Optimizing the Philos Mode-Switching Resynchronization: The Concept of the OPHIR Multicenter Study

A. HARTMANN, S. LÖSCHER
Department of Cardiology, Medical Center "St. Georg", Leipzig, Germany

S. HANSEN
Clinical Project Management, Biotronik, Berlin, Germany

On Behalf of the OPHIR Multicenter Study Group

Summary

Automatic mode-switching algorithms allow the use of dual-chamber pacemakers in patients with paroxysmal atrial tachyarrhythmias: Automatic switching from an atrial controlled (e.g., DDD) to a ventricular controlled mode (e.g., DDI) prevents the pacemaker-mediated conduction of an atrial tachyarrhythmia to the ventricle. The dual-chamber pacemakers Philos DR, D, and SLR are equipped with a flexible mode-switching algorithm based on the X-out-of-Y concept, in which the switch-off criterion (Z-out-of-8 criterion) is programmed independent of the selection for the switch-on criterion (X-out-of-8 criterion). This allows for adapting the mode-switching function to the individual needs of the patient in order to achieve an optimal speed, specificity, and sensitivity during de- and resynchronization, which should prevent mode oscillations. The recently started, prospective, randomized OPHIR multicenter study aims at determining a Z value for the Z-out-of-8 switch-off criterion that enables an adequate resynchronization without mode oscillations. This article describes and discusses the goals and methods of the OPHIR study.

Key Words

Mode switching, X/Z-out-of-Y, resynchronization, atrial tachyarrhythmia, mode oscillation

Introduction

According to the literature, paroxysmal atrial tachyarrhythmias occur in 30 to 60 % of all cardiac pacemaker patients [1]. Automatic mode-switching algorithms allow the use of dual-chamber pacemakers in these patients [2,3]. The automatic mode-switching function describes the capability of a pacemaker both to detect the presence of atrial tachyarrhythmias and to switch automatically from a triggering mode (e.g., DDD) to a non-triggering one (e.g., DDI) for the duration of the tachyarrhythmia (desynchronization). It should detect when the atrial tachyarrhythmia terminates and switch back to the triggering mode (resynchronization). In this manner, mode switching prevents the pacemaker-mediated conduction of an atrial tachyarrhythmia to the ventricle and, thus, the unfavorable hemodynamic and symptomatic effects of rapidly conducted atrial tachycardias [4]. Correct de- and resynchronization of the ventricular depolarization is decisive for the optimal function of the mode-switching algorithm.

Flexible mode-switching functions based on the X-out-of-Y concept are increasingly used in the newer pacemaker systems. Due to the variability of their programming, they enable an individual adaptation of the algorithm in regard to its speed, specificity, and sensitivity for detecting atrial tachyarrhythmias [5]. For example, the X value of the X-out-of-8 switch-on criterion can be programmed in the Logos pacemaker system (Biotronik, Germany), allowing a free choice between high sensitivity (e.g., 2-out-of-8) and a high specificity (e.g., 7-out-of-8) [6]. However, in most systems with a mode-switching function, resynchroniza-

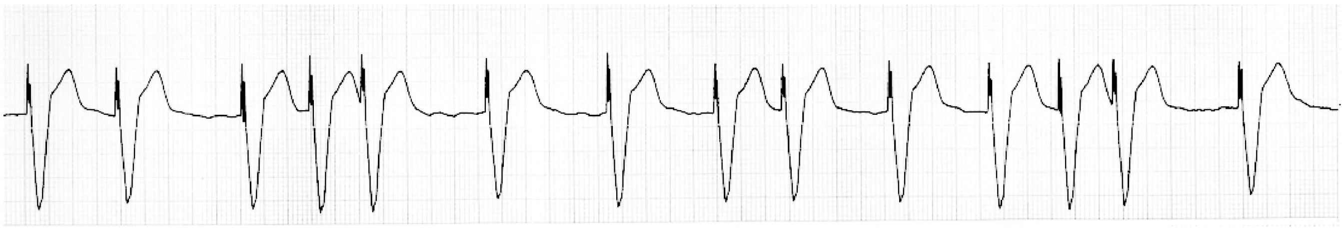

Figure 1. Example of a mode oscillation.

tion is either set to a fixed value or coupled to the programming of the switch-on criterion for the desynchronization. The Philos DR, D, and SLR dual-chamber pacemakers (Biotronik) are currently the only pacemakers that contain a novel, additional mode-switching function (Z-out-of-8) to control the speed of resynchronization individually and, thus, to prevent resynchronization failures. Frequent false-positive resynchronization is a major cause of mode oscillations [4,7-9]. Mode oscillation is the constant back-and-forth switching between conduction and blocking the conduction, despite a still ongoing atrial tachyarrhythmia. Figure 1 shows an example of a mode oscillation. Typical circumstances that can lead to an incorrect resynchronization are:

- The signal amplitude in the atrium is too low to be sensed (e.g., during atrial fibrillation) [5,8-11].
- An atrial event occurs during the post-ventricular atrial blanking period (PVAB) [2,9].

If a low value is programmed for the switch-off criterion (resynchronization), the period of AV dissociation after termination of the tachyarrhythmia is shortened; however, the probability of an incorrect resynchronization and, consequently, of mode oscillation, also increases [4,7,9]. Especially in patients with episodes of atrial flutter, who are switched to DDIR and in whom the momentary pacemaker rate equals a half, a third, or more of the flutter rate, programming of a low switch-off criterion can lead to incorrect resynchronization. This is caused by the fact that a part of the atrial signals is regularly not evaluated, due to the PVAB and/or far-field blanking.
A high switch-off criterion can help avoid incorrect resynchronization and mode oscillation during atrial fibrillation with low signal amplitudes and, thus, unreliable sensing [1,7,12]. However, if the switch-off criterion is set too high (e.g., 8-out-of-8), this can lead to the problem that resynchronization takes place only a considerable time after termination of the atrial tachyarrhythmia. The period during which no conduction of the normal sinus rhythm is possible should, however, be as short as possible (AV dissociation). This applies in particular to patients with atrial tachycardias with amplitudes that can be sensed well. In the DVI(R) mode, competitive pacing in the atrium can occur, and in the VVI mode, there is the possibility of a retrograde conduction (pacemaker syndrome).
The described problems in selecting an optimal Z value are shown schematically in Figure 2.

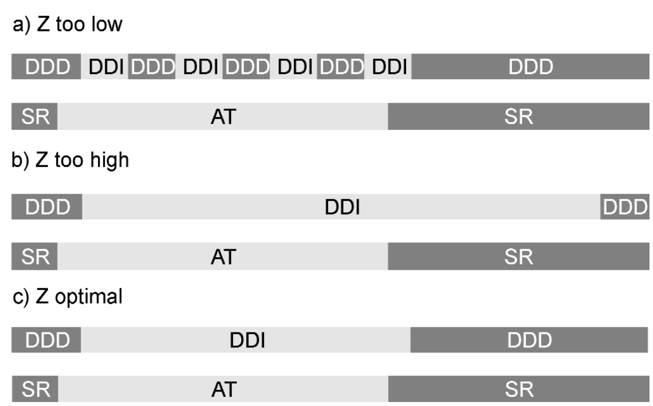

Figure 2. Schematic depiction of the problems in optimizing the Z-out-of-8 switch-off criterion. Abbreviations: DDD and DDI represent all atrial and ventricular triggered modes, respectively; SR = sinus rhythm; AT = atrial tachy-arrhythmia. Explanation: a) If the Z value is too low, this can result in a false-positive resynchronization, possibly leading to a mode oscillation. b) If the Z value is set too high, there is the problem of an unnecessary long AV dissociation. c) With an optimally programmed Z value, correct resynchronization occurs shortly after the AT terminates.

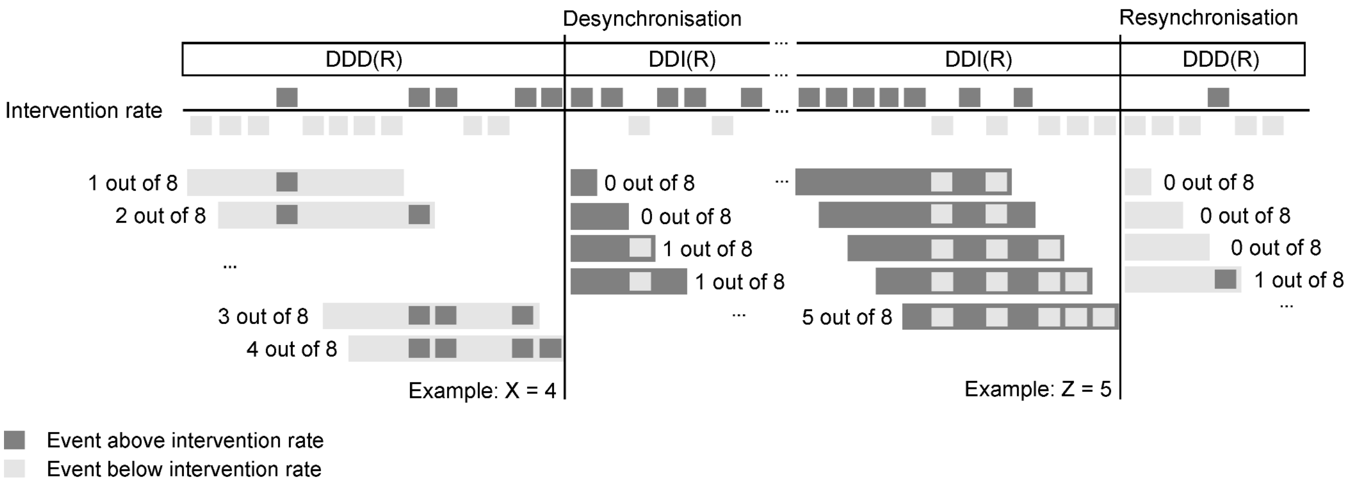

Figure 3. Automatic mode switching in the dual-chamber pacemakers Philos DR, D, and SLR: Schematic depiction of the functioning of the X/Z-out-of-8 algorithm, with the switch-on criterion X set to 4, and the switch-off criterion Z, to 5.

Description of the Mode-Switching Algorithm

During mode switching (X/Z-out-of-8 algorithm), the pacemaker switches to a ventricular controlled mode (e.g., DDI) for the duration of the arrhythmia episode after detecting an atrial tachyarrhythmia. Switching back to the AV-synchronous mode (e.g., DDD) is also called resynchronization or resolution. Figure 3 shows an example of how the X/Z-out-of-8 algorithm functions in the Philos DR, D, or SLR.

Switch-on criterion X-out-of-8 (desynchronization): If the pacemaker is in a mode that allows the conduction of atrial signals to the ventricle (DDD, DDDR, VDD and VDDR), the X-out-of-8 counter remembers the number of atrial cycles within the last eight atrial cycles, for which the rate was higher than the programmable intervention rate (tachy cycles). As soon as this switch-on criterion is met, mode switching is triggered in the pacemaker. The mode, to which the pacemaker switches after a mode switching, can be programmed. The AV delay is set to a fixed value of 100 ms during operation in the DDI(R) mode (after mode switching).

Switch-off criterion Z-out-of-8 (resynchronization): To avoid mode oscillations, the switch-off criterion Z-out-of-8 is set to 0 after mode switching (triggered by the atrial tachycardia), i.e., all eight previous cycles are regarded as tachy cycles, no matter how many were actually necessary for mode switching. From that point on, the Z-out-of-8 counter remembers the number of atrial cycles within the last eight atrial cycles, for which the rate was below the programmable intervention rate (brady cycles). As soon as the programmed switch-off criterion Z-out-of-8 is met, resynchronization is triggered in the pacemaker. To avoid mode oscillations, the switch-on criterion X-out-of-8 is set to 0 after the resynchronization, i.e., all eight previous cycles are regarded as brady cycles, no matter how many were actually necessary for resynchronization.

Rationale of the OPHIR Study

When the physician activates the mode-switching function during pacemaker programming of a Philos DR, D, or SLR, the pre-programmed default setting for the Z-out-of-8 switch-off criterion is 5-out-of-8. Depending on the individual needs of the patient, it should be possible to reprogram the Z value if necessary. Application monitoring performed in late 2000 recorded the pacemaker programming of Philos during the discharge follow-up in 24 patients. It showed that the default setting for the Z-out-of-8 switch-off criterion was not changed in the 13 patients (54 %) in whom the mode-switching function was activated. The following conclusions were drawn from this result:

- Due to lacking clinical experience with programming a flexible switch-off criterion, the attending physician first retains the default setting in order to then keep changing the patient-individual setting of the Z value in the case of symptomatic mode oscil-

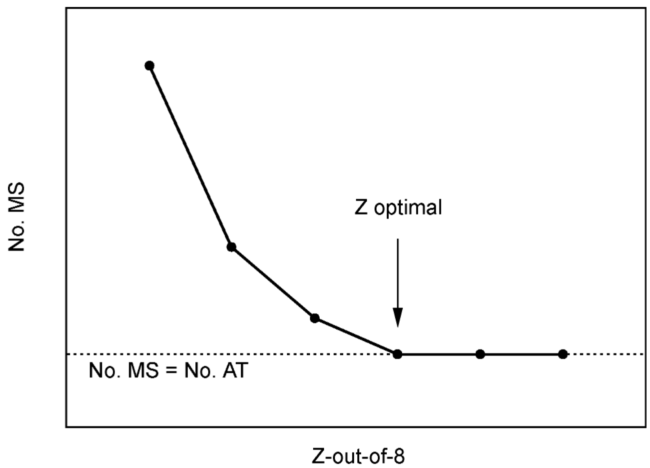

Figure 4. Schematic depiction of the hypothetic assumption for determining an optimal Z value using the Philos statistics function mode-switching counter. Abbreviations: No. MS = number of mode-switching events measured by the mode-switching counter (y-axis); No. AT = real number of atrial tachycardias; Z-out-of-8 = programmable Z values 3...(1)...8 (x-axis).

lations until no more mode oscillations occur. Since atrial tachyarrhythmias in these patients occur only rarely during a follow-up, it can take several follow-ups until the Z value is individually optimized. This means that the pacemaker does not optimally provide for the patient over a longer time period, and this might be accompanied by a decrease in the patient's quality of life.

- There are no retrospective or prospective data that would allow a reliable definition of a Z value that is optimal for most patients. A safe programming recommendation could, however, increase the number of patients who ideally profit from an optimal supply by the pacemaker immediately after the implantation, which avoids mode oscillations and, thus, guarantees a high quality of life.

Therefore, a prospective, randomized, multicenter study for Optimizing the Philos Mode Switching Resynchronization (OPHIR) has the goal of finding an optimal setting of the Z-out-of-8 switch-off criterion. That Z value is regarded as the optimal setting that is large enough to prevent mode oscillations due to false-positive resynchronization, and is at the same time small enough to guarantee the fastest possible return of the pacemaker to the AV-synchronous mode (see Figure 2).

The statistics memory of the Philos does not provide information about the absolute number of mode oscillations if the number of all mode-switching events in a follow-up period is greater than 64 (the statistics function tachy episode protocol shows the date, time at termination, and duration only for the last 64 mode-switching events). However, it has to be assumed that this number is quickly surpassed, especially when mode oscillations occur. In this case, the statistics function mode-switching counter needs to be used for analyzing the data. This function counts all mode-switching events within a follow-up period, without differentiating between correct mode switching (= one mode-switching event per atrial tachyarrhythmia) and mode oscillation. When judging whether mode oscillations occur with a certain Z value, the OPHIR study therefore works with the hypothetic assumption that the average number of atrial tachyarrhythmias per time interval remains constant for a sufficiently large sample of patients. If this is true, then the number of mode-switching events should first decrease when the Z value is increased step by step, starting with the smallest value Z = 3, because the average number of mode oscillations will decrease due to the reduction in false-positive resynchronizations. Starting with the Z value at which no more mode oscillations occur, the number of mode-switching events should no longer decrease even if the Z value is further increased since the number of mode-switching events and the number of atrial tachyarrhythmias remain equal on average due to the correct resynchronization. This value is then the optimal Z value because a further increase of the Z value only leads to an unnecessary increase in the time in AV-asynchronous mode. Figure 4 schematically depicts the principle of the described hypothetic assumption.

Pilot Study for the OPHIR Study

The pilot study has the goal of proving the principal efficacy of flexible mode-switching resynchronization in the Philos DR, D, and SLR dual-chamber pacemakers for minimizing the undesired mode oscillations. Using the statistics data stored in the pacemaker, it shall be tested whether differences exist between the smallest (Z = 3) and greatest (Z = 8) programmable Z value in regard to the frequency of mode oscillations, according to the hypothetic assumption described above. There are three possible result variants:

- The frequency of mode oscillations is higher at Z = 3 than at Z = 8. This result is expected to be the most probable, and it is assumed that the number of mode oscillations at Z = 8 approaches zero or a range that is insignificant for the patient. If preventing mode oscillations or keeping them within patient-acceptable limits should be impossible even at Z = 8, changes to the algorithm would be necessary. However, according to the previous clinical experiences with the Inos[2] CLS pacemaker (Biotronik), which operates with a fixed 8-out-of-8 switch-off criterion, hardly any mode oscillations should occur at Z = 8. In case of this result variant, the subsequently planned OPHIR study will aim to find the Z setting optimal for most patients (= smallest Z value at which no mode oscillations occur).
- The frequency of mode oscillations is the same at Z = 3 and Z = 8 and approaches zero in both cases (control: the last 64 recorded events in the tachy episode protocol document correct mode switching without mode oscillations). In case of this result variant, Z = 3 is sufficient to prevent mode oscillations (= optimal), making the OPHIR study unnecessary.
- The frequency of mode oscillations is the same at Z = 3 and Z = 8, and it is too high in both cases (in the sense of patient tolerance). This result variant is not expected because a high number of mode oscillations is unlikely for Z = 8 (see first variant); it would necessitate a modification of the algorithm and would make the OPHIR study untenable for the time being.

Another goal of the pilot study is to optimize the study design for the planned OPHIR study. In particular, it shall be tested whether the kind of atrial tachyarrhythmia (e.g., atrial fibrillation, atrial flutter) has an influence on the results, which would require specifying the inclusion criteria for the OPHIR study. Furthermore, suitable time intervals between follow-ups are to be determined using the average frequency of atrial tachyarrhythmias or, respectively, the number of mode-switching events per time period. Since the planned OPHIR study will aim to record the influence of programming the switch-off criterion on the quality of life, the suitability of the SF-36 health survey questionnaire is tested in this pilot study. The SF-36 has been chosen because this questionnaire for assessing the quality of life is generally accepted.

Materials and Methods

The pilot study for the OPHIR study is carried out as a

study in the German-speaking region. A total of 30 patients will be included in this study, and the study par ticipation period for each patient will be for 7 months after implantation. The two settings for the switch-off

other in a 2-arm study design with crossover.
Aside from a pacemaker indication [12,13], patients

anamnesis of paroxysmal atrial tachyarrhythmias dur-
-

graphic or clinical diagnosis). They must be scheduled

SLR dual-chamber pacemaker, and they require a bipolar atrial lead with a tip-ring distance of ≤ 15 mm

patients must be able to principally tolerate any setting

the physician, and their medication should be stable at

of the study. Furthermore, only such patients are

who have read and understood the patient information

their written consent to participate in the study, and
-
-
-

symptomatic chronotropic incompetence, and unre solved atrial sensing problems (the latter applies from

The study design of the pilot study is shown schemati cally in the flow chart in Figure 5. Data are collected at

implantation, discharge follow-up, 1-, 4- and 7-month
-

from the Philos statistics memory. The patients are ran domized into two groups (A and B) as part of the inclu sion phase according to principle of randomness (ran dom list). The period between discharge follow-up and

electrodes (wash-in) and for testing the principal toler ance of the setting Z = 3 by the respective patient.

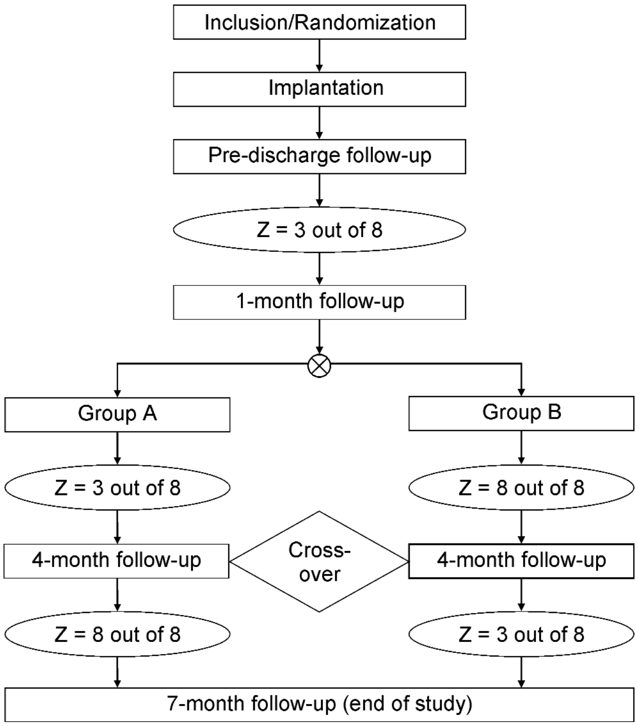

Figure 5. Flow-chart of the pilot study for the OPHIR study.

patients from group A is programmed to Z = 3, and that

4-month follow-up, a crossover of the Z-out-of-8 set tings takes place; group A: Z = 8 and group B: Z = 3.

follow-up. Besides the defined settings of the Z-out-of-

-

= DDIR, intervention rate = 160 beats/min, X-out-of-8

selected in such a manner that far-field sensing is

-

-

-

-

SF-36 questionnaire (German version, Hogrefe Verlag,

phase, the 4- and the 7-month follow-up, respectively.

-

switch-off criterion to 3-out-of-8 and 8-out-of-8. The

-

-

switch-off criterion to 3-out-of-8 and 8-out-of-8, and

36) between setting the switch-off crite-

parameters from the Philos statistics memory are used

protocol, and ADR. The ADR serves as control whether

last nine occurred atrial tachyarrhythmias. The statisti cal analysis is performed with a Wilcoxon test, applied α 2-tailed). The sec ondary objectives are descriptively analyzed in an

Results and Discussion

available data are not yet sufficient to discuss any ini tial results in regard to the study goal.

-

patients with paroxysmal atrial tachyarrhythmias opti mally. A programming recommendation for an optimal

adapted pacemaker output for most patients, can make

that guarantees optimal resynchronization in the

indication. Such an optimal Z value could then be pre-

passed on to the physicians as a programming recom mendation. If there should be no uniform optimal

-

diseases if the patient population of the study is large

with atrial flutter and atrial fibrillation). For instance, it

fibrillation, which were classified, among others, in the

affect the resynchronization behavior of mode-switch ing algorithms in general and whether there is a uni form Z value for all types.

Z values, sensitivity and specificity are decisive for the

arrhythmias to minimize the risk of inadequate thera pies [6,16]. The OPHIR multicenter study and the recently started OPHIR pilot study are intended to make a major clinical contribution to this.

Conclusion

Today, cardiac pacemakers offer a number of functions and programming options, which allow in many cases a pacemaker output that is individually optimized to the patient. Due to the multitude of different algorithms available for a certain therapy in the pacemaker models on the market, it is often difficult for the attending physician to find the optimal programming, especially if there are no safe recommendations based on clinical data.

The Philos DR, D, and SLR dual-chamber pacemaker models are the first to offer a freely programmable switch-off criterion (Z-out-of-8) as part of the mode-switching function, which is designed to guarantee the correct resynchronization to the AV-synchronous mode and can, thus, prevent undesired mode oscillations. The planned prospective, randomized, multicenter study OPHIR will attempt to validate a scientifically proven programming recommendation for an optimal Z value, which guarantees a correct resynchronization without mode oscillation in the majority of the potential patients. To clarify important questions about the conception of the study design (e.g., principal efficacy, follow-up intervals, influence of the indication), a pilot study is first performed, which has been recently started.

Current Participants of the OPHIR Multicenter Study Group

A. Hartmann (Principal Investigator) and S. Löscher (Leipzig, Germany); B.-D. Gonska, H. Baumann and M. Müller (Karlsruhe, Germany); E. Meisel (Dresden, Germany); R. Pospiech and B. Wille (Berlin, Germany); G. Hoh (Lutherstadt Wittenberg, Germany); F. Saborowski and H.W. Angenent (Cologne, Germany).

References

[1] Levy S, Breithardt G, Campbell RW, et al. Atrial fibrillation: Current knowledge and recommendations for management. Working Group on Arrhythmias of the European Society of Cardiology. Eur Heart J. 1998; 19: 1294-1320.

[2] Nowak B. Taking advantage of sophisticated pacemaker diagnostics. Am J Cardiol. 1999; 83: 172D-179D.

[3] Sutton R, Stack Z, Heaven D, et al. Mode switching for atrial tachyarrhythmias. Am J Cardiol. 1999; 83: 202D-210D.

[4] Ellenbogen KA, Mond HG, Wood MA, et al. Failure of automatic mode switching: Recognition and management. PACE. 1997; 20: 268-275.

[5] Israel CW. Mode-Switch-Algorithmen: Programmierbarkeit und Nutzen. Herz. 2001; 26: 2-17.

[6] Israel CW, Lawo T. Use of an advanced mode switching algorithm in Inos2 CLS and Logos dual chamber pacemakers. Herzschr Elektrophys. 1999; 10: I/72-I/80.

[7] Koglek W, Suntinger A, Wernisch M, et al. Automatische Modusumschaltung (Auto-Mode-Switch, AMS). Herzschr Elektrophys. 1998; 9: 108-119.

[8] Bonnet JL, Brusseau E, Limousin M, et al. Mode switch despite undersensing of atrial fibrillation in DDD pacing. PACE. 1996; 19: 1724-1728.

[9] Palma EC, Kedarnath V, Vankawalla V, et al. Effect of varying atrial sensitivity, AV interval, and detection algorithm on automatic mode switching. PACE. 1996; 19: 1734-1739.

[10] Lam CT, Lau CP, Leung SK, et al. Improved efficacy of mode switching during atrial fibrillation using automatic atrial sensitivity adjustment. PACE. 1999; 22: 17-25.

[11] Levine PA, Bornzin GA, Barlow J, et al. A new automode switch algorithm for supraventricular tachycardias. PACE. 1994; 17: 1895-1899.

[12] Lembke B, Fischer W, Schulten HK. Richtlinien zur Herzschrittmachertherapie – Indikation, Systemwahl, Nachsorge – der "Kommission für Klinische Kardiologie" der Deutschen Gesellschaft für Kardiologie – Herz-und Kreislaufforschung. Z Kardiol. 1996; 85: 611-628.

[13] Gregoratos G, Cheitlin MD, Epstein AE, et al. ACC/AHA guidelines for implantation of cardiac pacemakers and antiarrhythmia devices: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Pacemaker Implantation). J Am Coll Cardiol. 1998; 31: 1175-1209.

[14] Wells JL, Karp RB, Kouchoukos NT, et al. Characterization of atrial fibrillation in man: Studies following open heart surgery. PACE. 1978; 1: 426-438.

[15] Allessie MA, Konings K, Kirchhof CJ, et al. Electrophysiologic mechanisms of perpetuation of atrial fibrillation. Am J Cardiol. 1996; 77: 10A-23A.

[16] Barbaro V, Bartolini P, Calcagnini G, et al. Automated classification of human atrial fibrillation from intraatrial electrograms. PACE. 2000; 23: 192-202.

Contact
Prof. Dr. Andreas Hartmann
1. Klinik für Innere Medizin
Städtisches Klinikum "St. Georg" Leipzig
D-04129 Leipzig
Germany
Telephone: +49 341 909 23 01
Fax: +49 341 909 23 23
E-mail: Andreas.Hartmann@sanktgeorg.de