

# The Atrial Pacing Peri-ablation for Paroxysmal Atrial Fibrillation (PA<sup>3</sup>) Study

## Rationale and study design

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The Canadian Atrial Pacing Peri-Ablation for Paroxysmal Atrial Fibrillation Study tested the hypotheses that atrial pacing prevents paroxysmal atrial fibrillation (PAF) in patients without symptomatic bradycardia and that DDDR pacing is more likely to prevent PAF following total atrioventricular (AV) node ablation compared to VDD pacing. Patients with PAF who were refractory to or intolerant of antiarrhythmic drug therapy received a Medtronic Thera DR pacemaker 3 months prior to a planned total AV node ablation. Patients were randomized to atrial pacing or no pacing therapy. The time to first

recurrence of sustained PAF was the primary study outcome event. Following AV node ablation, patients were randomized to the DDDR or VDD mode in a crossover study design. Patients were followed in each mode for 6 months. The time course of PAF recurrence was compared for each pacing mode.

(Europace 1999; 1: 40–42)

**Key Words:** Paroxysmal atrial fibrillation, atrial pacing, dual chamber pacing, ventricular pacing, rate-responsive pacing.

## Introduction

Present pharmacological strategies for maintenance of sinus rhythm or control of ventricular rate response are frequently ineffective or unsatisfactory for many patients with paroxysmal atrial fibrillation (PAF). In this setting, total atrioventricular (AV) node ablation with implantation of a VVIR or DDDR pacing system may be considered as a therapeutic option<sup>1,2</sup>. However, there is a small risk of sudden cardiac death following total AV node ablation<sup>3,4</sup> and many patients may lapse into chronic atrial fibrillation<sup>2,5</sup>. There is some clinical evidence that atrial pacing prevents the development of chronic atrial fibrillation in patients with sinus node disease<sup>6–12</sup> and in patients with bradycardia-induced PAF<sup>13–15</sup>. Accordingly, atrial pacing modalities for the prevention of PAF have been proposed<sup>15–18</sup>.

The Atrial Pacing Peri-Ablation for Paroxysmal Atrial Fibrillation Study, a Canadian multicentre randomized trial, also known by the acronym, the PA<sup>3</sup> Study, began in July 1994. The study was designed to: (1) determine if atrial pacing might prevent PAF in

patients with a history of PAF in the absence of symptomatic bradycardia as an indication for pacing; (2) determine if DDDR pacing compared to VDD pacing alters the time course of recurrence of PAF in patients following total AV node ablation; and (3) determine the time course of development of chronic atrial fibrillation following total AV node ablation in patients with PAF following implantation of a DDDR pacing system.

## Method

### *Study population*

The study population consisted of patients with a history of symptomatic PAF who were unresponsive to or intolerant of antiarrhythmic drug therapy. Consequently, these patients were referred for total AV node ablation and would require a permanent pacemaker.

### *Study protocol*

The study consisted of two phases. Phase I compared the effects of atrial pacing to no pacing therapy in patients with a history of PAF without symptomatic bradycardia. Consenting patients received a Medtronic Thera DR pacemaker 3 months prior to a planned total AV

Supported by a grant from Medtronic, Inc., Minneapolis, Minnesota. Dr Gillis is a Senior Scholar of the Alberta Heritage Foundation for Medical Research.

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node ablation. The Thera DR device was selected because of the high rate atrial tachyarrhythmia detection feature which permits storage in the device memory of the time, date and duration of up to 15 episodes of an atrial tachyarrhythmia. This feature was used for detection of the primary study outcome event — the time to first episode of sustained PAF<sup>[19,20]</sup>. Following pacemaker implantation, patients were randomized to no pacing therapy or to rate-adaptive atrial pacing therapy. To enable the high rate atrial tachyarrhythmia detection feature, the pacemaker was programmed to DDI rate 30 beats · min<sup>-1</sup> in patients in the no pacing group and to DDIR lower rate, 70 beats · min<sup>-1</sup> in the atrial pacing group. These pacing modalities were selected to ensure that patients in the no pacing group would not be paced and that patients in the atrial pacing group would be paced in the atrium but not the ventricle most of the time. Following a 2 week stabilization period to allow atrial lead stabilization, the diagnostic counters were cleared and patients were followed for an additional 10 weeks. At the 3-month follow-up, the high rate atrial tachycardia data was retrieved from the pulse generator memory. Patients had 2-D echocardiograms and 24-h ambulatory ECGs performed at baseline and at the 3 month follow-up visit.

Phase II compared the effects of DDDR pacing to VDD pacing on the time course of recurrence of PAF following total AV node ablation, and discontinuation of antiarrhythmic drug therapy. Following total AV node ablation, patients were randomized to the DDDR or the VDD mode. The high rate atrial tachyarrhythmia data was retrieved from the pacemaker every 2 months during a follow-up visit. After 6 months, patients were crossed over to the alternate pacing mode and the high rate atrial tachyarrhythmia data was retrieved every 2 months during an additional 6 months follow-up period. Ambulatory ECGs were performed 6 and 12 months postablation.

### Outcome events

The study outcome events included: (1) the time to first episode of sustained PAF (>5 mins duration); (2) the intervals between successive episodes of sustained PAF; (3) the frequency of PAF; (4) the total duration of PAF; (5) atrial arrhythmias on ambulatory ECG; and (6) quality of life.

### Results

As of 1 June 1997, 97 patients had been randomized to Phase I of this study. Phase I follow-up was completed in September 1997 and the results were presented early in 1998<sup>[21]</sup>. Seventy-six patients have been enrolled in Phase II and follow-up was completed in September 1998. It is anticipated that final Phase II study results will be presented in the spring 1999.

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