Results of the Protos Survey: Effectiveness of the New Closed-Loop Pacemakers in Clinical Practice

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Summary

The new Protos DR/CLS dual-chamber and Protos VR/CLS single-chamber pacemakers have an extended indication and functionality range compared to earlier rate-adaptive pacemaker systems based on monitoring the myocardial contraction dynamics by means of intracardiac impedance measurement. During the Protos survey, 66 patients with DDD(R) or VVI(R) pacemaker indication were followed for 4 weeks after implantation. A total of 60 patients (mean age 72.5 ± 9.9 years, 32 female) with the rate adaptation by means of Closed Loop Stimulation (CLS) activated at hospital discharge were included in the analysis. At the 4-week follow-up, the rate adaptation of 16 out of a total of 43 documented and evaluated exercise tests was classified as adequate. In 26 patients, it was impossible to evaluate the rate adaptation due to a present intrinsic rhythm. In one case, cardiac pacing was observed only at the basic rate despite statistical data of the pacemaker memory that demonstrated a typical histogram with pacing rates higher than the basic rate. Rate adaptation achieved by CLS was comparable to the heart rate variation in chronotropically competent patients with dominating intrinsic rhythm (rest 70.5 ± 10.5 beats/min versus 74.1 ± 13.2 beats/min, 5-min walk test 111.6 ± 22.1 beats/min versus 101.0 ± 19.6 beats/min, stair descending 100.0 ± 7.1 beats/min versus 104.4 ± 20.3 beats/min, stair ascending 106.0 ± 32.1 beats/min versus 109.6 ± 26.0 beats/min). The Protos survey has demonstrated that rate adaptation using the CLS mode in the new Protos DR/CLS dual-chamber and Protos VR/CLS single-chamber pacemakers results in adequate behavior. Additionally, due to a reduction in the effort required to program the device, the follow-up procedure is facilitated.

Key Words

Closed Loop Stimulation (CLS), rate-adaptive pacing, atrioventricular delay

Introduction

To establish an appropriate therapy using rate-adaptive pacemaker systems, the sensor parameters have to be adapted to the individual needs of each patient. Many of these sensor systems require an inappropriately high programming effort to achieve appropriate rate adjustment, prolonging the follow-up procedure in daily clinical routine. An ideal sensor which reacts quickly and adequately to metabolic demands should therefore also be easy to program, and it should not require frequent readjustments [1]. In this context, closed-loop sensors have the advantage of detecting a cardiovascular parameter which is influenced by the heart rate via negative feedback. Consequently, a rise in the sensor signal leads to an increase in the pacing rate, which in turn results in a decrease in the sensor signal. In this manner, the pacing rate can be optimally controlled [2].
The concept of Closed Loop Stimulation (CLS, Biotronik, Germany) is based on an intracardiac imped-

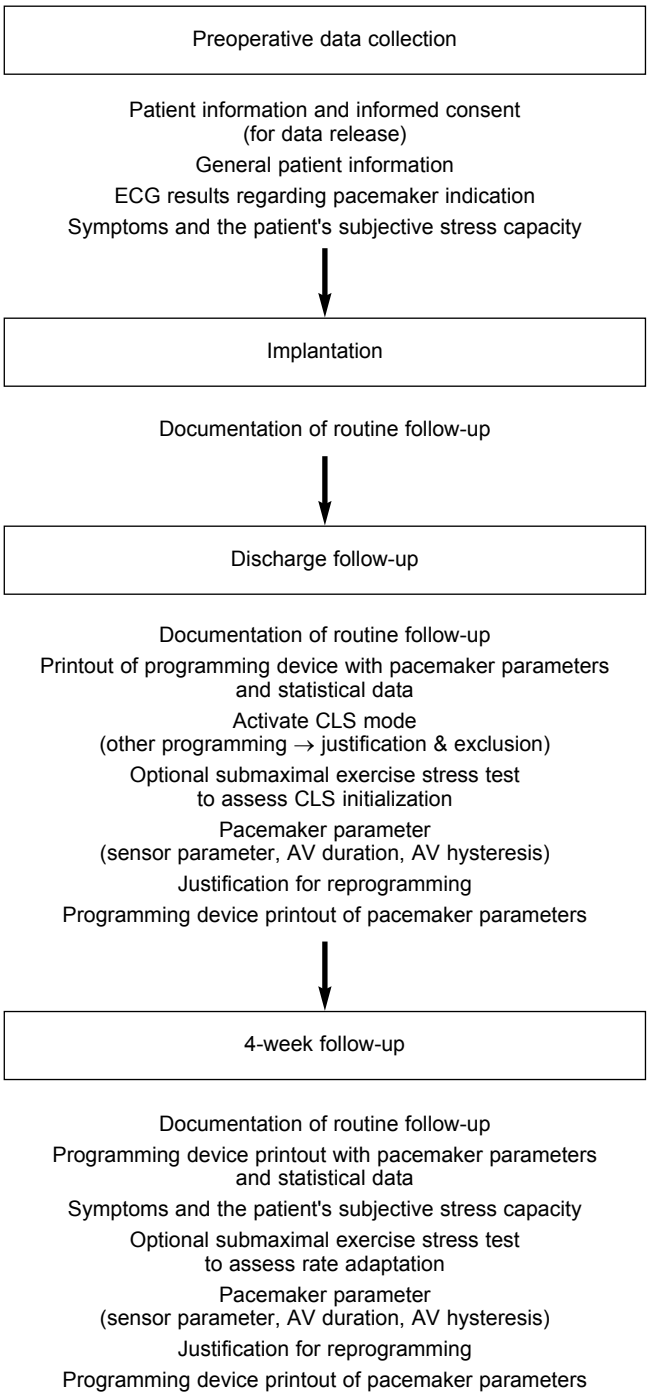

Figure 1. Flow-chart of the Protos survey. AV = atrioventricuar.

ance measurement utilizing the contraction dynamics of the myocardium for rate adaptation [2-5]. Previous realizations of the concept in the Inos^{2} CLS and Inos^{2+} CLS pacemakers required permanent ventricular pacing. This limitation no longer applies to the new Protos DR/CLS dual-chamber and Protos VR/CLS single-chamber pacemakers (Biotronik), thus making CLS therapy also available to patients with intrinsic activation of the ventricle. The goal of the Protos survey was to evaluate if the Protos DR/CLS dual-chamber and Protos VR/CLS single-chamber pacemakers meet the requirements for rate-adaptive pacemaker systems in clinical practice and if the default setting of the rate-responsive parameters had been optimally chosen. To this end, the routine examinations (pre-operative, implantation, discharge follow-up, 4-week follow-up) and the evaluation of the pacemaker's functionality were documented.

Materials and Methods

Closed Loop Stimulation

The CLS concept [3-6] offers a therapy for the rate-variable electrostimulation of the heart on the basis of the closed-loop principle. Rate control is based on continuous monitoring of the contraction dynamics of the myocardium by means of intracardiac impedance measurements using a standard ventricular lead. During the different phases of the cardiac cycle (filling phase, isovolumetric contraction, ejection), the blood-to-myocardium ratio and thus the local impedance in the vicinity of the electrode tip varies, making the corresponding impedance changes during metabolic stress characteristic for the rise in ventricular contraction and the cardiac load [7]. By comparing an impedance curve at a given time (impedance values in a range of 50 to 250 ms following ventricular pace or sense) with a reference impedance curve recorded at rest, the pacemaker determines the necessary pacing rate. In this way, the CLS pacemaker is capable of using the intrinsic cardiovascular control for rate adaptation to react adequately to physical [8-13] as well as mental stress [14] and thus to increase the patient's quality of life [15,16]. The new CE-marked (European conformity) Protos DR/CLS dual-chamber and Protos VR/CLS single-chamber pacemakers use an automatic initialization feature that adopts the rate adaptation approximately to the individual patient about 15 min after activating the CLS mode and optimizes it within a few days. A continuous automatic adjustment [17] compensates for changes in the intracardiac impedance due to the grow-in behavior of the ventricular lead or a change in inotropic drug therapy. To compensate extreme levels of activity, the CLS dynamics can be attenuated or amplified in two steps.

		No. of patients
Implantation	New	42 (70.0%)
	Replacement	18 (30.0%)
Pacemaker	Protos DR/CLS	49 (81.7%)
	Protos VR/CLS	11 (18.3%)
Mode	DDD-CLS	48 (80.0%)
	VVI-CLS	12 (20.0%)

Table 1. Pacemaker indication, type, and mode for 60 patients.

Pacemaker relevant ECG diagnosis	No. of patients	
SSS not sepecified	2	(3.3%)
SSS bradycardia	16	(26.7%)
SSS sinus arrest	5	(8.3%)
SSS chronotropic incompetence	5	(8.3%)
SSS brady-tachy syndrome	10	(16.7%)
AV block II	10	(16.7%)
AV block III	12	(20.0%)
Atrial fibrillation	23	(38.3%)
Right bundle branch block	1	(1.7%)
Left bundle branch block	3	(5.0%)

Table 2. Pre-implantat ECG diagnosis in the 60 patients analyzed (multiple entries are possible). SSS = sick sinus syndrome.

Like the surface ECG, the shape of the intracardiac impedance curve depends strongly on the ventricular event type and can differ considerably between ventricular sensing and pacing. Following successful pre-examinations [18], the impedance curves of all event types can be successfully analyzed in the Protos DR/CLS and Protos VR/CLS. In the Protos DR/CLS dual-chamber pacemaker, intrinsic atrioventricular (AV) conduction with intermittent AV block is supported by an automatic AV hysteresis [19]. The hysteresis also has the purpose of performing a regular update of the various impedance reference curves of ventricular paced and sensed events in order to continuously compensate for changes in myocardial contractility. Since fusion beats [20] cannot be analyzed by the CLS algorithm due to the irregular contraction sequence, the programmed dynamic AV delay that takes into account the sense compensation should be more than 39 ms below the respective intrinsic AV delay. To simplify AV-delay and AV-hysteresis programming, the Protos DR/CLS dual-chamber pacemaker offers new AV-delay statistics that provide information on the delay of the intrinsic AV conduction after atrial paced or sensed eveents, especially classified in relationship to the underlying heart rate.

Project Design

The study was performed as a prospective, multicenter survey, without setting any special requirements. The schedule and scope of the follow-up examinations were in accordance with medical standards, and patient guidance was left to the discretion of the attending physician. Data acquisition was performed preoperatively, during implantation, at the hospital discharge follow-up, and at the 4-week follow-up (Figure 1). The required documentation was limited to a standard pacemaker follow-up and an evaluation of pacemaker functionality based on an optional submaximal exercise test [21]. For this purpose, a baseline measurement of the heart rate at the end of a resting phase of at least 2 min and measurements of the maximum heart rate when ascending stairs, descending stairs, or walking for at least 5 min was recommended.

The effectiveness of the new automatic CLS initialization had to be evaluated during the discharge follow-up. In case of pacing rates above the basic rate, rate adaptation was classified as detectable. If the intrinsic rate was too low and there were still no pacing rates above the basic rate, the rate adaptation was classified as not detectable for the time shortly after the initialization (due to the fact that an approximate start value was used for determing the pacing rate). The intrinsic rhythm category contains all other cases in which a rise in the pacing rate could not be detected and was also not necessary due to an existing intrinsic rhythm.

At the 4-week follow-up, the rate adaptation was evaluated qualitatively. An increasing intrinsic rate during the exercise test was classified as intrinsic rhythm. Cases were judged adequate when a rise in the pacing rate was necessary and also occurred at the necessary magnitude. Accordingly, cases were judged inadequate when a rise in the pacing rate was necessary but did not occur at the necessary magnitude.

Results

Patients

The survey was performed in the period between the first pre-operative data collection on March 20 and the last 4-week follow-up on May 22, 2003, in eight

	No. of classified tests	Intrinsic rhythm	Rate-adaptive pacing verifiable	Rate-adaptive pacing non-verifiable
DDD-CLS	30	14 (46.7%)	12 (40.0%)	4 (13.3%)
VVI-CLS	10	3 (30.0%)	6 (60.0%)	1 (10.0%)
Total	40	17 (42.5%)	18 (45.0%)	5 (12.5%)

Table 3. Results of the submaximal exercise test at the discharge follow-up.

	No. of classified tests	Intrinsic rhythm	Rate-adaptive pacing appropriate	Rate-adaptive pacing not appropriate
DDD-CLS	33	21 (63.6%)	12 (36.4%)	0 (0%)
VVI-CLS	10	5 (50.0%)	4 (40.0%)	1 (10.0%)
Total	43	26 (60.5%)	16 (37.2%)	1 (2.3%)

Table 4. Results of the submaximal exercise test at the 4-week follow-up.

German centers and one Austrian center. Between hospital discharge follow-up and the 4-week follow-up, the following occurred in 13 patients:

- 12 additional follow-ups unrelated to the specific properties of the pacemakers, and
- four adverse effects (ineffective pacing, sensing loss) caused by lead problems.

Six out of the 66 patients enrolled were classified as dropouts for the following reasons:

- Two patients did not appear for a follow-up.
- One patient died.
- One patient was re-hospitalized.
- There were two cases of reprogramming during special follow-ups which were unrelated to the specific properties of the pacemakers.

Implant data and pre-implantation ECG diagnosis of the remaining 60 patients (32 female, mean age 72.5 ± 9.9 years) are shown in Tables 1 and 2.

Exercise Test at the Discharge Follow-up
According to Table 3, automatic initialization could not be evaluated in 17 of 40 cases (42.5%) due to the presence of an intrinsic rhythm. In 18 of 40 patients (45%), a rate adaptation could be observed 15 min after activating the CLS mode, but this was not possible in five of 40 patients (12.5%).

CLS Parameters at the End of the Discharge Follow-up
The default settings of the CLS parameters were only reprogrammed in a few patients. The results were as follows:

- Two cases of reprogramming the maximum closed-loop rate (maximum sensor rate) from 120 ppm to 110 ppm and 130 ppm, respectively;
- Six activations of the parameter Vp required in patients who needed permanent ventricular pacing;
- Two attenuations of the CLS dynamics (equivalent to a sensor gain adjustment).

Exercise Test at the 4-week Follow-up
At the 4-week follow-up, evaluation of the rate adaptation was not possible due to the presence of an intrinsic rhythm in 26 of 43 cases (60.5%), as demonstrated in Table 4. The rate adaptation of 16 of 43 exercise tests (37.2%) was judged adequate when observing permanent ventricular pacing, permanent intrinsic conduction, as well as intermittent intrinsic conduction or intrinsic ventricular rhythm (Figure 2). In total, 1 of 43 cases (2.3%) was judged inadequate because there was no detectable increase in the pacing rate above the basic rate in the VVI-CLS mode with permanent ventricular pacing. In contrast to the exercise test, the rate trend and the rate histogram obtained between discharge and the 4-week follow-up showed a typical rate adaptation (Figure 3). Additionally, during the surveillance period, the symptoms of the patient, who had been included due to an exchange indication, had improved (Table 5).
There was no significant difference in resting heart rate and the maximum heart rate during submaximal exercise (e.g., 5 min walking, stair descending, stair ascending) comparing the group with intrinsic rhythm and the paced patients with rate adaption classified as adequate (Figure 4a). The intraindividual differences between the various exercise tests and the basic rate, i.e., the rate increase during exercise, are also in the same range in both groups (Figure 4b).

CLS Parameters at the End of the 4-week Follow-up
At the 4-week follow-up, the final mode setting was as follows:

- DDD/VVI mode in 23 patients, demonstrated as chronotropically incompetent [21,22]
- One patient had a change to the DVI mode

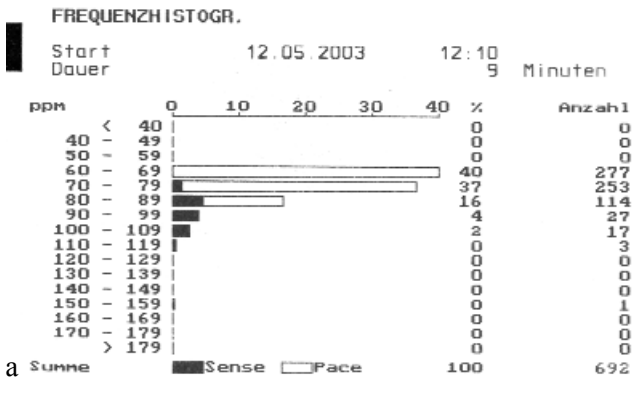

Figure 2. Pacemaker statistical data (Protos VR/CLS, Biotronik) from a 5-min walk test. Rate histogram (panel a) and rate trend (panel b) show appropriate pacing associated with intrinsic ventricular rhythm.

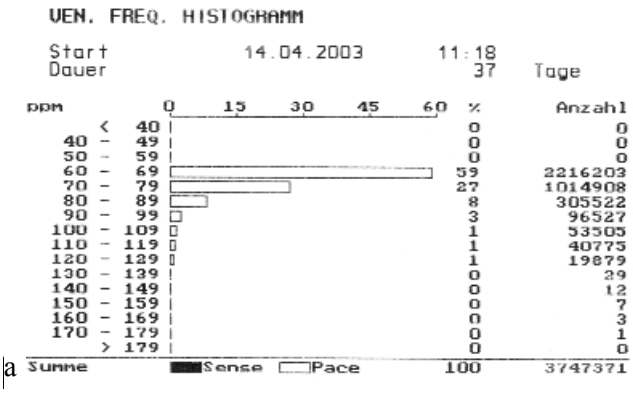

Figure 3. Protos VR/CLS rate histogram (panel a) and rate trend (panel b) of the period from discharge to the 4-week follow-up from the patient without rate adaptation during a 5-min walk test.

- From three patients there is no information on the final mode.
- Four patients had a change to the accelerometer-based, rate-responsive mode for investigational purposes due to the discretion of the attending physician.

The remaining 30 patients retained the CLS mode with the following modifications:

- Four cases of reprogramming the maximum closed-loop rate (maximum sensor rate) from 120 ppm to 130 ppm
- Two activations of the parameter Vp required in patients needing permanent ventricular pacing
- One increase of the CLS dynamics (equivalent to a sensor amplification).

AV-delay Measurement at the 4-week Follow-up

Figure 5 shows the default settings for the dynamic AV delay and the AV hysteresis. The area shaded in light grey shows the permitted range for intrinsic conduction. The dark grey area is considered a risk range for potential fusion beats that can occur in the case of an intermittent AV block. As part of the survey, the intrinsic AV delay was measured after atrial intrinsic events (66 ± 14 beats/min), during slight overdrive pacing (81 ± 11 beats/min), and during higher overdrive pacing (102 ± 10 beats/min). Taking into account the programmed sense compensation (default value –45 ms, mean value 41 ± 14 ms) for comparison of the intrinsic AV delay after atrial sensing and atrial pacing, a longer AV delay results with increasing overdrive pacing at rest compared to the physiologic shortening at

Symptoms	Preoperative diagnosis	4-week follow-up
General condition	low	good
Exertion tolerance	low	adequate
Heart rate	normal	normal
Palpitation of the heart	at no time	at no time
Difficult breathing/dyspnea	frequent	at no time
Syncopes	at no time	at no time
Dizziness	infrequent	infrequent
Chest pain/angina pectoris	at no time	at no time
Cerebral symptoms	infrequent	at no time

Table 5. History of the patient without rate adaptation during an exercise test at the 4-week follow-up.

stress [23]. Therefore, the dynamic AV delay for higher heart rates can only be optimally programmed with simultaneous or previous stress. As an alternative, the AV-delay statistical data of the Protos DR/CLS pacemaker can be used to program sense compensation, dynamic AV delay, and AV hysteresis. This statistical information on the intrinsic AV delays after atrial paced and sensed events is in accordance with the previously described measurements (Figure 6).

Discussion

The new automatic initialization for CLS provides an approximate start value for determining the pacing rate from the intracardiac impedance values, which may not be too high for safety reasons. Therefore, the few cases of undetectable rate adaptation directly after activating the CLS mode are within expectations.

At the 4-week follow-up, the DDD-CLS and VVI-CLS modes were adequate in 16 of 43 patients (37.2%). Only one of 43 (2.3%) exercise tests was inadequate because no increase in the pacing rate above the basic rate could be observed. All existing data indicate that this patient was still adequately supplied over a longer period because the patient history showed an improvement compared to the preoperative diagnostics, and the rate adaptation was comparable to that of other chronotropically incompetent patients according to the statistical data in the period between the discharge and 4-week follow-ups. Because the patient had a change to the accelerometer-based, rate-responsive mode for investigational purposes due to the discretion of the attending physician, further analysis of the CLS mode can be performed earliest at the next regular follow-up. The additional follow-ups, adverse effects, or the only

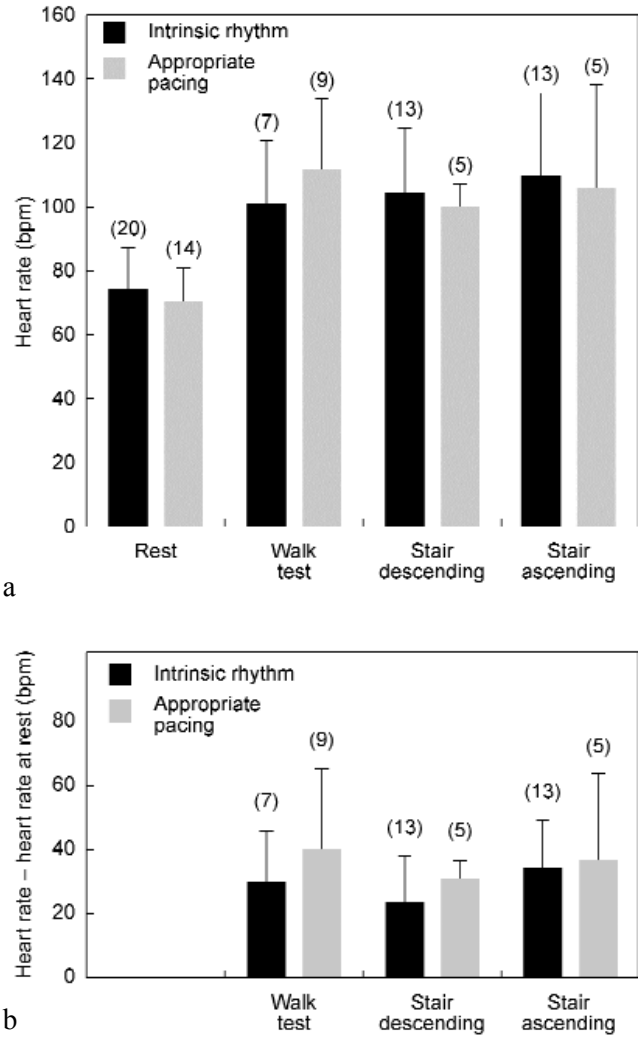

Figure 4. Panel a) Mean heart rate at rest and maximum heart rate during various exercise test for two subgroups with intrinsic rhythm and with adequate pacing as classified by the inverstigators. Panel b) Mean intraindividual difference values between the various exercise tests and the basic rate and corresponding standard deviations. For each value, standard deviations and number of cases are presented.

death within the surveillance period were not related to the specific pacemaker properties. There were no sensor-specific events causing a reprogramming of the mode setting.

At the end of the 4-week follow-up, the CLS mode was the final mode setting in 50% of the patients which reflects the wide use of pacemaker systems with incorporated sensor for rate-responsive pacing [24]. These results indicate that preoperative diagnosis of chorontropic incompetence is limited, e.g., due to changes in

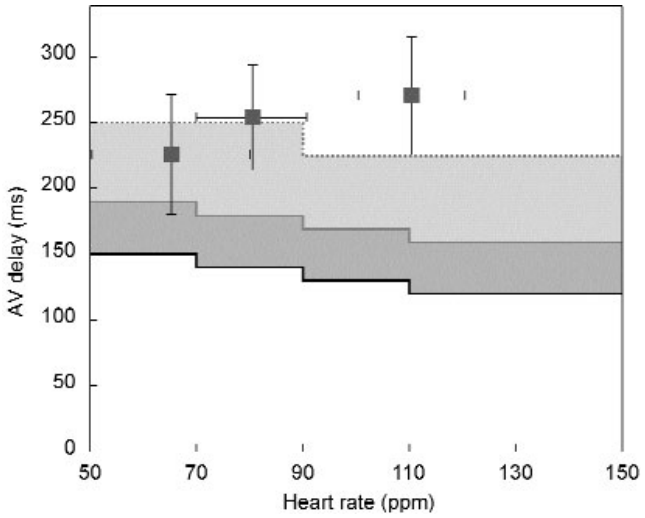

Figure 5. Atrioventricular (AV) delay versus heart rate. Default dynamic AV delay (lower line), default AV hysteresis (upper line). Symbols are representing mean AV delay and standard deviation from ECG measurements of atrial sensed events (AV delay + programmed sense compensation), slight overdrive pacing, and higher overdrive pacing.

a

INTRINSISCHE AV-ÜBERL.

	As Vs	Ap Vs	Summe
< 70 ppm	57268	192e3	249e3
70 bis 90 ppm	300e3	254e3	555e3
91 bis 110 ppm	3035	895	3930
111 bis 130 ppm	50	45	95
> 130 ppm	3	0	3
Summe	361e3	448e3	809e3

b

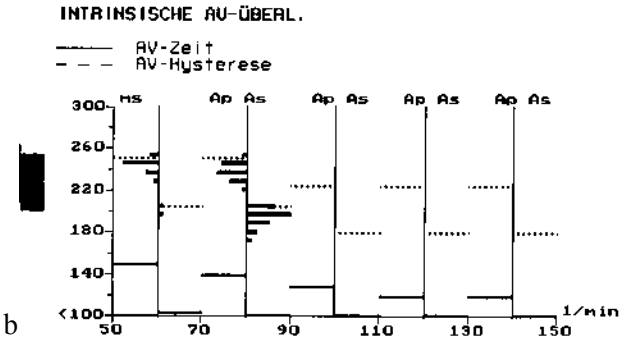

Figure 6. Statistics of the intrinsic atrioventricular (AV) delay between current and last follow-up. Panel a) Number of intrinsic AV-conduction events after atrial sensed (As Vs) and paced (Ap Vs) events for five heart rates ranges (rows). For each column and row the corresponding total number ("Summe") is given. Panel b) The AV histogram shows a difference between atrial pacing (Ap) and sensing (As) of 40 − 60 ms, which is in accordance with the programmed default sense compensation of 45 ms as well as with data obtained from ECG measurements (As Vs = 187 ms, Ap Vs = 256 ms, difference = 59 ms).

antiarrhythmic medication. On the other hand, postoperative diagnosis including pacemaker statistics will improve sensitivity and specificity. Thus, rate-adaptative pacemakers are the method of choice, whereby activating or deactivating the rate-adaptive mode should be decided individually on the base of all information available.

Conclusion

The Protos survey has demonstrated that the CLS mode in the new Protos DR/CLS dual-chamber and Protos VR/CLS single-chamber pacemakers allow appropriate rate-responsive pacing with minimal programming effort. Due to the extended functionality and indication of the new pacemaker family, studies with a large sample size can be performed.

Limitations

To complete this project within a short time, the indication for DDD(R) or VVI(R) pacemaker therapy was selected as the enrollment criterion, allowing for the inclusion of chronotropically competent patients, as long as activating the rate-adaptive mode over 4 weeks was not contraindicated. A survey does not allow for a protocol with fixed parameter settings and also no interventions into the therapy decisions of the study physicians. Thus, only optional, non-standardized tests were used, not allowing a specific statistical analysis of the data. This approach was justified by the intention to test the CLS properties of the new Protos DR/CLS and Protos VR/CLS in everyday clinical practice.

References

[1] Lau CP. The range of sensors and algorithms used in rate adaptive cardiac pacing. PACE. 1992;15: 1177-1211.

[2] Leung SK, Lau CP. Developments in sensor-driven pacing. Cardiol Clin. 2000; 18:113-155.

[3] Schaldach M, Ebner E, Hutten H, et al. Right ventricular conductance to establish closed-loop pacing. Eur Heart J. 1992; 13 (Suppl E): 104-112.

[4] Schaldach M. Automatic adjustment of pacing parameters based on intracardiac impedance measurements. PACE. 1990; 13: 1702-1990.

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

[6] Pichlmaier AM, Braile D, Ebner E, et al. Automatic nervous system controlled closed loop cardiac pacing. PACE. 1992; 15: 1787-1791.

[7] Osswald S, Cron T, Grädel C, et al. Closed loop stimulation using intracardiac impedance as a sensor principle: correlation of right ventricular dP/dt max and intracardiac impedance during dobutamine stress test. PACE. 2000; 23: 1502-1508.

[8] Hilti P, Cron T, Osswald S. Das ‚closed-loop' Sensorsystem mit intrakardialer Impedanzmessung als Parameter für die myokardiale Kontraktilität. Herzschrittmacher. 2000; 5: 345-352.

[9] Martinelli Filho M, Nishioka SA, Lopes H, et al. Neurohumoral behavior in recipients of cardiac pacemakers controlled by a closed-loop autonomic nervous system-driven sensor. PACE. 2000; 23: 1778-1782.

[10] Griesbach L, Gestrich B, Wojciechowski D, et al. Clinical performance of automatic Closed Loop Stimulation systems. PACE. 2003; 26: 1432-1437.

[11] Vijay N, de Metz K, Dolan M, et al. A prospective multicenter study demonstrating safety and effectiveness of closed loop stimulation. Prog Biomed Res. 2001; 6: 397-401.

[12] Hamilton D, Cook L, Tomczak C, et al. Assessment of the chronotropic/metabolic relationship in patients with the Inos2+ CLS closed loop pacemaker. Prog Biomed Res. 2002; 7: 231-241.

[13] Cook L, Hamilton D, Busse E, et al. Impact of adaptive rate pacing controlled by a right ventricular impedance sensor on cardiac output in response to exercise. PACE. 2003; 26: 244-247.

[14] Malinowski K. Interindividual comparison of different sensor principles for rate adaptive pacing. PACE. 1998; 21: 2209-2213.

[15] Gestrich B, Meyer P, Schleich A, et al. Influence of closed-loop pacemaker implantation on patients' quality of life: RAPID study findings. Prog Biomed Res. 2002; 7: 55-62.

[16] Menezes Jr A, Daher M, Nascente C, et al. Correlation among closed loop stimulation, cardiopulmonary capacity, and quality of life. Prog Biomed Res. 2003; 8: 119-124.

[17] Lawo T, Lemke B. Rateadaptation durch Sensorerkennung: Sensorsysteme und Einstellung. Herz. 2001; 26: 75-78.

[18] Pieragnoli P, Colella A, Michelucci A, et al. A new algorithm for closed-loop stimulation: A feasibility study. PACE. 2003; 26: 229-232.

[19] Stierle U, Kruger D, Vincent AM, et al. An optimized AV delay algorithm for patients with intermittent atrioventricular conduction. PACE. 1998; 21: 1035-1043.

[20] Fischer W, Ritter Ph. Praxis der Herzpacemakertherapie, 2. Auflage. Berlin: Springer Verlag; 1997: 225-340.

[21] Vorstand der Deutschen Gesellschaft für Kardiologie - Herz- und Kreislaufforschung. Richtlinien zur Herzpacemakertherapie Indikationen, Systemwahl, Nachsorge. Z Kardiol. 1996; 85: 611-628.

[22] Epperlein S, Kreft A, Siegert V, et al. DDD- versus DDDR-Pacemakerstimulation: Vergleich der kardiopulmonalen Leistungsfähigkeit, der Häufigkeit von Vorhofarrhythmien und der Lebensqualität. Z Kardiol. 1996; 85: 226-236.

[23] Meine M, Hexamer M, Werner J, et al. Relationship between atrioventricular delay and oxygen consumption in patients with sick sinus syndrome: relevance to rate responsive pacing. PACE. 1999; 22: 1054-1063.

[24] Danish pacemaker Registry. Annual Report 2002. Available from URL: http://www.pacemaker.dk/pdf.htm

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