

## Preventive Pacing in Atrial Fibrillation

W. KAINZ

Department of Cardiology, Hanusch Hospital, Vienna, Austria

### Summary

*Patients with paroxysmal atrial fibrillation are often highly symptomatic, are frequently in need of hospital treatment, and are subject to considerable complications. Though drug therapy is the generally accepted standard in treating atrial fibrillation, the efficacy and safety of antiarrhythmic drugs has remained questionable. Aside from other forms of therapy, in recent years pacemaker therapy has gained in importance for preventing atrial fibrillation. Preventive pacing in paroxysmal atrial fibrillation has the goal of modulating the electrical activity of the atria in order to prevent recurrences of fibrillation. Supraventricular extrasystoles, bradycardias, special initiation sequences (short-long-short), and so-called early recurrence of atrial fibrillation are the onset mechanisms that are responsible in more than 90 % of cases. Today special pacing algorithms are available to suppress these onset scenarios, and their efficacy is currently evaluated in numerous studies. Stimulating at certain locations in the right atrium, such as at the interatrial septum and in the region of the Bachmann bundle, allows resynchronization of the atria, similar to the biatrial pacing method by means of two leads; this method also makes it possible to achieve a reduction of atrial fibrillation episodes. Numerous smaller studies and the preliminary results of large, randomized trials concerning the efficiency of preventive pacing were able to confirm a significant reduction in the AF-burden, as well as an improvement in the patients' quality of life.*

### Key Words

Atrial fibrillation, atrial overdrive pacing, atrial rate stabilization, atrial resynchronization

### Introduction

Atrial fibrillation is the most frequent cardiac arrhythmia that physicians confront in clinical practice. The loss of the atrial contribution to the stroke volume and the coarse irregularity of the ventricular complexes cause a worsened hemodynamic situation, which, together with embolic complications, leads to a significant morbidity and mortality. Current drug therapy strategies aim at rate control, on the one hand, and at conversion to a stable sinus rhythm by treatment with class I/III antiarrhythmics, on the other hand. Both strategies are often ineffective, and the prescribed medication frequently has to be discontinued because of serious side effects. Therefore, non-pharmacological therapy concepts have been considered with increasing interest in recent years. Aside from ablative and surgical methods, this includes the use of pacemakers.

### Rationale for Prevention by Pacing

The substrate for atrial fibrillation is formed by the atria's capability to sustain various, simultaneously existing excitation waves. Under normal electrophysiologic conditions, this requires a considerable increase in atrial size. However, a slowed spread of excitation and/or shortening of the atrial refractory period can also cause atrial fibrillation in cases involving a normal atrial dimension. Patients with atrial fibrillation have always exhibited an abnormal constellation in their atrial electrophysiology, such as a shortening of the action potential duration, delayed conduction, and a disturbed rate adaptation of these parameters. Under such conditions, supraventricular extrasystoles that are conducted abnormally and split into multiple excitation waves can trigger atrial fibrillation. The spread of these premature impulses depends, in turn, on the location of their origin and the previous cycle lengths,

<b>Targets</b>	
Atrial substrate	Abnormal repolarisation: shortened refractory period, lacking rate adaption, increased dispersion of the refractory periods  Abnormal conduction: delayed mostly when heart rate is low, anisotropy and increased dispersion of the conduction velocity
Trigger	Supraventricular extrasystoles  Pauses  Specific triggering sequences; e.g., short-long-short
<b>Methods</b>	
Fixed-rate pacing (AAI)	Conventional rate: prevents pauses  Higher rate: "overdrive" pacing
Physiologic pacing (AAIR)	Constant overdrive
Triggered pacing	Special algorithms to prevent supraventricular extrasystoles and pauses
Biatrial/multisite pacing	Resynchronisation of the atria

Table 1. Prevention of atrial fibrillation by pacing – targets and methods according to Murgatroyd [1].

which define the state of refractoriness and heterogeneity of the atria. As shown in Table 1, the development of atrial fibrillation can therefore be seen as an interaction of structural and functional factors, modified by variations in the cycle length and premature atrial complexes, which function as triggers [1]. The monitoring phase of the atrial fibrillation therapy (AFT) study has provided comprehensive data about the various onset mechanisms for atrial fibrillation. This multicenter, randomized crossover study, the final results of which are not yet available, investigated the onset scenarios in its first phase. In more than 43 %, the atrial tachyarrhythmias were preceded by supraventricular extrasystoles; in a third of the cases – so-called early recurrences that occurred within a few minutes after termination – about 20 % were induced by a bradycardia, and the rest were either sudden onsets or triggered by a tachycardia [2].

### Prevention of Atrial Fibrillation by Fixed-Rate Atrial Pacing

The preventive effect of atrial pacing in atrial fibrillation has been documented in numerous retrospective studies. Already in 1986, Rosenquist et al. [3] published the result of a comparative study of AAI versus VVI pacing in patients with sick sinus syndrome. Patients with VVI pacing had significantly more frequent episodes of atrial fibrillation compared to patients

with AAI pacing (30 % vs. 4 %, p-value < 0.01). These data could be confirmed in a later study [4] after a longer follow-up period (atrial fibrillation: 47 % vs. 6.7 %, p-value < 0.005). Sasaki [5] reported on a population of 103 patients with sick sinus syndrome that had been subdivided into non-paced, ventricular paced, or physiologically paced (atrial or dual-chamber pacing) groups. Atrial fibrillation was significantly more frequent in the group with VVI pacing than in the two others. Many other publications came to concurring results. In 1997, Andersen et al. [6] confirmed the preventive effect of atrial pacing regarding the incidence of atrial fibrillation in sick sinus syndrome when compared to VVI pacing in the first randomized and prospectively designed study.

### Overdrive Pacing

#### Constant Overdrive Pacing

As early as 1983, Coumel et al. [7] reported on the positive effect of atrial pacing with a constant rate of 90/min in patients with vagally induced atrial fibrillation. In a study that was only presented recently on the effect of atrial overdrive pacing in patients with paroxysmal atrial fibrillation and without indications of a sinus node disease and with normal AV conduction, Wiberg et al. [8] were able to prove a significant reduction of symptomatic atrial fibrillation attacks. The patients were paced in the right atrial appendage

'with various fixed rates. The pacemakers were programmed to AAI medium rate, i.e., 10 – 19 beats/min above the mean heart rate (MHR), AAI high rate, meaning 20 – 29 beats/min above the MHR, and OAO (no stimulation). All symptomatic atrial fibrillation episodes were recorded by the patients in a diary and documented with an event recorder.

#### *Dynamic Overdrive Pacing*

In the last few years, several pacemakers have been equipped with algorithms for pacing just above the intrinsic heart rate. These systems allow an almost complete suppression of spontaneous atrial depolarization, but they do not impair patients by pacing at a rate that is too high. The preliminary results of the ADOPT-ALL study have shown a 39 % reduction in the burden caused by atrial fibrillation during the phase with activated overdrive algorithm [9]. The data of the ADOPT-ALL study, presented during the Late Breaking Clinical Trials Session of the NASPE meeting on May 5, 2001, are also remarkable. The primary endpoint of this study was "AF burden," defined as the percentage of days during the follow-up period on which symptomatic atrial fibrillation occurred. To assure that the symptoms were actually caused by atrial fibrillation, the patients documented the episodes with an event recorder. By activating the overdrive mode, an atrial pacing percentage of 92.2 % could be achieved, compared to 67.9 % when the algorithm was not active. Overdrive pacing was able to achieve a 25.03 % reduction of the "AF burden." In a subgroup analysis that excluded those patients in whom no symptomatic atrial fibrillation episodes had occurred in the first 30 days after implantation, the "AF burden" was reduced by 36 %. This clinical study proved the preventive effect of dynamic overdrive pacing, as well as a significant improvement in the patient's quality of life. A lower re-hospitalization rate was also observed. A 34% reduction in mode switch episodes and a shortening of the average atrial arrhythmia duration by 48 % were also found by the PROVE study [10]. The Italian AT500 Registry, while documenting a significant decrease in supraventricular extrasystoles, showed only a trend towards a reduction of atrial tachyarrhythmias [11].

#### **Discontinuous Triggered Pacing**

These pacing algorithms are activated by supraventricular extrasystoles and are supposed to prevent further

premature atrial depolarization and avoid post-extrasystolic pauses by discontinuous overdrive pacing, thus causing the rate to stabilize. It also attempts to prevent early recurrences of atrial fibrillation following a mode switch episode by temporary, faster atrial pacing. A sudden and abnormally fast rate drop after a load situation triggers another algorithm. Since these algorithms have only been available for a short time, no data from large clinical trials have yet been published. The results of the multicenter AFT study are to be presented at the European Cardiology Congress in Stockholm in September 2001 (personal note by Prof. Camm; June 2001, Europace; Copenhagen, Denmark).

#### **Biatrial/Multisite Pacing**

These pacing techniques aim at resynchronizing the atria by:

- Dual right-atrial pacing;
- Biatrial pacing;
- Septal pacing;
- Bachmann bundle pacing.

Dual right-atrial pacing for the prevention of therapy-refractory paroxysmal atrial fibrillation has been studied by Saksena [12]. This method paces the right atrium with two electrodes. One lead is anchored in the high right atrium, and the other at the entry to the coronary sinus. The results of the DAPPAF study document a clear reduction of tachyarrhythmias during dual-atrial overdrive pacing compared to pacing solely in the high right atrium and conventional AAI pacing [13]. The SYNBIAPACE study attempted to pace both atria simultaneously by implanting one lead in the right atrium and placing a second one in the coronary sinus, thus achieving a resynchronization. Patients with therapy-refractory paroxysmal atrial fibrillation and a clearly prolonged P-wave duration – 184 ms on average – as an expression of a higher-degree, interatrial conduction delay were included in the study. The time until a recurrence of atrial fibrillation was slightly, but not statistically significant, extended when using biatrial pacing with a basic rate of 70 beats/min, compared to right-atrial pacing with 70 beats/min and a mostly inhibited mode (DDI 40 beats/min) [14]. Resynchronization of the atria can also be achieved by pacing at the interatrial septum in the vicinity of the entry to the

coronary sinus. Padeletti and his colleagues compared the preventive effect of septal pacing (IAS) with pacing in the high right atrium (HRA) in patients with paroxysmal atrial fibrillation. Prior to pacemaker implantation, an average of six episodes per month had occurred in the HRA group, and an average of 5.4 episodes in the group with IAS pacing. While the incidence of atrial fibrillation episodes also clearly decreased to 2.0 episodes per month during HRA pacing, this decrease was even more pronounced in the group with IAS pacing with only 0.2 atrial fibrillation paroxysms [15]. Equally remarkable are the results of a study published by Padeletti et al. on the preventive effect of septal pacing in patients with chronic atrial fibrillation and a primarily successful electrocardioversion, which enabled sinus rhythm for 2 – 24 hours. During a mean follow-up period of  $17 \pm 5$  months, 11 (65 %) of 17 patients remained in sinus rhythm – six with paroxysmal atrial fibrillation attacks and five without a symptomatic fibrillation episode. Recurring chronic atrial fibrillation was observed in the remaining six patients [16]. In a prospective, randomized, multicenter study, Bailin et al. studied the effect of pacing at the high interatrial septum – at the Bachmann bundle – in patients with paroxysmal atrial fibrillation in comparison to pacing at the right atrial appendage. A significant decrease in P-wave duration could be documented during pacing at the Bachmann bundle, as well as a statistically significant decrease (75 % vs. 52 %;  $p$ -value < 0.003) in the progression to chronic atrial fibrillation [17].

### Discussion and Conclusion

A wealth of data supports the use of atrial pacing for reducing atrial fibrillation attacks in patients with sick sinus syndrome and vagally induced atrial fibrillation. While sufficient facts about the efficacy in other forms of atrial fibrillation are not yet available, the results of smaller studies and the preliminary results of ongoing studies are nevertheless quite promising. Special algorithms for atrial overdrive pacing and for suppressing supraventricular extrasystoles and pauses increase the efficacy of this therapy. Resynchronizing the atria by septal, dual right-atrial, and biatrial pacing causes a further reduction of atrial arrhythmias. In combination with various antiarrhythmic drugs, these modern pacing methods constitute a promising alternative for patients with therapy-refractory paroxysmal atrial fibrillation.

### References

- [1] Murgatroyd FD. Modes of onset of spontaneous episodes of atrial fibrillation: Implications for the prevention of atrial fibrillation by pacing. In: Daubert JC, Prystowsky E, Ripart A (editors). *Prevention of Tachyarrhythmias with Cardiac Pacing*. Armonk, NY: Futura Publishing Company; 1997.
- [2] Hoffmann E. Analysis of onset scenarios prior to atrial fibrillation (abstract). *PACE*. 2000; 23: 415.
- [3] Rosenquist M, Brandt J, Schüller H. Long-term pacing in sinus node disease: A treatment comparison study. *Am Heart J*. 1986; 111: 292-297.
- [4] Rosenquist M, Brandt J, Schüller H. Long-term pacing in sinus node disease: Effects of stimulation mode on cardiovascular morbidity and mortality. *Am Heart J*. 1988; 116: 16-22.
- [5] Sasaki Y, Shimotori M, Akahane K, et al. Long-term follow-up of patients with sick sinus syndrome: A comparison of clinical aspects among unpaced, ventricular inhibited paced and physiologically paced groups. *PACE*. 1988; 11: 1575-1583.
- [6] Andersen HR, Nielsen JC, Bloch-Thomsen PE, et al. Long-term follow-up of patients from a randomized trial of atrial versus ventricular pacing for sick sinus syndrome. *Lancet*. 1997; 350: 1210-1216.
- [7] Coumel P, Friocourt P, Mugica J, et al. Long-term prevention of vagal atrial arrhythmias by atrial pacing at 90/min: Experiences with 6 cases. *PACE*. 1983; 6: 552-560.
- [8] Wiberg S, Lönnerhalm S, Jensen S, et al. Overdrive atrial pacing in symptomatic paroxysmal atrial fibrillation (abstract). *Europace*. 2001; 35 (Suppl B): 592.
- [9] Beinhauer A, Vock, P, Nobis H, et al. DAO algorithm reduced AF-burden by 39% in Patients in ADOPT-ALL trial (abstract). *Europace*. 2001; 34 (Suppl. B): 635.
- [10] Funck RC, Adamec R, Lurje L, et al. Atrial overdriving is beneficial in patients with atrial arrhythmias: First results of the PROVE study. *PACE (Part II)*. 2000; 23: 1891-1893.
- [11] Pieragnoli P, Santini M, Ricci R, et al. Pacing prevention of atrial tachyarrhythmias: Preliminary results from the Italian AT 500 registry (abstract). *Europace*. 2001; 35 (Suppl B): 824.
- [12] Saksena S, Prakash A, Hill M, et al. Prevention of recurrent atrial fibrillation with chronic dual-site right atrial pacing. *J Am Coll Cardiol*. 1996; 28: 687-694.
- [13] Saksena S, Prakash A, Fitts S, et al. Dual site atrial pacing of atrial fibrillation (DAPPAF) trial: substudy on device-based detection of recurrent atrial fibrillation (abstract). *PACE (Part II)*. 2001; 24: 595.
- [14] Mabo P, Daubert JC, Bouhour A. Biatrial synchronous pacing for atrial arrhythmia prevention: the Synbiapace Study (abstract). *PACE (Part II)*. 1999; 22: 221.
- [15] Padeletti L, Porciani C, Santini M, et al. Comparison of interatrial septum pacing with right atrial appendage pacing for prevention of paroxysmal fibrillation (abstract). *PACE (Part II)*. 2000; 23: 118.

- 
- [16] Padeletti L, Porciani MC, Michelucci A, et al. Prevention of short term reversible chronic atrial fibrillation by permanent pacing at the triangle of Koch. *J Interv Card Electrophysiol.* 2000; 4: 575-583.
- [17] Bailin SJ, Gudici M, Solinger B, et al. Pacing from Bachmann's bundle prevents chronic atrial fibrillation: Final results from a prospective randomized trial (abstract). *PACE (Part II).* 2001; 24: 595.

**Contact**

Dr. Walter Kainz  
2. Med. Abteilung/Kardiologie  
Hanusch-Krankenhaus  
Heinrich Collinstrasse 30  
A-1140 Wien  
Austria  
Telephone: +43 1 91021 2339  
Fax: +43 1 91021 2656  
E-mail: walter.kainz@wgkk.sozvers.at