significant advantage in the re-establishment of the physiological circulatory control mechanisms that maintain an appropriate MABP.

Furthermore, the effects of the higher cerebral functions on cardiac activity are also recognized. The ANS-controlled pacemaker operates under the direction of systemic control processes and, therefore, places a more controlled stress on a patient's circulatory reserves.

Advancements in ANS-controlled pacemakers

In late 1995, the next generation of ANS pacemakers was introduced. The Inos pacemaker systems are new devices which incorporate the ANS closed-loop concept with additional refinements gained from the initial investigational devices, Neos-PEP and Diplos-PEP.

The Inos^2 DDDR pacemaker has now been implanted in 12 patients. This device is based on a new software-controlled pacemaker platform and has the capability of allowing rate-adaptive pacing using either the ANS impedance-based sensor or an accelerometer-based (motion) sensor. The early clinical data using the ANS sensor indicate excellent rate-adaptive performance.

The Inos family of pacemakers have the flexibility to be a clinical investigational tool for the academic researcher as well as a fully functional rate-adaptive pacemaker for the pacemaker clinician.

References

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

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

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

[4] Schaldach M, Urbaszek A, Ströbel JP, Heublein B. Rate-adaptive pacing using a closed-loop autonomous nervous system controlled pacemaker. J HK Coll Cardiol 1995; 2:131.

Inos^2 DR - Technical Data

General	
Size	8.8 x 57 x 45 mm^2
Weight	40 g
Battery	Li/I, 2.8V, 2.0 Ah
Life Time	5-6 years
Pacing	
Dual Chamber Pacing	✓
Pulse Amplitude Control System	✓
Pulse Amplitude Fine Adjust	0.2 .. 7.2 V smallest step: 0.1 V
Pulse Width Fine Adjust	0.05 .. 2.0 ms smallest step: 0.05 ms
Safety Period	✓
PVARP	200 .. 300 step size: 25 ms
PVARP Extension	0 .. 300 ms step size: 25 ms
Dynamic AV-Delay	programmable
Sense Compensation	0, -30, -40, -50, -60 ms
AV-Delay	20 .. 300 ms smallest step 20 ms
Rate Adaptation	
Closed-Loop Concept	✓
Sensor	Unipolar intracardiac impedance
Algorithm Implementation	Software in RAM
Auto-Adjust Function	✓
Follow-Up	
User Guidance	✓
Patient Data Memory	Implant data, lead configuration, 16 char. patient string, serial number
Event Counters	As, Ap, Vs, Vp, VES date/time of VES-clusters date/time of ERI-detect
Rate Histogram	Sensed and paced events
Trend Recording	18 min, 38 h, arbitrary
Impedance Recording	6 min
Programmer	PMS 1000