

# Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION



**Role of Permanent Pacing to Prevent Atrial Fibrillation: Science Advisory From the American Heart Association Council on Clinical Cardiology (Subcommittee on Electrocardiography and Arrhythmias) and the Quality of Care and Outcomes Research Interdisciplinary Working Group, in Collaboration With the Heart Rhythm Society**

Bradley P. Knight, Bernard J. Gersh, Mark D. Carlson, Paul A. Friedman, Robert L. McNamara, S. Adam Strickberger, Hung Fat Tse, Albert L. Waldo and for the AHA Writing Group

*Circulation* 2005;111;240-243

DOI: 10.1161/01.CIR.0000151800.84945.47

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 72514

Copyright © 2005 American Heart Association. All rights reserved. Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://circ.ahajournals.org/cgi/content/full/111/2/240>

Subscriptions: Information about subscribing to *Circulation* is online at  
<http://circ.ahajournals.org/subscriptions/>

Permissions: Permissions & Rights Desk, Lippincott Williams & Wilkins, 351 West Camden Street, Baltimore, MD 21202-2436. Phone 410-5280-4050. Fax: 410-528-8550. Email:  
[journalpermissions@lww.com](mailto:journalpermissions@lww.com)

Reprints: Information about reprints can be found online at  
<http://www.lww.com/static/html/reprints.html>

## Role of Permanent Pacing to Prevent Atrial Fibrillation Science Advisory From the American Heart Association Council on Clinical Cardiology (Subcommittee on Electrocardiography and Arrhythmias) and the Quality of Care and Outcomes Research Interdisciplinary Working Group, in Collaboration With the Heart Rhythm Society

Bradley P. Knight, MD; Bernard J. Gersh, MD; Mark D. Carlson, MD; Paul A. Friedman, MD;  
Robert L. McNamara, MD; S. Adam Strickberger, MD; Hung Fat Tse, MD, MBBS;  
Albert L. Waldo, MD; for the AHA Writing Group

**Abstract**—This advisory summarizes the current database on pacing modalities and algorithms used to prevent and terminate atrial fibrillation (AF). On the basis of the evidence indicating that ventricular pacing is associated with a higher incidence of AF in patients with sinus node dysfunction, a patient who has a history of AF and needs a pacemaker for bradycardia should receive a physiological pacemaker (dual chamber or atrial) rather than a single-chamber ventricular pacemaker. For patients who need a dual-chamber pacemaker, efforts should be made to program the device to minimize the amount of ventricular pacing when atrioventricular conduction is intact. Many pacemakers and implantable defibrillators have features designed to prevent AF and to terminate AF with rapid atrial pacing. The evidence to support their use is limited, although these algorithms appear to be safe and usually add little additional cost. For patients who have a bradycardia indication for pacing and also have AF, no consistent data from large randomized trials support the use of alternative single-site atrial pacing, multisite right atrial pacing, biatrial pacing, overdrive pacing, or antitachycardia atrial pacing. Even fewer data support the use of atrial pacing in the management of AF in patients without symptomatic bradycardia. At present, permanent pacing to prevent AF is not indicated; however, additional studies are ongoing, which will help to clarify the role of permanent pacing for AF. (*Circulation*. 2005;111:240-243.)

**Key Words:** AHA Science Advisory ■ fibrillation ■ pacing ■ pacemakers ■ electrophysiology

Rhythm control continues to be an appropriate strategy for the treatment of patients with symptomatic atrial fibrillation (AF). Because antiarrhythmic drug therapy has many limitations, nonpharmacological therapies have been developed. Pacing techniques that have been proposed as treatments for AF include standard atrial pacing, alternative single-site atrial pacing, multisite atrial pacing, pacing algorithms to increase the amount of atrial pacing and to prevent atrial pauses, and antitachycardia atrial pacing to terminate AF (Table). Despite the commercial availability of many of these options, the role of permanent pacing to prevent AF is controversial. Therefore, the Council of Clinical Cardiology believed that it would be useful to develop an advisory that

summarizes the current database on pacing modalities and algorithms used to prevent and terminate AF.

### Mechanisms of AF

AF is probably the result of several mechanisms.<sup>1</sup> One theorized mechanism is that of the multiple reentrant wavelet,<sup>2,3</sup> in which AF results from a critical number of randomly circulating reentrant wavelets. The pathways of these wavelets are not anatomically determined but rather are determined by local atrial refractoriness and excitability. In this mechanism, wavelets can collide and annihilate, divide, or fluctuate in size and velocity. A critical number of wavelets

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

This statement was approved by the American Heart Association Science Advisory and Coordinating Committee on October 22, 2004. A single reprint is available by calling 800-242-8721 (US only) or writing the American Heart Association, Public Information, 7272 Greenville Ave, Dallas, TX 75231-4596. Ask for reprint No. 71-0310. To purchase additional reprints: up to 999 copies, call 800-611-6083 (US only) or fax 413-665-2671; 1000 or more copies, call 410-528-4121, fax 410-528-4264, or e-mail kgray@lww.com. To make photocopies for personal or educational use, call the Copyright Clearance Center, 978-750-8400.

Expert peer review of AHA Scientific Statements is conducted at the AHA National Center. For more on AHA statements and guidelines development, visit <http://www.americanheart.org/presenter.jhtml?identifier=3023366>.

© 2005 American Heart Association, Inc.

*Circulation* is available at <http://www.circulationaha.org>

DOI: 10.1161/01.CIR.0000151800.84945.47

**TABLE 1. Device-Based Approaches for the Prevention of AF**

|  |
|--|
| Standard atrial pacing   |
| Multisite atrial pacing  |
| Pacing algorithms to increase frequency of atrial pacing           |
| Pacing algorithms to maximize native ventricular conduction        |
| Novel atrial pacing sites (Bachmann bundle, coronary sinus ostium) |
| Combination of prevention/termination algorithms                   |
| Hybrid approaches (device with medications or ablation)            |

must be circulating to sustain the AF. A second mechanism is an atrial focus that generates a rhythm sufficiently rapid that some or much of the remainder of the atria cannot follow with 1:1 activation, resulting in fibrillatory conduction.<sup>1,4</sup> Theoretically, atrial pacing could prevent AF resulting from reentry or fibrillatory conduction by preventing the changes in refractoriness caused by pauses or bradycardia, reducing intra-atrial conduction times, reducing dispersion of atrial refractoriness, or reducing atrial ectopy.

With regard to a relationship between the mechanism of AF and the potential role of pacing to terminate AF, termination by rapid pacing would make sense if the AF mechanism was such that pacing could interrupt the rhythm, because pacing can interrupt reentrant and triggered rhythms. The key, of course, is that the paced impulses must be able to invade the tissue that generates the rhythm. In a canine model of AF resulting from an apparent, stable, reentrant circuit of short cycle length, pacing in that region uniformly interrupts that rhythm (the driver), so that with termination of the burst pacing, the AF also terminates.

### Effect of Pacing on AF in Patients With Bradycardia

Compared with ventricular pacing alone, atrial pacing is supported by both electrical and mechanical theory in preventing the onset of AF. Atrial pacing prevents potential triggers for AF such as bradycardic episodes and ectopic atrial beats, and atrial pacing avoids the atrial stretching caused by increased atrial pressure that is associated with atrioventricular (AV) dyssynchrony. Observational studies have suggested that the incidence of AF is between 0% and 3% per year in patients with dual-chamber pacemakers as compared with an incidence of 6% to 15% per year in patients with single-chamber ventricular pacemakers. These studies carry the numerous biases associated with nonrandomized and retrospective studies, however.

Five prospective randomized controlled trials comparing single- (atrial or ventricular) or dual-chamber pacing have evaluated the incidence of AF, usually as a secondary end point, in patients with a history of bradycardia.<sup>5-9</sup> The evidence from these trials suggests that atrial pacing is superior to ventricular pacing in the prevention of AF in patients with sinus node dysfunction and normal AV conduction. In this group of patients, atrial pacing alone may be superior to dual-chamber pacing, but the data are limited. In the subgroup of bradycardic patients with AV conduction disease, including patients undergoing AV node ablation, the evidence is conflicting.

### Multisite Pacing to Prevent AF

The association between atrial tachyarrhythmias and inter- and intra-atrial conduction delay has led investigators to consider pacing therapies that could decrease the total atrial activation time.<sup>10,11</sup> Two such options include biatrial pacing, which is accomplished by pacing simultaneously through leads placed at the high right atrium and at the coronary sinus ostium, and dual-site right atrial (RA) pacing.<sup>12</sup> Studies of these 2 pacing modes have been performed in patients with a bradycardia indication for pacing and a history of atrial tachyarrhythmias. Both pacing modes have been shown to decrease atrial activation time. The only multicenter randomized controlled trial of long-term biatrial pacing, however, failed to show benefit compared with single-site or no atrial pacing.<sup>13</sup> Several small studies have shown that dual-site RA pacing decreases the incidence of atrial tachyarrhythmias when compared with no pacing or single-site RA pacing; however, a multicenter randomized trial of dual-site atrial pacing versus high RA or support (DDI or VDI) pacing did not reveal a statistically significant benefit of dual-site atrial pacing.<sup>14</sup> The requirement for 2 atrial leads and a Y connector may limit the usefulness of both biatrial and dual-site RA pacing. Furthermore, whether these pacing modes are superior to atrial septal pacing is unknown.

### Alternative Site Pacing to Prevent AF

Pacing at RA sites at which preferential interatrial conduction exists will preexcite the left atrium to shorten the total atrial activation time and may reduce the susceptibility for AF. Bachmann's bundle, a band of muscular fibers that crosses the roof of the atrial septum, and the low interatrial septum near the triangle of Koch or coronary sinus ostium have been studied as alternative pacing sites for AF prevention. Studies of atrial pacing at high or low septal locations suggest that these sites are as feasible and as safe as conventional pacing from the RA appendage.<sup>15-18</sup> During an intermediate period of follow-up, RA septal pacing may prevent the progression of AF in patients with bradycardia and AF who have indications for conventional pacing. Furthermore, the additional use of atrial overdrive pacing algorithms appears to further enhance the beneficial effect of septal pacing.<sup>18</sup> As compared with multisite atrial pacing, these alternative pacing sites require less hardware. The relative efficacy of RA high versus low atrial septal pacing for AF prevention remains unknown; however, the use of high septal pacing is associated with a lower risk of ventricular far-field sensing. Despite these findings, it is important to note that no large multicenter clinical trial of alternative site pacing to prevent AF has been performed. Until these types of data are available, the use of alternative site pacing should be considered unproven and experimental.

### Pacing Algorithms to Prevent AF

The observation that atrial (AAI) or physiological (DDDR) pacing in patients with sinus node dysfunction retards the development of AF as compared with ventricular (VVI) pacing has created an interest in increasing the "dose" of atrial pacing. To accomplish this while avoiding the continuously elevated heart rate that is associated with increasing the pacing lower-rate limit, a number of algorithms have been developed. Although variable in design, algorithms in general aim to prevent brady-

cardia and to avoid large atrial cycle length variations. Specific algorithms have included rate-adaptive pacing that periodically assesses the underlying intrinsic rate to pace just above it, elevation of the pacing rate after spontaneous atrial ectopy, transient high-rate pacing after mode switch episodes, and increased postexercise pacing to prevent an abrupt drop in heart rate. These algorithms have been added to the armamentarium of device-based approaches for preventing AF and have been shown to increase the frequency of atrial pacing compared with conventional rate-responsive pacing.<sup>19</sup>

The studies of preventive algorithms have yielded mixed results, possibly because they have used different trial designs, therapies, patient populations, and end points.<sup>19–21</sup> Some trials have assessed multiple algorithms simultaneously, further clouding the role of the pacing algorithms themselves.<sup>21</sup> Another limitation of these trials has been the absence of information about the frequency of ventricular pacing. Right ventricular apical pacing introduces elevated filling pressures, valvular regurgitation, and changes in ventricular geometry that may adversely affect the atria. An analysis of the MOST (MOde Selection Trial) study demonstrated a linear increase in the risk of AF in association with cumulative percentage of ventricular pacing.<sup>22</sup> This suggests that the ventricular dyssynchrony introduced by ventricular pacing increases the risk of AF in sinus node dysfunction even when AV synchrony is preserved. Although algorithms to enhance intrinsic ventricular conduction have been developed, data about their efficacy are lacking. Therefore, in patients with a bradycardia indication for pacing, pacing algorithms play at most a modest adjunctive role in arrhythmia control. In the absence of such a bradycardia indication, device implantation is not warranted.

### Pacing Algorithms to Terminate AF

Although AF may be secondary to reentry in many patients, it has been difficult to show that atrial pacing can terminate AF that is induced in the electrophysiology laboratory; however, atrial pacing appears able to terminate spontaneous atrial tachyarrhythmias, especially when the rhythm is rela-

tively organized. Implantable pacemakers and defibrillators are available with antitachycardia atrial pacing therapies. It has been difficult to interpret studies of the effectiveness of antitachycardia atrial pacing for AF, in part because the therapy often is studied in combination with atrial pacing therapies designed to prevent AF. In large trials, atrial pacing therapies have been shown to reduce arrhythmia burden only when used in combination with shock therapy.<sup>23</sup>

### Summary

A patient who has a history of AF and needs a pacemaker for bradycardia should receive a physiological pacemaker (dual chamber or atrial) rather than a single-chamber ventricular pacemaker. This conclusion is based on evidence that ventricular pacing appears to be associated with a higher incidence of AF in patients with sinus node dysfunction. For patients who need a dual-chamber pacemaker, efforts should be made to program the device to minimize the amount of ventricular pacing when AV conduction is intact by extending the AV delay, programming the device to a nonatrial tracking mode such as DDIR, or implanting a device with an algorithm that minimizes ventricular pacing. Many pacemakers and implantable defibrillators have features designed to prevent AF and to terminate AF with rapid atrial pacing. The evidence supporting their use is limited, although these algorithms appear to be safe and usually add little additional cost.

For patients who have a bradycardia indication for pacing and also have AF, no consistent data from large randomized trials support the use of alternative single-site atrial pacing, multisite RA pacing, biatrial pacing, overdrive pacing, or antitachycardia atrial pacing. Even fewer data support the use of atrial pacing in the management of AF in patients without symptomatic bradycardia. At present, permanent pacing to prevent AF is not indicated. Additional studies are ongoing, which will help to clarify the role of permanent pacing for AF. Until data from these clinical trials are available, pacing to prevent AF in patients without a bradycardia indication for a pacemaker should be considered unproven.

### Disclosures

| Writing Group Member Name | Research Grant   | Speakers Bureau/Honoraria             | Stock Ownership | Consultant/Advisory Board                | Other |
|---------------------------|--|---------------------------------------|-----------------|--|-------|
| Dr Bradley P. Knight      | Guidant, Medtronic, St. Jude, Boston Scientific            | Guidant, Medtronic                    | None            | Guidant, Medtronic, CardioOptics         | None  |
| Dr Bernard J. Gersh       | None   | None                                  | None            | AstraZeneca, Cardiovascular Therapeutics | None  |
| Dr Mark D. Carlson        | None   | Reliant                               | None            | Guidant, St. Jude, Cameron Health        | None  |
| Dr Paul A. Friedman       | Guidant, Medtronic, St. Jude, CR Bard, Hewlett Packard     | Guidant, Medtronic, St. Jude, CR Bard | None            | None                                     | None  |
| Dr Robert L. McNamara     | None   | None                                  | None            | None                                     | None  |
| Dr S. Adam Strickberger   | Medtronic, Guidant, St. Jude                               | None                                  | None            | None                                     | None  |
| Dr Hung Fat Tse           | CryoCor, Guidant, Medtronic, Pfizer, AstraZeneca, Medwaves | None                                  | None            | St. Jude                                 | None  |
| Dr Albert L. Waldo        | None   | AstraZeneca, Reliant Pharma           | None            | CryoCor, AstraZeneca, Reliant Pharma     | None  |

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group were required to complete and submit.

## References

- Waldo AL. Mechanisms of atrial fibrillation. *J Cardiovasc Electrophysiol.* 2003;14:S267–S274.
- Moe GK, Rheinbolt WC, Abildskov JA. A computer model of atrial fibrillation. *Am Heart J.* 1964;67:200–220.
- Allessie MA, Lammers W, Smeets J, Bonke F, Hollen J. Total mapping of atrial excitation during acetylcholine-induced atrial flutter and fibrillation in the isolated canine heart. In: Kulbertus HE, Olsson SB, Schlepper M, eds. *Atrial Fibrillation: Proceedings of a Symposium Held in Kiruna, Sweden, June 24-27, 1981.* Molndal, Sweden: AB Hässle; 1982:44–59.
- Nattel S. Atrial electrophysiology and mechanisms of atrial fibrillation. *J Cardiovasc Pharmacol Ther.* 2003;8:S5–S11.
- Skanes AC, Krahn AD, Yee R, Klein GJ, Connolly SJ, Kerr CR, Gent M, Thorpe KE, Roberts RS; Canadian Trial of Physiologic Pacing. Progression to chronic atrial fibrillation after pacing: the Canadian Trial of Physiologic Pacing. CTOPP Investigators. *J Am Coll Cardiol.* 2001;38:167–172.
- Lamas GA, Orav EJ, Stambler BS, Ellenbogen KA, Sgarbossa EB, Huang SK, Marinchak RA, Estes NA III, Mitchell GF, Lieberman EH, Mangione CM, Goldman L. 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;338:1097–1104.
- Andersen HR, Nielsen JC, Thomsen PE, Thuesen L, Mortensen PT, Vesterlund T, Pedersen AK. Long-term follow-up of patients from a randomised trial of atrial versus ventricular pacing for sick-sinus syndrome. *Lancet.* 1997;350:1210–1216.
- Nielsen JC, Kristensen L, Andersen HR, Mortensen PT, Pedersen OL, Pedersen AK. A randomized comparison of atrial and dual-chamber pacing in 177 consecutive patients with sick sinus syndrome: echocardiographic and clinical outcome. *J Am Coll Cardiol.* 2003;42:614–623.
- Gillis AM, Connolly SJ, Lacombe P, Philippon F, Dubuc M, Kerr CR, Yee R, Rose MS, Newman D, Kavanagh KM, Gardner MJ, Kus T, Wyse DG. Randomized crossover comparison of DDDR versus VDD pacing after atrioventricular junction ablation for prevention of atrial fibrillation. The atrial pacing peri-ablation for paroxysmal atrial fibrillation (PA (3)) study investigators. *Circulation.* 2000;102:736–741.
- Bayes de Luna A, Cladellas M, Oter R, Torner P, Guindo J, Marti V, Rivera I, Iturralde P. Interatrial conduction block and retrograde activation of the left atrium and paroxysmal supraventricular tachyarrhythmia. *Eur Heart J.* 1988;9:1112–1118.
- Daubert JC, Leclercq C, Pavin D, Mabo P. Biatial synchronous pacing: a new approach to prevent arrhythmias in patients with atrial conduction block. In: Daubert JC, Prystowsky EN, Ripart A, eds. *Prevention of Tachyarrhythmias With Cardiac Pacing.* Armonk, NY: Futura Publishing Co.; 1997:99–119.
- Israel CW, Hohnloser SH. Pacing to prevent atrial fibrillation. *J Cardiovasc Electrophysiol.* 2003;14:S20–S26.
- Levy T, Walker S, Rochelle J, Paul V. Evaluation of biatrial pacing, right atrial pacing, and no pacing in patients with drug refractory atrial fibrillation. *Am J Cardiol.* 1999;84:426–429.
- Saksena S, Prakash A, Ziegler P, Hummel JD, Friedman P, Plumb VJ, Wyse DG, Johnson E, Fitts S, Mehra R; DAPPAF Investigators. Improved suppression of recurrent atrial fibrillation with dual-site right atrial pacing and antiarrhythmic drug therapy. *J Am Coll Cardiol.* 2002;40:1140–1150.
- 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;12:912–917.
- Padeletti L, Purerfellner H, Adler SW, Waller TJ, Harvey M, Horvitz L, Holbrook R, Kempen K, Mugglin A, Hettrick DA; Worldwide ASPECT Investigators. Combined efficacy of atrial septal lead placement and atrial pacing algorithms for prevention of paroxysmal atrial tachyarrhythmia. *J Cardiovasc Electrophysiol.* 2003;14:1189–1195.
- Padeletti L, Pieragnoli P, Ciapetti C, Colella A, Musilli N, Porciani MC, Ricci R, Pignalberi C, Santini M, Puglisi A, Azzolini P, Spampinato A, Martelli M, Capucci A, Boriani G, Botto G, Proclemer A. 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;142:1047–1055.
- De Voogt W, De Vusser P, Lau CP, van den Bos A, Koistinen Y, Mairesse G, Agren PL, Geelen P, on behalf of the OASES study group. Overdrive atrial septum stimulation in patients with paroxysmal atrial fibrillation (AF) and class 1 and 2 pacemaker indication (OASES). Paper presented at: Annual Scientific Sessions of the Heart Rhythm Society; May 17, 2003; Washington, DC.
- Carlson M, Ip J, Messenger J, Beau S, Kalbfleisch S, Gervais P, Cameron DA, Duran A, Val-Mejias J, Mackall J, Gold M; Atrial Dynamic Overdrive Pacing Trial (ADOPT) Investigators. A new pacemaker algorithm for the treatment of atrial fibrillation: results of the Atrial Dynamic Overdrive Pacing Trial (ADOPT). *J Am Coll Cardiol.* 2003;42:627–633.
- Savelieva I, Camm AJ. The results of pacing trials for the prevention and termination of atrial tachyarrhythmias: Is there any evidence of therapeutic breakthrough? *J Interv Cardiol Electrophysiol.* 2003;8:103–115.
- Friedman P, Dijkman B, Warman EN, Xia HA, Mehra R, Stanton M, Hammill SC. Atrial therapies reduce atrial arrhythmia burden in defibrillator patients. *Circulation.* 2001;104:1023–1028.
- Sweeney MO, Hellkamp AS, Ellenbogen KA, Greenspon AJ, Freedman RA, Lee KL, Lamas GA; MODO Selection Trial Investigators. Adverse effect of ventricular pacing on heart failure and atrial fibrillation among patients with normal baseline QRS duration in a clinical trial of pacemaker therapy for sinus node dysfunction. *Circulation.* 2003;107:2932–2937.
- Lee MA, Weachter R, Pollak S, Kremers MS, Naik AM, Silverman R, Tuzi J, Wang W, Johnson LJ, Euler DE; ATTEST Investigators. The effect of atrial pacing therapies on atrial tachyarrhythmia burden and frequency: results of a randomized trial in patients with bradycardia and atrial tachyarrhythmias. *J Am Coll Cardiol.* 2003;41:1926–1932.