



## Pacing for atrial fibrillation

Chu-Pak Lau

*Heart* 2003;89:106-112  
doi:10.1136/heart.89.1.106

---

Updated information and services can be found at:  
<http://heart.bmj.com/cgi/content/full/89/1/106>

---

*These include:*

**Data supplement**

"Web-only References"  
<http://heart.bmj.com/cgi/content/full/89/1/106/DC1>

**References**

This article cites 19 articles, 13 of which can be accessed free at:  
<http://heart.bmj.com/cgi/content/full/89/1/106#BIBL>

3 online articles that cite this article can be accessed at:  
<http://heart.bmj.com/cgi/content/full/89/1/106#otherarticles>

**Rapid responses**

You can respond to this article at:  
<http://heart.bmj.com/cgi/eletter-submit/89/1/106>

**Email alerting service**

Receive free email alerts when new articles cite this article - sign up in the box at the top right corner of the article

---

**Topic collections**

Articles on similar topics can be found in the following collections

[Heart Education](#) (252 articles)  
[Atrial fibrillation](#) (7 articles)  
[Arrhythmias](#) (700 articles)

---

**Notes**

---

To order reprints of this article go to:  
<http://www.bmjournals.com/cgi/reprintform>

To subscribe to *Heart* go to:  
<http://www.bmjournals.com/subscriptions/>

# PACING FOR ATRIAL FIBRILLATION

Chu-Pak Lau

106

*Heart* 2003;89:106–112

**E**pidemiological data from the Framingham heart study indicate that the cumulative incidence of atrial fibrillation (AF) over a 22 year follow up was 2.1% in men and 1.7% in women. The prevalence of AF increases with age, doubling with each successive decade, and 70% of people with AF are between 65–85 years old. AF is associated with a three- to fivefold increased risk of stroke, a threefold increased risk of congestive heart failure, and a significant 1.5- to 1.9-fold mortality risk even after adjusting for underlying cardiovascular conditions. Pacemaker follow up physicians often have to deal with AF as a co-morbidity. AF may also be associated with brady-tachy syndrome. A high incidence of AF will be present when we use pacemaker therapy after atrioventricular (AV) nodal ablation for medically refractory AF.

## ▶ PHARMACOTHERAPY FOR AF: HOW SUCCESSFUL ARE WE?

Conventional pharmacological treatments includes rate control with AV nodal blockers, maintenance of sinus rhythm, and anticoagulation. While rate control and anticoagulation is a recognised treatment strategy, proarrhythmia using class I antiarrhythmic agents to maintain sinus rhythm remains a concern. A recent study<sup>1</sup> has shown that low dose amiodarone, when compared to either sotalol or propafenone, is more efficacious in maintaining sinus rhythm. However, amiodarone had to be discontinued for cardiac and non-cardiac side effects in 18% of patients, while 35% of patients still developed AF at 16 months. While newer antiarrhythmic agents may enhance our success in these refractory cases, the current experience underscores the difficulties of long term pharmacological treatment to maintain sinus rhythm. Indeed, the preliminary results of the AFFIRM (atrial fibrillation following investigation of rhythm management) trial did not show the superiority of rhythm maintenance using drugs over rate control alone (late breaking news, American College of Cardiology annual meeting, 2002). Thus, the use of pacing, either alone or in a hybrid fashion with other treatments, has recently gained favour for treating AF.

## MECHANISMS OF PACING FOR PREVENTING AF

AF develops as a result of the interaction between the triggers (atrial premature beat (APB)), the substrate (atrial effective refractory period (AERP), and conduction velocity), and mediation by the autonomic nervous system. Several groups have examined the changes in sinus rhythm and APB prematurity in patients developing AF (table 1).<sup>2,3</sup> Most data in patients without sinus node disease (sick sinus syndrome (SSS)) suggest that the prevailing sinus rate before the onset of AF is normal or only slightly faster than normal. Thus a single rate support algorithm to prevent bradycardia is unlikely to be effective in suppressing AF in the majority of cases. There are three patterns of APB induced AF onset: APBs that initiate AF after a pause, and APBs that trigger AF with a closely coupled interval, or after a short-long-short cycle.<sup>3</sup> The majority of AF episodes are triggered by closely coupled APBs that have a coupling interval shorter than those APBs that do not induce AF (table 1). Apart from initiating AF, APBs arising from the pulmonary veins may also act as a perpetuator of AF. As AF episodes frequently recur within minutes of termination, high rate overdrive pacing after AF termination may be useful to suppress AF reinitiation.

Atrial electrical remodelling occurs when AF is sustained, leading to a shortening of AERP and slowing of conduction velocity that promotes AF (AF begets AF). Atrial remodelling is inhomogeneous, with more shortening of AERP in the left atrium than the lower right atrium (RA). There is also prolonged interatrial conduction time and suppressed sinus node function. Pacing, particularly delivered at multi-sites, may homogenise electrical conduction properties of the atrium and promote sinus rhythm. For example, distal coronary sinus (CS) pacing has been shown to suppress APBs from inducing AF by limiting their prematurity at the triangle of Koch, which is a region of local conduction delay and re-entry. Simultaneous RA and distal CS pacing reduced atrial conduction delay and increased electrogram width at this region and could prevent AF.<sup>4</sup> By overdrive atrial pacing after AF, pacing may avoid AERP dispersion mediated by abrupt cycle length changes, thereby allowing time for reverse atrial remodelling to occur before AF is reinitiated.

Correspondence to:  
Professor Chu-Pak Lau,  
Cardiology Division, University  
of Hong Kong, Queen Mary  
Hospital, Hong Kong;  
cplau@hkucc.hku.hk

**Table 1** Characteristics of atrial fibrillation (AF) onset<sup>2,3</sup>

References	Number of episodes (patients)	Preceding sinus rate (%)			APB coupling interval (ms)	
		Fast	Normal	Slow	AF	No AF
Killip (1965)	18 (14)		NA		0.48*	0.68*
Bernett (1970)	32 (8)		NA		300	371
Capucci (1992)	168 (20)	15	77	8	412	470
Murgatroyd (1993)	1126 (78)	8.5	82.8	8.7	–	–
Mehra (1996)	193 (80)	12	79	9	432	806
Tse (1999)	58 (53)	0	91	9	333	396

\*Ratio of atrial premature beat (APB) coupling interval to preceding sinus cycle length.

Very little is written on the role of the autonomic nervous system on AF mediation. A vagally mediated type of AF has been described, and overdrive pacing suppresses AF by counteracting the bradycardia.<sup>5</sup> A vagolytic effect of pacing the carotid sympathetic chain has been suggested to suppress certain types of AF or to control the ventricular rate in animals. The role of extracardiac stimulation to control AF in humans remains to be determined.

### HOW CAN PACING BE DELIVERED?

Pacing can be delivered either in a *passive* or an *active* manner at a variety of *sites* (table 2). “Passive pacing” is conventional pacing to prevent or alter the response to AF. For example, different types of pacing modes have been compared to minimise the development of AF. Pacing is used in patients who have a clear bradycardia induced AF. If AF develops in a dual chamber pacemaker (DDD), rapid ventricular response up to the programmed maximum rate can occur as atrial activities are tracked. This is handled in modern DDD pacemakers by an algorithm known as automatic mode switching. When AF is detected or diagnosed, the pacemaker changes automatically to a non-atrial tracking mode (for example, DDI or VVI), so that a rapid ventricular rate does not occur. A clinically proven strategy to treat medically refractory AF is the use of AV nodal ablation followed by permanent DDD(R) or VVI(R) pacing. Both treatments are effectively a type of AF rate control and

pacing does not act on the AF itself. Pacing is often used as an adjunct to drug treatment: antibradycardia pacing in the case of successful drug treatment causing sinus bradycardia, partial control with drugs and bradycardia that requires backup pacing so that larger doses of drugs can be used, and intermittent slow rate during AF from drugs used for rate control. An irregular ventricular rate in AF contributes to adverse symptoms and haemodynamics, and ventricular pacing delivered at a rate slightly faster than the average ventricular pacing rate in AF (known as ventricular regularisation pacing) can be used to achieve rate regularisation.

“Active pacing” involves either fixed or dynamic (based on the current sinus or a sensor mediated rate) overdrive of the normal sinus rhythm. Active pacing intervention using algorithms to counteract the mode of APB onset have been developed. These algorithms can be triggered by the onset of APBs, with treatment that aims at minimising the changes of atrial rate.

“Alternative atrial pacing sites” different from the conventional RA appendage or high lateral RA have been evaluated to modify the underlying substrate. Pacing has also been delivered from more than one site in the atrium. It is intuitive that some form of overdrive rate rather than the standard pacing rate will be necessary to maximise the “dose” of pacing to these sites, making them a form of active pacing therapy.

Pacing for AF prevention has been applied to the following patient populations: (1) pacing after AV nodal ablation; (2) vagally/bradycardia related AF; (3) patients with SSS; (4) patients with AF with or without sinus bradycardia; and (5) AF after cardiac surgery. Additionally, pacing methods have now been used to terminate AF precursors, and to control the ventricular rate irregularity once AF develops.

**Table 2** Types of pacing intervention for atrial fibrillation

- ▶ “Passive pacing”
  1. Pacing modes for AF prevention in sinus node disease
    - AAI (R) v VVI(R)
    - DDD(R) v VVI(R)
    - DDD(R) v AAI(R)
  2. Ventricular rate control
    - Automatic mode switching
    - AV node ablation and pacing
    - Support pacing for concomitant drug treatment
    - Ventricular rate stabilisation pacing
- ▶ “Active pacing”
  - Automatic atrial overdrive pacing
  - Post-ectopic atrial overdrive pacing
  - Post-AF atrial/overdrive pacing
  - AF termination
- ▶ “Alternative sites”
  - Bachmann’s bundle region pacing
  - Low interatrial septal pacing (outside coronary sinus os)
  - Biatrial endocardial pacing (right atrial and coronary sinus)
  - Biatrial epicardial pacing (right and left atrium)
  - Dual site atrial pacing (right atrial appendage and low interatrial septum)

### PACING AFTER AV NODAL ABLATION

One of the most effective ways to treat the fast and irregular rate of AF is to use catheter ablation to interrupt the normal AV conduction system, and leave the patient’s rhythm to be controlled by a pacemaker. Several studies have documented the use of this “ablate and pace” strategy in improving symptoms, heart failure, and well being of patients over conventional drug treatment.<sup>6</sup> In the North American registry that prospectively collected 156 patients followed up for one year, sustained improvement in quality of life was observed. Also, left ventricular ejection fraction was improved in those with a low ejection fraction (< 45%).

A disadvantage of this strategy is pacemaker dependency, with the need for replacement and associated morbidity. In addition, there is a high incidence of progression to permanent AF, likely to be caused by withdrawal of antiarrhythmic agents. For example, in one study,<sup>6</sup> AF developed in 24% of patients within six months after “ablate

## Abbreviations

**AERP:** atrial effective refractory period  
**AF:** atrial fibrillation  
**APB:** atrial premature beat  
**ATP:** antitachycardia pacing  
**AV:** atrioventricular  
**CS:** coronary sinus  
**ERAF:** early reinitiation of atrial fibrillation  
**ICD:** implantable cardioverter-defibrillator  
**PAF:** paroxysmal atrial fibrillation  
**RA:** right atrium  
**SSS:** sick sinus syndrome

108

and pace", but in none of the controls in the continued drug arm. A mortality rate of 15%, with 3% of patients dying suddenly, was reported. Recent evidence suggests that in the absence of previous myocardial infarction, congestive heart failure, and the use of cardiac medications after pacing, patients after ablate and pace had similar survival to age and sex matched populations when followed up for three years. These factors should be considered when prescribing this treatment for an individual patient.

A DDDR device is commonly prescribed after AV nodal ablation, together with automatic mode switching to avoid rapid ventricular tracking of AF. Arguably, because of poor long term sinus maintenance in this resistant group of patients, and in patients with persistent AF before ablation, a VVIR device may be an alternative.

### VAGALLY/BRADYCARDIA MEDIATED AF

In some patients, AF episodes typically occur after meals or exercise, or during sleep and after prolonged sinus pauses. The use of class Ic agents such as propafenone is the recommended treatment.  $\beta$  Blockers should be avoided as they may aggravate the associated bradycardia. An early study by Coumel and colleagues showed in 4/6 patients that atrial pacing prevented these AF episodes during 5.5 years of follow up, although almost all patients took disopyramide. This group<sup>5</sup> subsequently used DDD pacing in 10 patients with SSS in whom AF onset was related to bradycardia, and 7/10 patients also exhibited interatrial conduction delay that was reversed with higher rate atrial pacing. By overdrive pacing at a rate slightly above the mean diurnal rate, this group reported successful control of AF. These studies suggest that in a small group of patients in whom AF was clearly related to bradycardia, atrial based pacing could be effective in preventing AF episodes.

### SICK SINUS SYNDROME

AF occurs in a significant proportion of patients with SSS after pacing. Retrospective studies suggested the use of atrial pacing in these patients was associated with a lower incidence of AF compared to ventricular pacing (6.8% v 2.6% annually). In three prospective randomised studies, AF was also reduced by atrial pacing. In the Danish study,<sup>7</sup> 225 patients with SSS were randomised to either single chamber atrial (AAI) pacing or ventricular (VVI) pacing, with a follow up of eight years. The relative risk for AF (0.35 v 0.54), thromboembolic events, and heart failure were lower with AAI pacing. Similarly, in a Canadian study<sup>8</sup> involving 1474 patients randomised to VVI(R) pacing and 1094 to atrial based pacing, the annual rate of AF was reduced from 6.6% to 5.5% with physiological pacing, with a relative risk reduction of AF of 18% by three years.

The effect on AF was only apparent after two years. In the elderly population, DDD systems also improved quality of life and reduced the progression to chronic AF.<sup>9</sup> However, in all of these studies, conventional pacing is used and a control group is not possible as all of the involved patients required pacing therapy. It can be argued that atrial pacing does not actually suppress AF, rather it is ventricular pacing that is proarrhythmogenic.

Nevertheless, both retrospective and prospective data teach us that when prescribing pacemaker therapy for SSS, an atrial based pacing mode is preferred to ventricular pacing to minimise the incidence of AF. The impact of pacemaker prescription on AF incidence in patients with complete AV block is less certain, and is the subject of several ongoing studies (for example, UK PACE). As a high percentage of patients developed AF even with atrial pacing, some would advocate prophylactic use of additional strategies (hardware and software) to combat future AF episodes. These are described below.

### AF WITH OR WITHOUT ASSOCIATED BRADYCARDIA

There are several situations in which a pacemaker is used in patients with AF. Paroxysmal AF (PAF) is present in about half of patients with SSS and a third of patients with AV block at the time of pacing implantation. Antiarrhythmic medications can depress sinus node function that requires pacing backup, and this is now increasingly an indication for pacing in many centres. In refractory cases, some would argue for implanting a pacemaker first, and delay or avoid AV nodal ablation if AF can be controlled with a device. Finally, a device to treat AF in patients without bradycardia has been tested in several clinical studies. The above categories of patients represent the largest body of data on which pacing therapy has been tested, either alone or more often in combination with antiarrhythmic medications. Data are also emerging for AF as a co-morbidity in patients receiving implantable cardioverter-defibrillators (ICDs) or cardiac resynchronisation devices for heart failure.

#### Conventional pacing

In patients with medically refractory PAF pending AV nodal ablation, the PA<sup>3</sup> (atrial pacing periablation for paroxysmal AF) study randomised patients to either no pacing (DDI at 30 beats/min (bpm)) or to DDIR pacing at a lower rate of 70 bpm, with continuation of antiarrhythmic drugs.<sup>10</sup> Unexpectedly, pacing did not prolong the time to the first AF recurrence (1.9 days v 4.2 days with no pacing,  $p = \text{NS}$ ). In fact, pacing was associated with a trend for higher AF burden. Potential limitations in this study are the use of a pacing mode (DDIR) that did not guarantee AV synchrony, the lack of an overdrive algorithm to ensure a high percentage of atrial pacing (the atrium was paced in only 67% in this study), the use of atrial pacing at the conventional single site at the RA appendage, and the relatively short follow up (10 weeks).

The PA<sup>3</sup> study suggests that in patients with medically refractory AF who do not have bradycardia, conventional atrial pacing at 70 bpm in the short term is not effective in preventing AF.

#### Atrial overdrive

In patients with conventional pacing with a DDDR pacemaker, it is simple to just increase the backup rate to suppress AF. Ward and colleagues<sup>11</sup> randomised 18 patients with PAF and SSS to a backup rate of 60, 75, and 90 bpm, each for a two month period to test this hypothesis. While the percentage of atrial pacing increased by 44%, 57.5%, and 73.5%, respectively,

the incidence of AF (as defined by mode switching episodes) were not affected. On the other hand, one third of the patients developed angina when programmed to 90 bpm. It seems that the use of a high fixed lower rate to overdrive the atrium is not effective and is poorly tolerated.

If a fixed rate is ineffective, perhaps an algorithm to automatically overdrive the atrium may be more effective. In the Continuous Atrial Pacing algorithm (Medtronic Inc, Minneapolis, Minnesota, USA), for each P wave sensed the device shortens the atrial escape interval (for example, 30 ms) up to a programmable consistent overdrive rate limit to ensure atrial pacing. In 15 patients with such an algorithm, the percentage of atrial pacing is significantly increased from 57% to 86%, the incidence of APBs is reduced, and a trend to a lower incidence of mode switching and fewer AF symptoms was observed.<sup>12</sup> These benefits were not associated with a change in the mean atrial rate during the day or at night time.

The Dynamic Atrial Overdrive (DAO, St Jude, Minneapolis, USA) algorithm has been tested in a randomised study in 250 patients—the atrial dynamic overdrive pacing to treat paroxysmal AF study (ADOPT A study, late breaking news, North American Society of Pacing and Electrophysiology Society meeting, 2001). Preliminary results suggest that overdrive pacing was more effective than conventional pacing in reducing AF burden (60% *v* 45% suppression of baseline AF burden after six months of pacing) and improved symptoms of AF. The algorithm was well tolerated. Thus if there is evidence of AF in patients with pacemakers, it is reasonable to activate an automatic atrial overdrive mechanism if available that varies its rate according to the prevailing sinus rhythm rate. Further results are pending to see if the beneficial effect of atrial overdrive is algorithm specific.

#### Algorithms specific to APB/AF triggers

Experience with algorithms that overdrive the atrium when APBs occur suggests these are effective in reducing APB frequency, but not the overall AF episodes. After spontaneous or defibrillation-achieved AF termination, AF could occur in up to 34% of patients. Again, closely coupled ectopy is the cause of early reinitiation of AF (ERAF), which limits long term sinus rhythm maintenance. Tse and colleagues<sup>13</sup> tested, in a randomised manner, the use of atrial overdrive pacing post-defibrillation in suppressing APBs and ERAF in 12 patients with reproducible ERAF. Pacing at 400 ms and 300 ms were equally effective in preventing ERAF (42%), or delaying its onset (58%). APB density was reduced from 16.4/min to 3.4/min with pacing, and the mean coupling interval of these APB to sinus rhythm was significantly prolonged (from 398 ms to 420 ms) by pacing (fig 1). The design of the “post-mode-switch” overdrive (Medtronic Inc) is specifically based on this observation, although the optimal pacing rate and duration of pacing remain uncertain.

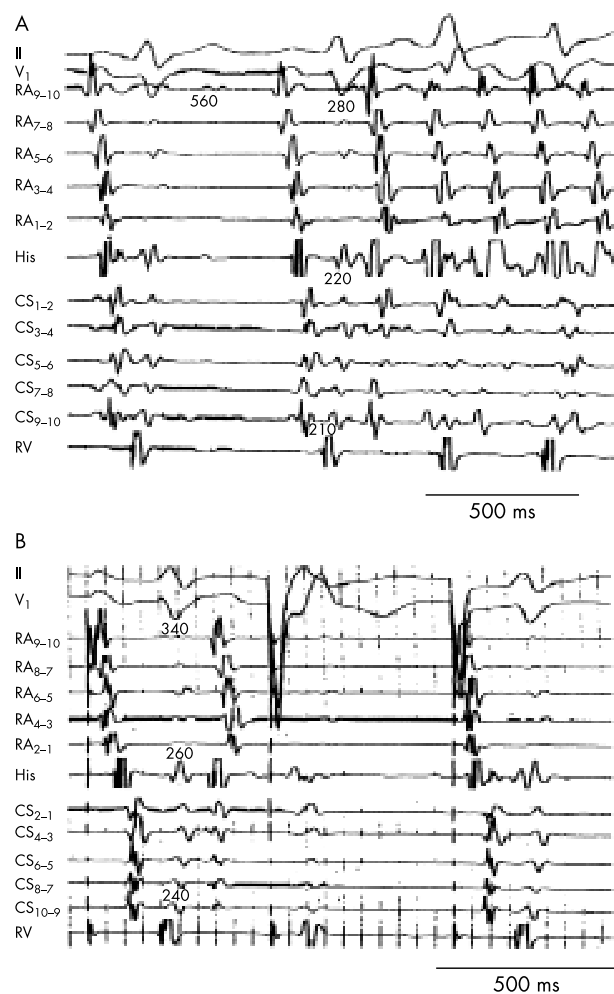
A variety of other algorithms such as rate smoothing post-APBs have been instrumented in different devices. There are as yet little data on their efficacy on top of automatic atrial overdrive pacing. In combination with antitachycardia pacing (ATP), these algorithms can contribute to reduction of AF burden (see below).

#### Alternative and multiple site atrial pacing

These include Bachmann’s bundle region/interatrial septal pacing, biatrial pacing (RA appendage and distal CS), and dual site atrial pacing (RA appendage and low atrial septum).

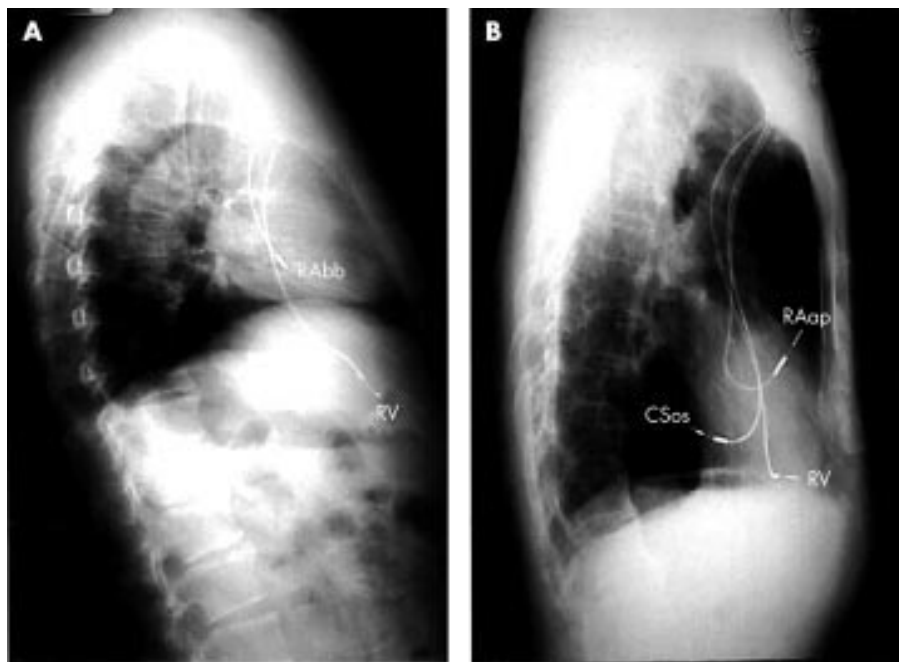
#### Bachmann’s bundle region or interatrial septal pacing

The existence of the Bachmann’s bundle is controversial. Nevertheless, acute testing suggests that pacing at the anterior



**Figure 1** Pacing in the suppression of early reinitiation of atrial fibrillation (AF). (A) AF occurred at baseline by an early atrial premature beat (APB) occurring in the left atrium (earliest recording at the distal CS: CS<sub>9-10</sub>). (B) Atrial pacing at 500 ms prevented AF from recurring. The coupling interval of the APB was also prolonged from 210 ms to 240 ms, which did not reinitiate AF. CS, coronary sinus; HIs, His bundle; RA, right atrium; RV, right ventricle. Reproduced from Tse *et al*<sup>13</sup> with permission.

superior interatrial septum leads to rapid conduction to either atrium, and may be a suitable site to suppress AF. Bailin and colleagues<sup>14</sup> randomised 120 patients with a mean age of 70 years to either RA appendage or Bachmann’s bundle region pacing. All patients had SSS and a history of paroxysmal AF, and half had a prior AV nodal ablation. The Bachmann’s bundle region was achieved by positioning an actively fixed lead in the highest point in the interatrial septum (using the fluoroscopic left anterior oblique view), with the lead pointing anteriorly in the right anterior oblique view (fig 2A). Compared to RA appendage pacing, pacing in the Bachmann’s bundle region significantly delayed the onset of permanent AF (75% *v* 47% at one year, *p* < 0.05). Interestingly, in most cases permanent AF developed within two months after pacing in the RA appendage group, and thereafter the onset of permanent AF was similar between the two groups. Both acute and long term atrial thresholds were similar between the two pacing sites. Bachmann’s bundle region pacing was also associated with a shortened P wave duration. These results are encouraging. However, there was a high incidence of AF in the RA appendage group, and withdrawal of antiarrhythmic drugs



**Figure 2** Lateral chest radiographs. (A) High interatrial septal pacing near the Bachmann's bundle region (RAbb). (B) Dual site atrial pacing with one atrial lead in the appendage (RAap) and the other outside the coronary sinus os (CSos). RV, right ventricular electrode.

might have influenced the outcome of this study. The proximity of the site to the aortic arch is a potential concern, although no complication related to the aorta was observed in this study. AF burden was not measured. Several studies are now underway to test the incremental benefit of automatic atrial overdrive in suppressing AF burden in the high septal region.

Padeletti and colleagues<sup>15</sup> reported the result of pacing at the low interatrial septum. This site was chosen as it is near the triangle of Koch (an area of slow conduction), and was approached by using a screw-in lead above the CS os. They studied 46 patients with paroxysmal AF, randomised to either RA appendage or low septal pacing. Either pacing mode reduced AF compared to pre-implantation frequency, but low interatrial septal pacing was superior to RA appendage pacing in reducing AF burden over a three month period. Again, P wave duration was significantly reduced compared to that in sinus rhythm.

Taken together, these studies suggest that pacing at the interatrial septum (high or low) shortens the P wave duration, and reduces the incidence of AF compared to the RA appendage site. At least in the short and medium term, the right interatrial septal site appears to be as stable and safe as the conventional appendage position. These sites may be an alternative pacing site for AF control in patients with SSS and AF if the issues of complexity in implantation and long term lead stability can be solved.

### Biatrial pacing

Daubert and his colleagues pioneered biatrial pacing by using a CS bipolar lead to achieve left atrial pacing simultaneously with conventional RA pacing. They tested the efficacy of biatrial pacing in patients with either prolonged P wave duration (> 120 ms) or interatrial conduction time ( $\geq$  100 ms). In a group of 86 patients with atrial tachyarrhythmias, they were able to reduce P wave duration (from mean (SD) 187 (29) ms to 160 (14) ms), and maintained sinus rhythm in 64% (with 33% free from any episode of AF).<sup>16</sup> However, in a multicentre European trial (the SYNBI-PACE (synchronous biatrial pacing for reduction of paroxysmal/permanent AF) study), such a

benefit in AF suppression was not reproduced. Thus this technique may be applicable to select patients with long interatrial conduction delay, and can also possibly contribute to better left heart AV interval programming and haemodynamic benefits. However, double sensing of A and V electrograms in the CS can be a problem, and special blanking is required. There is concern (as with biventricular pacing for heart failure) over the stability of the CS lead, and the ease with which lead extraction can be effected.

### Dual site atrial pacing

Delfaut and colleagues pioneered the use of RA appendage to RA low septal pacing (just outside the CS os) in suppressing AF<sup>17</sup> (fig 2B). Thirty patients with drug refractory symptomatic AF and documented primary or drug induced bradycardia underwent a crossover study to assess: (1) if pacing was useful to prevent AF compared to pre-implant history; (2) if single site (RA appendage or CS os pacing) were different; and (3) if dual site pacing had additional benefit to single site pacing. A fixed rate overdrive was used and event recorder documented first AF recurrence was used as the primary end point. The mean arrhythmia-free interval was increased from mean (SD) of 9 (10) days before implant, to 143 (110) days during single site periods, and to 195 (96) days during dual site crossover period. The authors did not find any difference between single site pacing at the RA appendage or CS os pacing in suppressing AF. Significantly, this study also documented long term safety of dual site pacing up to three years, with no case of CS os lead dislodgement after patient discharge from hospital, compared to a rate of dislodgement of up to 8% in dual site pacing. Although uncontrolled, the long term efficacy of maintaining sinus rhythm was 78% at one year and 56% at three years, which was remarkable in a very refractory group of patients. The limitations of this study were the lack of an unpaced controlled group, frequent crossover with potential carryover effect, and the need for antiarrhythmic medications to maintain sinus rhythm.

We have specifically addressed the use of dual site atrial pacing in patients with paroxysmal AF without conventional

indication for pacing, using pacemakers with the Continuous Atrial Overdrive algorithm.<sup>18</sup> Twenty two patients who had AF recurrence despite sotalol treatment underwent randomised crossover periods of 12 weeks with either pacing on (plus sotalol) or continuation of sotalol only. The end points were event recorder documented AF recurrence and pacemaker memory of AF burden. Dual site atrial pacing increased the percentage of atrial pacing (13 (18%) to 80 (30%)), reduced the number of APBs (from 8265/day to 2740/day), prolonged the time to the first documented AF (symptomatic or asymptomatic), and reduced AF burden (45 (34%) to 22 (29%)). Pacing reduced the risk of AF recurrence by 3.2 times. There was significant change in some measures of quality of life, but no overall change in AF symptoms. The DAPPAF (dual site atrial pacing for the prevention of AF) study prospectively randomised and crossed over patients between dual site and RA appendage pacing and support pacing in patients with PAF and pacing indications. The preliminary results suggested that dual site pacing with overdrive in combination with either class I or III antiarrhythmic agents was better tolerated and more effective in AF prevention than overdrive RA pacing or support pacing. Several other studies have also reported on the efficacy of dual site pacing.

Taken together, these trials indicate that pacing has an effect on the burden of AF in patients with or without the need of a pacemaker. Automatic atrial overdrive pacing is necessary for pacing to be effective, and multisite pacing may have an incremental benefit. However, the use of multiple leads (with their complexity of implantation and programming) should probably be reserved for those with AF of moderate severity. Use of a  $\beta$  blocker may provide an incremental benefit. Uncertainty remains as to the clinical predictors for a favourable response to dual site atrial pacing. Neither the P wave duration nor interatrial delay before pacing were predictive of an effective outcome.

### AF AFTER CARDIAC SURGERY

Approximately 20% of patients developed AF after bypass surgery. The causes are multifactorial, and may include the effects of cardiac bypass, changes in sympathetic tone, and postoperative infection. The development of AF is associated with an increase in stroke, heart failure, and length of hospital stay, which substantially increase management cost.  $\beta$  Blockers and amiodarone have been shown to be effective prophylactic agents for AF, but AF still developed in up to 30% of these patients despite amiodarone pre-treatment.

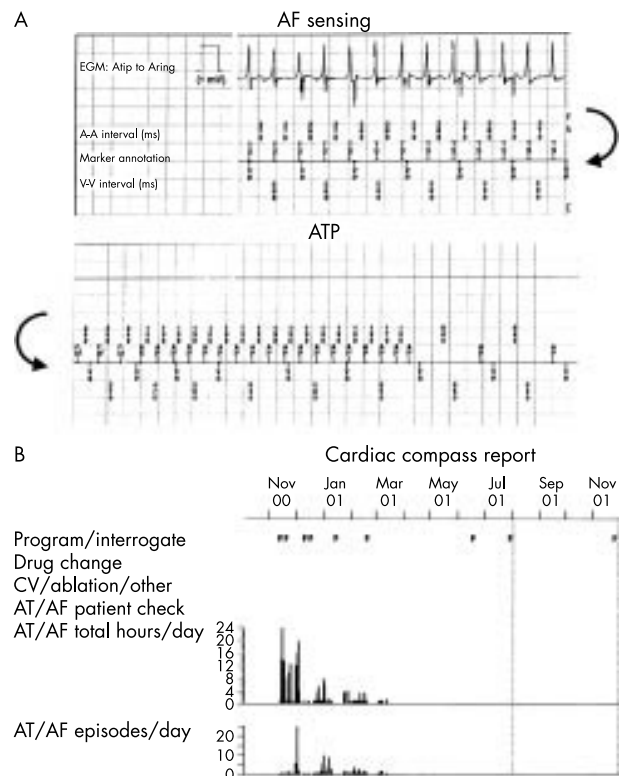
After cardiac surgery, epicardial pacing placement is often routine for support pacing, and it is of interest to assess if pacing may have effects on postoperative AF. Several studies have recently examined the effect of pacing (in addition to  $\beta$  blocker treatment) in suppressing postoperative AF. Fan and colleagues<sup>19</sup> randomised 132 patients to biatrial, RA, and left atrial pacing or control. Manual overdrive atrial pacing was performed for five days, at 10 bpm above the intrinsic rate up to 90 bpm. Only biatrial pacing reduced the development of sustained AF (42% in control *v* 12.5% during pacing), whereas single site pacing had no effect. The beneficial effect was attributable to a larger reduction of P wave dispersion during biatrial pacing compared with single site pacing or control, and only patients with AF prevention had a reduction in P wave duration. Postoperative intensive care stay and the associated cost were reduced. Several studies have since reported the efficacy of pacing, particularly biatrial pacing, in suppressing postoperative AF, with the left atrial lead in the posterior

atrium. The convenience and ease of instrumentation of biatrial pacing is a strong incentive to apply this technique to most patients after postoperative cardiac surgery.

### ANTITACHYCARDIA PACING

While the short excitable gap during sustained AF does not lend itself to pacing termination, ATP has several potential mechanisms to reduce AF burden. Many episodes of AF degenerate from atrial tachycardia or flutter, and early termination of these precursor rhythms may prevent AF from becoming established. Conversely, after antiarrhythmic agents (especially class Ic drugs), AF may be converted to flutter or a slower atrial tachycardia that can be terminated. It is logical to consider ATP in an implanted device to terminate these AF related rhythms.

Atrial ATP (burst, ramp, and 50 Hz stimulation) are now available in some ICDs and pacemakers. Several groups have reported on the efficacy of ATP, ranging from 33–86%, depending on the organisation of AF (fig 3A). Interestingly, “organised” rhythms were encountered in nearly half of all recorded episodes in patients with a clinical diagnosis of paroxysmal AF, suggesting that ATP may have a role in these patients. Twenty five per cent of patients with ICDs have associated AF. Friedman and colleagues<sup>20</sup> randomised 52/269 patients with a combined atrial and ventricular ICD to either ATP, atrial defibrillation, and preventive pacing versus only ventricular ICD function, each for a three month randomised period. Atrial therapies significantly reduced AF burden from



**Figure 3** (A) Pacemaker stored atrial electrogram (EGM) and marker annotation showing an episode of spontaneous “organised” atrial tachyarrhythmia which was sensed (Ts) (upper panel), and subsequently detected as fibrillation (Fb) and terminated by antitachycardia pacing (lower panel) (AT 500, Medtronic). A<sub>p</sub>, atrial pacing; V<sub>s</sub>, ventricular sensing. EGM not available during A<sub>p</sub>. (B) Telemetry recording of the AF history of the same patient indicating a decreasing trend of AF burden and AF episodes.

58.5 to 7.8 h/month. The efficacy of ATP for terminating slower and faster atrial tachyarrhythmias were 62% and 49%, respectively. While encouraging, these studies are limited by frequent patient exclusion and insufficient randomisation, and it is uncertain if burden reduction was related to pacing prevention or to ATP itself. Thus, in the absence of a well controlled randomised trial, it is uncertain whether ATP works or may be proarrhythmic.

### VENTRICULAR RATE STABILISATION

Apart from a rapid rate, irregularity in AF contributes to abnormal cardiac haemodynamics. By pacing the RV at a rate slightly faster than the mean ventricular rate of AF, it is possible to suppress shorter cycles and regularise the rate. This has been attributed to retrograde concealed activation in the AV node. Acute testing suggested that rate regularisation pacing can regularise AF at rest and to some extent during exercise. Ventricular rate stabilisation algorithms have been developed by several manufacturers. Clinical benefit in ambulatory patients remains to be confirmed, and the long term effect on left ventricular function because of pacing needs to be considered.

### FUTURE PERSPECTIVES

Pacing either in the treatment or prevention of AF should not be an isolated therapy. AF is a heterogeneous disease, and a hybrid approach is the standard. For example, concomitant antiarrhythmic medications are commonly used with pacing. Radiofrequency ablation can eliminate pulmonary vein ectopic foci for AF or modify the atrial substrate, and atrial defibrillation can further enhance the maintenance of sinus rhythm. The various types of hybrid therapy are under evaluation.

An important development in device therapy for AF is the ability to measure the total amount of AF (AF burden) that can be confirmed with stored atrial electrograms (fig 3B). This is a more accurate assessment of AF than the time to the first recurrence of AF itself. In addition, device based AF recording gives the clinician the possibility of objectively measuring the severity of AF, and may become a useful guide to assess interventional procedures, the need for anticoagulation, and to understand the symptomatology of AF itself.

### CONCLUSION

Ablation and pacing for medically refractory AF is clinically proven, and is an effective symptomatic therapy. In patients with SSS, an atrial based pacemaker should be prescribed to reduce future episodes of AF. An automatic atrial overdrive algorithm appears to be effective in reducing symptomatic AF. Dual site right atrial pacing, in the presence of overdrive and  $\beta$  blocker, confers additional benefit to single site pacing. Epicardial biatrial pacing is a useful technique to reduce the incidence of AF complicating cardiac surgery. While automatic mode switching and ventricular rate stabilisation will become programmable features of modern pacemakers, the role of ATP in patients with AF remains to be confirmed. It is likely that pacing efficacy will be enhanced when combined with strategies such as ablation, pharmacotherapy, and defibrillation.

### REFERENCES

- Roy D, Talajic M, Dorian P, *et al*. Amiodarone to prevent recurrence of atrial fibrillation. Canadian trial of atrial fibrillation investigators. *N Engl J Med* 2000;**342**:913–20.

- Mehra R, Hill MR. Prevention of atrial fibrillation/flutter by pacing techniques. In: Saksena S, Luderitz B, eds. *Interventional electrophysiology: a text book*. Armonk, New York: Futura Publishing, 1996:521–40.
- A good review article on the mechanism of AF onset and the background of multisite pacing.
- Tse HF, Lau CP, Ayers GM. Incidence and modes of onset of early reinitiation of atrial fibrillation after successful internal cardioversion, and its prevention by intravenous sotalol. *Heart* 1999;**82**:319–24.
- Yu WC, Chen SA, Tai CT, *et al*. Effects of different atrial pacing modes on atrial electrophysiology: implicating the mechanism of biatrial pacing in prevention of atrial fibrillation. *Circulation* 1997;**96**:2992–6.
- This describes the acute electrophysiology effect of biatrial pacing in the prevention of AF induction.
- Attuel P, Pellerin D, Mugica J, *et al*. DDD pacing: an effective treatment modality for recurrent atrial arrhythmias. *Pacing Clin Electrophysiol* 1988;**11**:1647–54.
- Brignole M, Menozzi C, Gianfranchi L, *et al*. Assessment of atrioventricular junction ablation and VVIR pacemaker versus pharmacological treatment in patients with heart failure and chronic atrial fibrillation: a randomized, controlled study. *Circulation* 1998;**98**:953–60.
- Andersen HR, Nielsen JC, Thomsen PE, *et al*. Long-term follow-up of patients from a randomised trial of atrial versus ventricular pacing for sick-sinus syndrome. *Lancet* 1997;**350**:1210–16.
- Stuart J, Connolly MD, Charles R, *et al*. Effects of physiologic pacing versus ventricular pacing on the risk of stroke and death due to cardiovascular causes. *N Engl J Med* 2000;**342**:1385–91.
- Lamas GA, Orav EJ, Stambler BS, *et al*. Quality of life and clinical outcomes in elderly patients treated with ventricular pacing as compared with dual-chamber pacing. Pacemaker selection in the elderly investigators. *N Engl J Med* 1998;**338**:1097–104.
- Gillis AM, Wyse DG, Connolly SJ, *et al*. Atrial pacing periblation for prevention of paroxysmal atrial fibrillation. *Circulation* 1999;**99**:2553–8.
- An important study which shows the lack of efficacy of conventional pacing alone in preventing drug refractory AF.
- Ward KJ, Willett JE, Bucknall C, *et al*. Atrial arrhythmia suppression by atrial overdrive pacing: pacemaker Holter assessment. *Europace* 2001;**3**:108–14.
- Lam CT, Lau CP, Leung SK, *et al*. Efficacy and tolerability of continuous overdrive atrial pacing in atrial fibrillation. *Europace* 2000;**2**:286–91.
- Tse HF, Lau CP, Ayers GM. Atrial pacing for suppression of early reinitiation of atrial fibrillation after successful internal cardioversion. *Eur Heart J* 2000;**21**:1167–76.
- This is the only randomised study to show that pacing can suppress early re-initiation of AF from atrial ectopic discharges.
- Bailin SJ, Adler S, Giudici M. Prevention of chronic atrial fibrillation by pacing in the region of Bachmann's bundle: results of a multicenter randomized trial. *J Cardiovasc Electrophysiol* 2001;**12**:912–17.
- A prospective study which demonstrates the efficacy of pacing the Bachmann's bundle region in preventing persistent AF.
- Padeletti L, Pieragnoli P, Ciapetti C, *et al*. Randomized crossover comparison of right atrial appendage pacing versus interatrial septum pacing for prevention of paroxysmal atrial fibrillation in patients with sinus bradycardia. *Am Heart J* 2001;**142**:1047–55.
- This randomised study investigated the use of low right atrial septal pacing in preventing AF.
- D'Allonnes GR, Pavin D, Leclercq C, *et al*. Long-term effects of biatrial synchronous pacing to prevent drug-refractory atrial tachyarrhythmia: a nine-year experience. *J Cardiovasc Electrophysiol* 2000;**11**:1081–91.
- One of several studies by this group which pioneered the use of biatrial pacing in preventing atrial tachyarrhythmias in patients with interatrial conduction delay.
- Delfaut P, Saksena S, Prakash A, *et al*. Long-term outcome of patients with drug-refractory atrial flutter and fibrillation after single- and dual-site right atrial pacing for arrhythmia prevention. *J Am Coll Cardiol* 1998;**32**:1900–8.
- The most important of several studies by this group which compared the relative efficacy of drug treatment, single site pacing, and dual site pacing on the development of AF.
- Lau CP, Tse HF, Yu CM, *et al*. Dual-site atrial pacing for atrial fibrillation in patients without bradycardia. *Am J Cardiol* 2001;**88**:371–5.
- A multicentre, randomised, controlled study that shows the efficacy of dual site pacing in preventing both symptomatic and asymptomatic AF over sotalol in patients without bradycardia.
- Fan K, Lee KL, Chiu CS, *et al*. Effects of biatrial pacing in prevention of postoperative atrial fibrillation after coronary artery bypass surgery. *Circulation* 2000;**102**:755–60.
- One of several studies recently published which demonstrates the role of multisite pacing in reducing the incidence of postoperative AF.
- Friedman PA, Dijkman B, Warman EN, *et al*. Atrial therapies reduce atrial arrhythmia burden in defibrillator patients. *Circulation* 2001;**104**:1023–8.



Additional references appear on the *Heart* website—[www.heartjnl.com](http://www.heartjnl.com)