

## Clinical Research

## Alternate Sites of Permanent Cardiac Pacing: A Randomized Study of Novel Technology

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**Introduction:** Several studies have suggested potential benefits from permanent cardiac pacing at alternate sites, such as the interatrial septum and the ostium of the coronary sinus for atrial pacing and various positions in the right ventricular outflow tract for ventricular pacing.

**Methods and Results:** During our participation in an international multicenter study, we randomized 30 patients with standard indications for permanent dual-chamber pacing to alternate site pacing with the use of a new, thin and compact, active fixation and steroid-eluting pacing lead and a steerable guiding catheter system. The study group comprised 18 men and 12 women, with a mean age of  $70 \pm 12$  years, afflicted by sick sinus syndrome ( $n=6$ ), Möbitz II or complete atrioventricular block ( $n=22$ ) or both ( $n=2$ ). The randomized pacing sites included the interatrial septum/high anterior right ventricular outflow tract ( $n=15$ ) and the coronary sinus ostium/low septal right ventricular outflow tract ( $n=15$ ). Implantation of the pacing system with the use of novel technology leads assisted by a steerable catheter system was successful in 28 patients (93%). There was one complication (pneumothorax) not related to the pacing system. Intraoperative measurements yielded an atrial pacing threshold of  $0.7 \pm 0.5V/0.5$  ms, ventricular pacing threshold of  $0.4 \pm 0.2V/0.5$  ms, atrial impedance of  $690 \pm 106 \Omega$  and ventricular impedance of  $807 \pm 193 \Omega$ , a P wave amplitude of  $2.8 \pm 1$  mV and R wave amplitude of  $15 \pm 5.5$  mV. Pacing parameters remained excellent during predischarge measurements, and at 2 weeks, 1 and 3 months of follow-up in all but two patients. During follow-up, in one patient an increase of ventricular pacing threshold was observed and in a second patient there was inappropriate ventricular capture from the atrial electrode at the coronary sinus os.

**Conclusions:** Alternate site, permanent cardiac pacing is feasible with high success (over 90%) with the use of a novel lead and guiding catheter pacing system without complications; the excellent pacing measurements obtained intraoperatively are maintained during short-term follow-up in the majority of patients.

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Permanent cardiac pacing at alternate atrial and/or ventricular sites has been proposed by several studies as superior to pacing at conventional sites.<sup>1-6</sup> Firstly, alternate sites have been studied for atrial pacing, such as the interatrial septum and/or the coronary sinus ostium, and compared with conventional pacing from the right atrial appendage for the prevention of atrial fibrillation.<sup>1-3</sup> Also the hemodynamic superiority of right ventricular outflow tract pacing has been suggested over conventional pacing from the

right ventricular apex.<sup>4-7</sup> Conventional, chronic, right ventricular apical pacing, particularly in patients with left ventricular dysfunction, could be harmful, as suggested by several recent studies.<sup>7-11</sup>

During our participation in an international multicenter study, 30 patients, with standard indications for permanent dual-chamber pacing, were randomly assigned to alternate atrial and ventricular pacing sites with the use of prototype pacing leads and novel guiding catheter technology.

## Patients, Materials and Methods

The study population comprised 30 patients, 18 men and 12 women, aged  $70 \pm 12$  years, with standard indications for permanent, dual-chamber cardiac pacing. Six patients had sick sinus syndrome, 22 patients had second-degree atrioventricular block, either Möbitz II or complete heart block, and 2 patients had both sinus node dysfunction and complete heart block. After written informed consent was obtained, all patients underwent DDDR pacemaker implantation. The study was approved by the local medical ethics committee and the institutional review board.

With regard to the technical characteristics, the new pacing lead (3830, Medtronic) is a bipolar, active fixation, thin (4.1 F) and compact (bearing no stylet) lead, with a titanium nitride cathode and an anode of titanium nitride covered by platinum-iridium. It has external insulation of polyurethane 55D and internal insulation of silicone, and bears a tip eluting beclomethazone. Lead placement was achieved with the assistance of a special steerable guiding catheter (10F), which allows the advancement and positioning of the lead at the specific endocardial site. After appropriate lead placement, the guiding catheter is removed with a special splitter which protects the lead.

The endocardial sites where lead placement was randomized included the combinations of the interatrial septum/high anterior right ventricular outflow tract and the coronary sinus ostium/low septal right ventricular outflow tract sites.

The implant procedures were performed by employing our routine methods of implanting dual-chamber pacing systems. In brief, all patients received prophylactic antibiotics before the procedure and for 5 days afterwards. Under strict aseptic/antiseptic conditions and with the use of local anesthesia, the cephalic vein cut down technique and/or subclavian vein puncture were used for the introduction of the guiding catheters and the pacing leads. The catheter delivery system was occasionally assisted by a steerable quadripolar electrode catheter for easier advancement through the tricuspid valve in cases where this was not feasible with use of the steerable guiding catheter alone. After the intraoperative measurements were taken and found satisfactory at the randomized sites, the guiding catheter was split off and removed. This was followed by securing the leads with sutures placed over sleeves in the infraclavicular area, where the pacemaker pocket was also fashioned. Fluoroscopy time and the duration of

the lead placement, as well as the duration of the whole procedure, were meticulously recorded. Three fluoroscopic views were recorded in all patients: a postero-anterior, a 30° right anterior oblique and a 45° left anterior oblique view.

Patients were routinely monitored for 2 days in the hospital and during this period intravenous antibiotics were administered. Prior to discharge, all patients had pacing and sensing thresholds measured with use of an external programmer. Also, a chest X-ray was obtained during the second day to confirm proper lead position and exclude lead dislodgment. Upon discharge, all patients were prescribed oral antibiotic therapy for an additional 3 days to receive at home. Subsequently, they were followed-up at the pacemaker clinic at 2 weeks, 1 month and 3 months after pacemaker implantation.

The data are presented as a mean value  $\pm$  1 standard deviation.

## Results

Of the 30 patients, 15 were randomized to the combined sites of interatrial septum/high anterior right ventricular outflow tract site (Figures 1 and 2) and 15 to the coronary sinus ostium/low septal right ventricular outflow tract sites. The procedure was successful in 28 patients (93%) with implantation of the novel technology leads at the assigned alternate sites assisted by the special steerable delivery catheter systems. The remaining 2 patients received the conventional pacing system.

In 60% of patients the atrial lead was inserted via the subclavian vein and in 40% via the cephalic vein. In 93% of patients the ventricular lead was introduced via the subclavian vein and in 7% via the cephalic vein. Access was obtained from the left side in 73% and from the right side in 27%. The mean fluoroscopy time was  $13.6 \pm 10$  min and the mean procedure time  $2 \pm 0.6$  hours.

After the procedure, one patient developed pneumothorax, a complication that was not related to the pacing system; it completely resolved with insertion of a chest tube. The results of the pacing parameters are presented in table 1. Measurements of pacing parameters obtained at pre-discharge, 2 weeks, 1 month and 3 months after implantation remained excellent. In 1 patient the ventricular pacing threshold determined at 1 month post-discharge was found to be elevated (exit block), while in another patient inappropriate ventricular capture from the coronary sinus os



**Figure 1.** 12-lead electrocardiogram obtained from pacing at alternate sites (interatrial septum/high anterior right ventricular outflow tract).

lead was detected. The former patient underwent explantation of the ventricular lead and replacement with a conventional lead, which was placed at the right ventricular apex. For the latter patient explantation of the displaced coronary sinus lead was scheduled to be performed after he had undergone repair or replacement of his mitral valve because of preexisting severe mitral valve regurgitation.

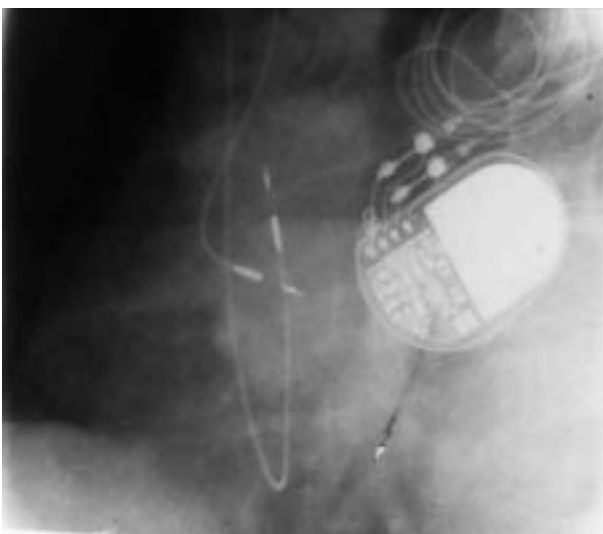
### Discussion

Alternate site cardiac pacing was performed successfully in the majority of patients (93%) in the present

study. The new bipolar pacing lead that was used has certain potential advantages. It is downsized (4.1F); it is compact without a lumen, thus having enhanced endurance and consequently less risk of possible fracture (crush) under the clavicle or by the securing sutures; it is steroid eluting and reduces the risk of threshold rise and exit block; it has a smaller contact surface and less current leakage and generally shows better performance and easier access to electrically and hemodynamically optimal sites and allows easier chronic lead extraction. In the present study the excellent intraoperative pacing measurements were maintained for at least the duration of the first 3 months post implantation.

Admittedly, the implantation procedure was generally more demanding than a conventional one, with difficulties during manipulation of the guiding catheter, especially during access from the right side. A major problem would arise if for any reason there was a need for lead repositioning after the catheter had been removed, which would entail lead removal and the use of a new guiding catheter system. However, technical modifications in the guiding catheter system have already been made by the manufacturer and are expected to further facilitate the procedure. Special caution was necessary in order to avoid air embolisation through the guiding catheter by continuous flush with heparinized normal saline. Nevertheless, with proper care exerted by the implanters, there were no complications related to the pacing system. Nor was there any significant delay in the duration of the procedure, with the mean implantation time being just 2 hours.

Of course, there was a learning curve for the procedure, as happens during the application of any new



**Figure 2.** Fluoroscopy view (45° left anterior oblique) of the novel pacing leads implanted at alternate sites: interatrial septum/high anterior right ventricular outflow tract.

**Table 1.** Pacing parameters

	Intraoperatively	Predischarge	2 weeks	1 month	3 months
A Thr	0.7±0.5 V/0.5ms	0.05±0.07ms/2.5V	0.08±0.1ms/2.5V	0.05±0.03ms/2.5V	0.04±0.02ms/2.5V
PW	2.8±1 mV	3.0±1 mV	3.5±1.6mV	3.7±1.6mV	4.2±2.3mV
A Imp	690±106 Ω	595±77 Ω	585±48 Ω	590±55 Ω	598±53 Ω
V Thr	0.4±0.2 V/0.5ms	0.05±0.07ms/2.5V	0.03±0.01ms/2.5V	0.04±0.05ms/2.5V	0.05±0.04ms/2.5V
RW	15±5.5 mV	9±4 mV	11±5mV	12±5mV	11±6mV
V Imp	807±193 Ω	652±127 Ω	637±92 Ω	648±98 Ω	640±109 Ω

A Imp=atrial impedance, A Thr=atrial pacing threshold, PW=P wave, RW= R wave, V Imp=ventricular impedance, V Thr= ventricular pacing threshold

technique, which varies according to the individual implanter. Thus, in the 2 patients in whom implantation of the prototype leads could not be carried out successfully, there was lead dislodgment during the procedure, which was subsequently turned into a conventional implant with standard leads. However, when similar problems were encountered in subsequent procedures, the prototype leads were then successfully re-introduced with the use of new guiding catheters.

The present study demonstrated that the use of this novel pacing technology is feasible and accomplishes alternate site pacing with high success both in the atrium and in the ventricle. It also shows that the performance of the new leads is excellent, at least during the short-term follow-up of 3 months (Table 1). This novel technology renders feasible the implantation of multiple endocardial leads for effecting multi-site pacing. During recent years, there has been an increased demand for multi-site pacing, which appears necessary both at the atrial level for the management of atrial fibrillation (atrial resynchronization), and at the ventricular level for the management of heart failure (ventricular resynchronization).<sup>1-6,9,11</sup>

With use of this novel technology, one can now avoid the apparent harmful effect of right ventricular apical pacing, which has already been demonstrated by many recent studies,<sup>7-11</sup> by implanting the ventricular lead at the right ventricular outflow tract. This adverse pacing effect does not seem to concern only patients with preexisting left ventricular dysfunction and/or heart failure, but also patients with normal left ventricular function who are paced chronically at the right ventricular apex.<sup>7</sup> It therefore seems likely that in the near future there will be a need to reconsider our current practice in permanent cardiac pacing with regard to choosing the right ventricular apex as our preferred site for chronic pacing in any

patient who is a pacemaker candidate. Of course, new comparative studies will be necessary in order to determine which alternate sites would be optimal in terms of hemodynamic and clinical benefits, but the mere avoidance of the conventional right ventricular apical site already looks significantly advantageous for permanent cardiac pacing, possibly in all patients.<sup>4-11</sup> Whether bifocal right ventricular pacing, combining the right ventricular apex and outflow tract, or monofocal pacing from the right ventricular outflow tract would be useful or equivalent to biventricular or left ventricular pacing in certain cases or in all patients, are questions that can be properly answered only by future studies.

Likewise, right atrial appendage pacing might need to be reconsidered in favor of alternate site pacing, either in the form of unifocal atrial pacing, e.g. at the interatrial septum, or in the form of bifocal pacing at alternate sites, such as those combining the right atrial appendage and the coronary sinus os. Preliminary results from studies concerning patients with atrial fibrillation are already in favor of pacing at alternate sites in the atrium.<sup>1-3</sup>

## Conclusions

Alternative site pacing proved feasible with the use of novel pacing technology, including a prototype lead and a special guiding catheter system, in 93% of patients in the present study without complications. The excellent intraoperative pacing measurements were maintained during short-term (1-3 months) follow-up in the majority of patients. Technological improvements in the guiding catheter system would further facilitate and expedite the procedure. Follow-up of these patients is continuing, and it is possible that the results of this study might have a significant impact on the way we approach permanent cardiac pacing in the future.

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