

# The effect of anti-tachycardia atrial pacing in patients with recurrent paroxysmal atrial fibrillation

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## Abstract

**Background:** *Atrial fibrillation (AF) is an arrhythmia with complex pathophysiological characteristics. The efficiency of various anti-tachyarrhythmic stimulation algorithms in patients with recurrent AF has become a subject of research and the aim of this analysis is to evaluate the success of treatment by continuous DDD(R) stimulation with an anti-tachyarrhythmic pacing algorithm in patients with paroxysmal AF.*

**Methods:** *In the period 2002–2004 19 patients (10 females and 9 males), aged 45–74 (with a mean age of  $64.2 \pm 7.6$ ), qualified for DDD(R) system implantation. The indication for implantation was tachy-brady syndrome with recurrent AF resistant to pharmacological treatment. All the patients had had at least three recurrences of symptomatic AF within the previous year. The follow-up period was 12 months. AF recurrences, outpatient visits and hospitalisation frequency were evaluated every 6 months and there were routine pacemaker controls. Baseline and final visit echocardiograms and a quality of life (QoL) questionnaire (SF-36) were obtained.*

**Results:** *One patient was excluded from the analysis owing to permanent AF with a final VVI pacing mode. In comparison with the pre-inclusion 12 months AF-related hospitalisation frequency within the 12-month follow-up period was 3.9 vs. 0.4 ( $p < 0.005$ ) and outpatient visits 2.1 vs. 0.8 ( $p < 0.05$ ). The mean atrial pacing percentage in all patients was  $95.7\% \pm 2.9\%$ , and the mode switch percentage during the first and second 6 month periods was 6.4% (1–50%, median 2) and 2.5% (0–7, median 2, NS) respectively. There were 483/month (0.44–5761, median 31) events defined as AF episodes during first 6 months and 84/month (0–480, median 17, NS) during the second 6 months. The AF burden was 1.92 days/month (7 h – 15 days, median 14 h), decreasing to 0.74 day/month (0–2.1 days, median 14 h, NS) in the second 6-month period. A significant 12-month improvement was achieved in QoL parameters.*

**Conclusions:** *An overdrive atrial algorithm can be a beneficial, safe and comfortable method in patients with paroxysmal drug-resistant AF and accepted indications for physiological pacing. (Folia Cardiol. 2006; 13: 590–595)*

**Key words:** paroxysmal atrial fibrillation, tachy-brady syndrome, overdrive, antitachyarrhythmic pacing

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## Introduction

Atrial fibrillation (AF) is the most common tachyarrhythmia observed in humans [1, 2] and morbidity increases in the elderly. AF is a recurrent supraventricular tachyarrhythmia and is frequently resistant to numerous introduced drugs. Its occurrence is associated with haemodynamic compromise and an increased risk of embolic events and thus results in increased mortality, morbidity and healthcare costs. One of the most important disadvantages of AF is a worsening of quality of life (QoL). Two main strategies of treatment, namely rhythm control and rate control, may be maintained and their effectiveness remains the subject of numerous trials. Both may provoke pharmacotherapeutical side effects which result in restrictions on drug use. As AF is a disease of complex origin, many alternative and hybrid modes of treatment have been considered [3–6] and permanent cardiac pacing with anti-tachycardiac atrial pacing algorithms is one of these, especially when AF is an element of tachy-brady syndrome.

The aim of the present analysis was evaluation of the permanent cardiac DDD(R) pacing mode with an algorithm of anti-tachycardiac atrial pacing in patients with tachy-brady syndrome and recurrent drug-resistant atrial fibrillation.

## Methods

In the period 2002–2004 DDD(R) pacemakers were implanted in 19 patients (10 females and 9 males), aged 45–74 (with a mean age of  $64.2 \pm 7.6$ ). The study population characteristics are presented in Table 1.

The indication for permanent pacing in all patients was tachy-brady syndrome with recurrent AF resistant to pharmacotherapy. The occurrence of at least three incidents of AF within the preceding year constituted a further criterion for inclusion in the study. The informed consent of all the patients was obtained.

The exclusion criteria were unstable angina, myocardial infarction within 3 months of the qualifying visit, heart failure assigned to NYHA classes III and IV, post-surgical right atrium abnormalities, artificial tricuspid heart valve, Wolff-Parkinson-White syndrome or AF with a reversible cause.

The study was designed as a prospective observation with a one year follow-up period. Every 6 months the following were evaluated:

- the frequency of recurrence of AF and the AF burden stored in the pacemaker Holter memory;

**Table 1.** The basic demographic, clinical and medication characteristics of the study population.

Age (years)	64.2 ± 7.6
Female/male	10/9
<b>Concomitant diseases</b>	
Arterial hypertension	14
Coronary artery disease	6
Diabetes	2
<b>Medication</b>	
Beta-blocker	16
Sotalol	1
Propafenone	8
Amiodarone	3
Calcium blockers	4
Digoxin	2
ACE-inhibitor	16
Diuretics	6

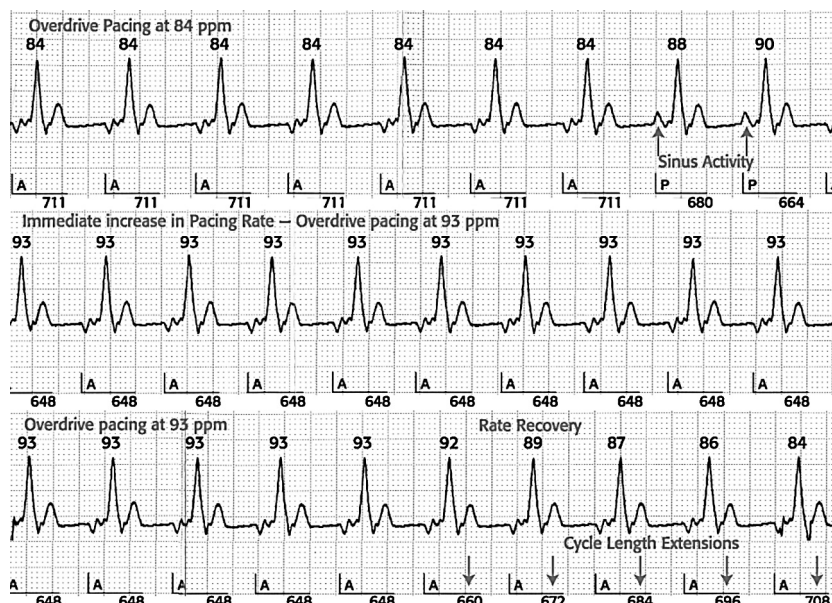
- the number of hospitalisations and outpatient visits following AF incidents;
- concomitant pharmacotherapy.

Each patient was asked to complete a quality of life (QoL) questionnaire (SF-36) at baseline and on the final visit. On the same visits M-mode and two-dimensional echocardiograms were taken. The protocol of the study was accepted by the local Bioethics Committee.

## Implantation procedure and special functions of the pacemaker

The pacemaker implantation procedure was always performed while the patients remained in sinus rhythm. If AF was diagnosed at admission, cardioversion was undertaken. All patients were given an Integrity AFxDR St. Jude Medical device, which was equipped with an AF suppression algorithm, enabling permanent right atrium overdrive. Atrial fibrillation suppression (AFS) is one of the anti-tachyarrhythmic features available among pacing products. Its operation is based on permanent spontaneous sinus activity detection. As soon as two consecutive atrial beats are sensed, a smooth overdrive is provided for the next 16 A-A intervals. Unless further atrial activity occurs, the atrial rate is then decreased to the basic programmed rate. Any atrial beats activate the atrial overdrive once more (Fig. 1).

The auto mode switch (AMS) causes automatic conversion from DDD(R) to DDI(R) mode if any atrial tachycardia occurs at a rate above that programmed. The atrial fibrillation suppression function is deactivated during this time. When a leading rhythm is



**Figure 1.** Atrial fibrillation suppression algorithm. At the DDD mode (initially A-R), overdrive at 84 ppm. Two P-P beats are detected (cycles 680 ms and 664 ms). Pacing rate is immediately accelerated to 93 ppm (A-A 648 ms) and sustained by 16 consecutive beats. Unless atrial activity is detected meanwhile, the pacing rate decreases to the basic programmed value.

found outside the AMS window, the pacing mode is restored to DDD(R). The pacemaker Holter memory provides data on mean heart rate, AMS frequency and the cumulative percentage of paced A-events which may correspond to AF occurrence.

**Statistics analysis**

Statistical analysis was made by SAS 8.0e. Wilcoxon score tests were used to compare continuous variables, the distribution of which was not Gaussian in the sample. Student’s t-test was used for the comparison of two population means with normal distribution.

Owing to differences in results, minimal and maximal values were given and medians calculated.

**Results**

In one patient AF was diagnosed as permanent after 1 month and the pacemaker was turned to VVIR mode. In the remaining patients dual-chamber pacing was sustained throughout the study period.

In the 12-month follow-up the frequency of AF hospitalisation decreased from 3.9 to 0.4 ( $p < 0.005$ ) and outpatient visits due to AF decreased from 2.1 to 0.8 ( $p < 0.05$ ) in comparison with the same period before implantation. In the pacemakers’ Holter memory the A-pacing rate was  $95.7 \pm 2.9\%$ , which demonstrated an acceptable overdrive func-

tion. The mean AMS activity rate was 6.4% (1–50%, median 2) during the first 6 months of observation, decreasing to 2.5% (0–7, median 2, NS) in the next 6 months. Events recorded as tachycardia decreased between the two halves of the follow-up period from a mean of 483 events/month (0.44–5761, median 31) to 84 events/month (0–480, median 17, NS). The AF burden was 1.92 days/month (7 h – 15 days, median 14 h), decreasing to 0.74 day/month (0–2.1 days, median 14 h, NS) in the second 6-month period.

Echocardiographic baseline and 12-month visit parameters did not differ. These were, respectively, left ventricle ejection fraction (EF) 42% (20–65, median 45, NS) and 43% (22–60, median 43, NS) and left atrium diameter 3.72 cm (2.5–5.4, median 3.5, NS) and 3.93 cm (3.0–5.7, median 3.9, NS).

The SF-36 questionnaire demonstrated a remarkable improvement in QoL in the population studied. These results were achieved in a global scale and, with the exception of the physical functioning and bodily pain criteria, were comparable in selected subgroups (Table 2).

During follow-up anti-arrhythmic drugs were modified in 8 patients: in 3 patients propafenone, calcium blocker and amiodarone were withdrawn, in 3 patients amiodarone (1) and digoxin (2) were added and in 2 patients propafenone and calcium blocker were replaced by amiodarone.

**Table 2.** Quality of life assessments.

SF-36	Parameter	Baseline	After 12 months	p (Student's t-test)	p (npar-test)
Scale 1	Physical functioning	12.2 ± 10.6 0–40, median 12.5	8.1 ± 10.9 0–40, median 5.0	0.0724 (NS)	0.0986
Scale 2	Role limitations due to physical problems	15.0 ± 7.3 (1.8) median 20	9.7 ± 8.1 (2.0) median 7.5	0.0097	0.0137
Scale 3	Social functioning	3.9 ± 2.3 (0.6) median 4	2.4 ± 2.1 (0.5) median 2.5	0.0256	0.0273
Scale 4	Bodily pain	3.5 ± 2.6 (0.7) median 3.5	3.3 ± 2.3 (0.6) median 3.5	NS	NS
Scale 5	General mental health	12.2 ± 4.7 (1.2) median 13	8.1 ± 3.3 (0.8) median 8	0.0024	0.0024
Scale 6	Role limitations due to emotional problems	7.5 ± 5.5 0–20, median 10	3.6 ± 5.5 (1.4) 0–20, median 0	0.0028	0.0078
Scale 7	Vitality	12.1 ± 3.8 (1.0) median 12	8.3 ± 2.4 (0.6) median 8.5	0.0011	0.0012
Scale 8	General health perception	12.7 ± 4.2 (1.0) median 11.5	9.9 ± 4.0 (1.0) median 10.5	0.0222	0.0294
Total		79.1 ± 29.7 (7.4) median 90.5	53.5 ± 25.6 (6.4) median 55	0.0005	0.0003

## Discussion

The initial suggestion that cardiac pacing may influence atrial tachyarrhythmias came from retrospective observations of patients treated with pacemakers as a result of sick sinus syndrome. Subjects implanted with physiological AAI or DDD systems had fewer AF incidents than those with VVI pacemakers [7–9]. This resulted in specially designed trials to determine whether physiological pacing demonstrates superiority over ventricular pacing alone in reducing AF paroxysms [10–12]. In the Canadian Trial of Physiologic Pacing [13], the Pacemaker Selection in the Elderly Trial [14] and the Mode Selection Trial [15] it was demonstrated that DDD pacing decreased incidents of arrhythmia and its conversion to permanent AF form. Physiological cardiac pacing may have a bidirectional haemodynamic and electrical effect. Sequential atrioventricular pacing decreased mean pressure in the atrial, reducing the strain and reverse remodelling. Electrical physiological activity could 1) eliminate or reduce brady-cardia-induced AF, 2) make activity homogenous to prevent atrial re-entry or 3) make refraction homogenous. In addition, the atrial overdrive mechanism can provide premature arrhythmogenic atrial beat suppression.

Our results may support the thesis that permanent atrial overdrive prevents AF incidents. As in the CAP [16] and PROVE [17] trials, the atrial

pacing percentage was high, reaching a mean value of 96%. This was followed by a decrease in AMS activity from 6.4% in the first 6 months after pacemaker implantation to 2.5% in the next 6 months. The AF burden was reduced from 1.92 days/month to 0.74 days/month respectively. The ADOPT trial [18] demonstrated that the AFS algorithm reduced the AF burden by 25% compared to controls. The AF burden in the AFS group was 3.19%, 1.93% and 1.37% after 1, 3, and 6 months respectively (by 60% compared to the first month of observation). In the ADOPT trial the first evaluation of the AFS mode was made after 1 month and the next after 3 months, when AF frequency reduction was greatest, exceeding our observations (from 3.19% to 1.93%, by 40%). The next visit took place 3 months later (in the 6<sup>th</sup> month) and the reduction was not so remarkable (from 1.93% to 1.37%, by 29%) and corresponded to our results.

AF incident reduction also resulted in a decrease in hospitalisations and outpatient visits. In our group reductions were achieved in hospitalisation and outpatient intervention of 90% and 62% respectively at one-year follow-up. The decrease in medical care interventions was probably related not only to the reduction in the absolute AF burden but also to amelioration of the characteristics of the AF incidents, which were shorter, well tolerated and often self-terminating. A common observation was that an arrhythmia stored in the device's Holter memory had not been perceptible.

It must be mentioned that AMS is not AF-specific and may be triggered by other supraventricular arrhythmias, frequent extra atrial beats or by atrial oversensing (R potential far-fields). Some of the AMS episodes might thus be an effect of other events. The absence of IEGM in the implanted pacemakers prevented verification and exclusion of falsely diagnosed AF events.

QoL, which qualifies only as a secondary endpoint in many studies, is a very important effect of treatment for the majority of patients. In AF patients the symptom spectrum is usually very broad and unspecific. A QoL questionnaire was a very helpful tool in assessing the results of therapy. In the group presented here QoL as assessed by SF-36 was improved in a way similar to the improvement demonstrated by the INOVA study [19]. All subscales improved except those describing physical functioning and bodily pain. In the INOVA study no statistical difference was achieved in a sub-scale concerning perception of general health.

The improvement in QoL was probably achieved as a result of a reduction in AF events, outpatient visits and hospitalisations, although the greater stabilisation of ventricular rhythm by DDI pacing might also have resulted in greater tolerance of arrhythmia.

### Study limitations

The patients were not randomised and the study population was relatively small.

Pharmacotherapy was at the discretion of the treating practitioners and in some patients treatment was modified. Because of the number of patients involved no conclusion can be drawn concerning the influence of drugs on the results.

The AMS is not AF-specific and the AFS algorithm function is not renowned for its optimal antiarrhythmic effect [20, 21].

We did not specify a site for right atrium pacing and the sites chosen may have varied according to the preference of the operating cardiologist. Because pacing site may *per se* be of importance this cannot be analysed in our study [22–24].

### Conclusions

1. Atrial overdrive pacing by preventing one of the atrial pro-arrhythmic mechanisms reduces the number of AF events, the AF burden, the number of hospitalisations and outpatient visits and improves the quality of life.
2. Atrial overdrive pacing is a safe and well tolerated feature.

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