Development and Prospective Evaluation of a Single-Lead Dual Chamber Temporary Pacing Catheter

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Abstract: Temporary DDD pacing has been neglected in emergency settings, despite the potential clinical benefits in haemodynamically compromised patients. This may relate to the major technical challenge of achieving stable temporary atrial and ventricular pacing. The hypothesis of this thesis is that a temporary pacing lead, incorporating electrodes for both atrial and ventricular pacing, that can be easily and rapidly deployed and achieve reliable dual-chamber pacing should benefit patients presenting with bradyarrhythmias and haemodynamic compromise. The hypothesis was tested by four studies. (i) A randomised trial comparing standard semi-rigid to fluoroscopically positioned balloon-flotation temporary pacing leads. Procedure and fluoroscopy times were reduced and lead positions were improved with balloon-flotation leads. (ii) Development and evaluation of a single-lead balloon flotation DDD temporary pacing catheter, incorporating Overlapping Biphasic Impulse (OLBI®) stimulation via non-contact atrial electrodes. The lead was inserted easily and achieved atrial pacing in 91 percent of patients. (iii) A randomised trial of temporary DDD pacing, comparing the single-lead system with standard atrial plus ventricular pacing leads: The single-lead system was inserted more quickly, with less fluoroscopy and was more reliable during follow-up. (iv) A comparison of the effects of VVI and DDD modes showed that optimal DDD pacing significantly improved the cardiovascular function of most patients presenting with bradyarrhythmia.

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This thesis is dedicated to Renée, Christopher and Mark.

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Statement of Candidate

I declare that the work of this thesis is original (except where acknowledgments have been made) and that neither the whole work nor any part of it has been, is being, or will be submitted for another degree in this or any other university.

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CHAPTER 1

A Review of Temporary Cardiac Pacing

INTRODUCTION

In just over four decades, pacemaker technology has progressed from the first elementary experiments in the human heart to the current era of device therapy. The earliest devices were simply able to stimulate the heart at a fixed rate to prevent bradycardia. [1-3] They were unreliable and prone to failure without warning. Pacemaker technology has progressed enormously since then and the diversity and capability of modern devices is impressive. They are now capable of anti-bradycardia pacing, detecting and recording arrhythmia, detecting and treating both ventricular and supraventricular tachyarrhythmia and resynchronisation of left and right ventricles for the treatment of heart failure. [1] The large research and development programmes of the pacemaker industry, coupled with advances in information technology and a growing knowledge of cardiac electrophysiology, is likely to add refinements to current devices and further expand their clinical utility.

Temporary cardiac pacing is a small but important part of the diverse field of pacemaker therapy and temporary transvenous pacing remains vital for the emergency treatment of certain patients presenting with bradyarrhythmia. [4,5] Compared to permanent pacing however, temporary cardiac pacing has changed very little over the last two decades and there has been little published data to influence clinical practice. This thesis explores the development and utility of a new pacing lead for temporary dual chamber cardiac pacing. To understand the rationale for the development of our temporary pacing lead, it is useful to consider a brief history of cardiac pacing and the development of current temporary pacing practice, clinical problems commonly encountered with temporary transvenous pacing and the theoretical reasons why temporary dual chamber pacing might be important in patients presenting with bradycardia and haemodynamic compromise.

THE DEVELOPMENT OF TEMPORARY CARDIAC PACING

A brief history of cardiac pacing

Since the mid 1800's it was known that the mammalian heart, either as a strip of muscle or as an intact organ, could contract in response to an electrical stimulus. [6,7] In 1932, a physician from New York City, Albert Hyman, [2] reported the resuscitation of asphyxiated guinea pigs with an electrode needle inserted through the chest wall into the right ventricle. The heart was then stimulated by a hand cranked 'Artificial Pace Maker for the Heart' and was reported to achieve reliable

ventricular stimulation. The name 'Pace Maker' was first used in the patenting of this device in 1930 and soon became the accepted term to describe such a device. [8] Three different versions of the pacemaker were made and used in animal experiments. They received much media attention but also criticism from prominent physicians, including accusations that this therapy might interfere with the natural history of disease.

There were no further developments until the 1950's when the first reports on human subjects were published. In 1952, Zoll described 'resuscitation of the heart in ventricular standstill using external electrical stimulation'. [3] He implanted electrodes into the subcutaneous tissue close to the cardiac apex of two patients with complete heart block who had failed to respond to intracardiac injections of epinephrine. Using a 'Thyratron' pulse generator to deliver electrical pulses of 15-100 Volts, he successfully achieved ventricular capture and restoration of cardiac output for 25 minutes in one patient and for several days in the other. Both patients only survived for a short period but the potential value of pacemaker therapy had been demonstrated.

Stimulation of the heart by electrodes placed on the chest wall required very high outputs and was restricted by 'convulsive contractions of the chest wall musculature'. Subsequently, Weirich[9] and Folkmann[10] demonstrated that much lower outputs (< 2 Volts) were required if the electrodes were embedded into the myocardium and stimulation of skeletal muscle could be avoided. The obvious

disadvantage of direct myocardial stimulation at that time was the requirement for a thoracotomy to apply the electrodes to the epicardial surface of the heart. In 1958, Furman adapted a Cournand cardiac catheter to transmit electrical impulses to the heart. [7] This catheter was introduced via the external jugular vein of sixteen mongrel dogs and inserted into the right ventricle to achieve endocardial stimulation. Although 'intracardiac' pacing had been previously reported in animal studies, [11] the publication of this report marked the beginning of the era of transvenous pacing in man.

In the same year the first report of a permanent pacemaker implantation was published. A Swedish thoracic surgeon Åke Senning with the help of an engineer Rune Elmquist had developed an implantable pulse generator. [12] This was first implanted using epicardial electrodes in a 40 year old patient with complete heart block in 1958. The system failed within a few hours and was replaced by another which lasted 6 weeks. The patient died forty-two years later after a total of 26 pacemaker implants! [1] Two years later in Buffalo, New York, a 77 year old man with recurrent Stokes-Adams attacks had a successful implantation of a permanent system, also using epicardial leads. William M. Chardack, the thoracic surgeon, performed a two stage procedure: he implanted the leads and after 2 months of stable pacing thresholds, he implanted the generator. [13] Prior to the implantation, the patient, Frank Henefelt, had suffered so many episodes of syncope and head injury that he took to wearing a football helmet for protection. With the pacemaker implanted, he returned to a moderately active lifestyle and was able to discard his

helmet. This story was elaborately reported in the New York Saturday Evening Post. [1]

These early reports attracted much attention and provoked an explosion in technological developments. The earliest pulse generators were cumbersome devices, prone to sudden malfunction. Powered by zinc-mercury oxide they delivered stimuli at a preset rate, regardless of the intrinsic electrical activity within the heart. The leads simply consisted of a pair of multi-strand stainless steel epicardial wires in a Teflon sleeve. The demand for smaller, lighter generators with longer battery life and leads which would be less likely to fracture, gave impetus to sustained technological development. Some of the important early milestones included [1,4] (i) Transvenous pacing leads, 1962[14] (ii) The J-lead for atrial pacing, 1969 (iii) The lithium iodide battery, 1972 (iv) Noninvasive rate and output programmability, 1973 (v) Hermetically sealed generators , 1976 (vi) Multiprogrammable pacemaker (at least 3 programmable parameters), 1978 (vii) DDD pacemaker,1980. Permanent pacemakers are now comparatively simple to implant and are routinely implanted by most cardiology services. Most operators insert ventricular and/or atrial leads via the transvenous approach and position the pulse generator (of usually less than 50cc), into a pre-pectoral pocket. Contemporary generators can provide reliable pacing for 8-12 years. By 1993, the number of permanent systems implanted in Europe and the USA approached 400 per million of the population. [4]

The practice of temporary cardiac pacing

In contrast to major advances in the field of permanent pacing, temporary cardiac pacing has changed little over the last 50 years, despite the fact that it remains essential for the management of acute bradyarrhythmias. [5,15] Seven years before the first reports of electrical stimulation of human hearts, Callaghan and Bigelow described temporary pacing of canine hearts using transvenous pacing electrodes and a portable pulse generator capable of biphasic electrical stimulation. [11] In fact, they achieved reliable stimulation of the 'sino-auricular' node and achieved 'physiological' pacing in dogs which had been cooled to 22°C to achieve sinus bradycardia. Five decades later temporary pacing is still most commonly achieved by the transvenous route, inserting a single lead into the right ventricle via a central vein and connecting it to an external temporary pacing generator for bipolar endocardial pacing. The simple ventricular-demand (VVI) pacing mode is used in the vast majority of cases,[16-18] even those exhibiting haemodynamic instability. [5] Although VVI pacing can be achieved in most patients, the haemodynamic effects of this mode have not been properly assessed in emergency settings. Studies in permanent pacing suggest that the dual chamber (DDD) pacing mode significantly increases cardiac output compared to the VVI mode. [19-22] However, the complexities of achieving and maintaining temporary DDD pacing, using conventional atrial plus ventricular leads, have precluded its use in routine clinical practice. In addition, major complications relating to even simple transvenous VVI

pacing are reported in up to a third of cases, [23,24] further discouraging the uptake of more complex temporary DDD pacing.

Alternatives to transvenous pacing have been described and are useful in specific circumstances but are not suitable for the majority of patients requiring temporary pacing. [4] Transcutaneous pacing is useful in emergencies as a bridge to temporary transvenous or permanent pacing. [25] Epicardial pacing is routinely used after open heart surgery but obviously requires a thoracotomy to position the leads. Other approaches such as transoesophageal, coronary or subcutaneous electrodes may be appropriate in specific circumstances but have not been widely adopted. Transthoracic pacing using percutaneous needle-stick of the left ventricle has largely been abandoned because of the high risk of complications.

Temporary transvenous pacing lead design

In 1951, Callaghan and Bigelow described the use of a 12 French bipolar pacing lead for stimulation of the canine heart. [11] This consisted of a plastic covered 'metal' lead with two closely spaced electrodes at the tip and looked remarkedly similar to modern temporary pacing leads (see Figure 1.1). Furman adapted a conventional Cournand catheter by passing a stainless steel suture through its lumen for his experiments with canine hearts. [7] Later, and in his first experiments on human subjects, he used a No. 6 Cournand electrode catheter (United States Catheter Company, Glens Falls, New York) which had been designed to obtain

intracardiac electrograms. This lead consisted of a conventional Courmand catheter with a copper central core and a metallic tip.

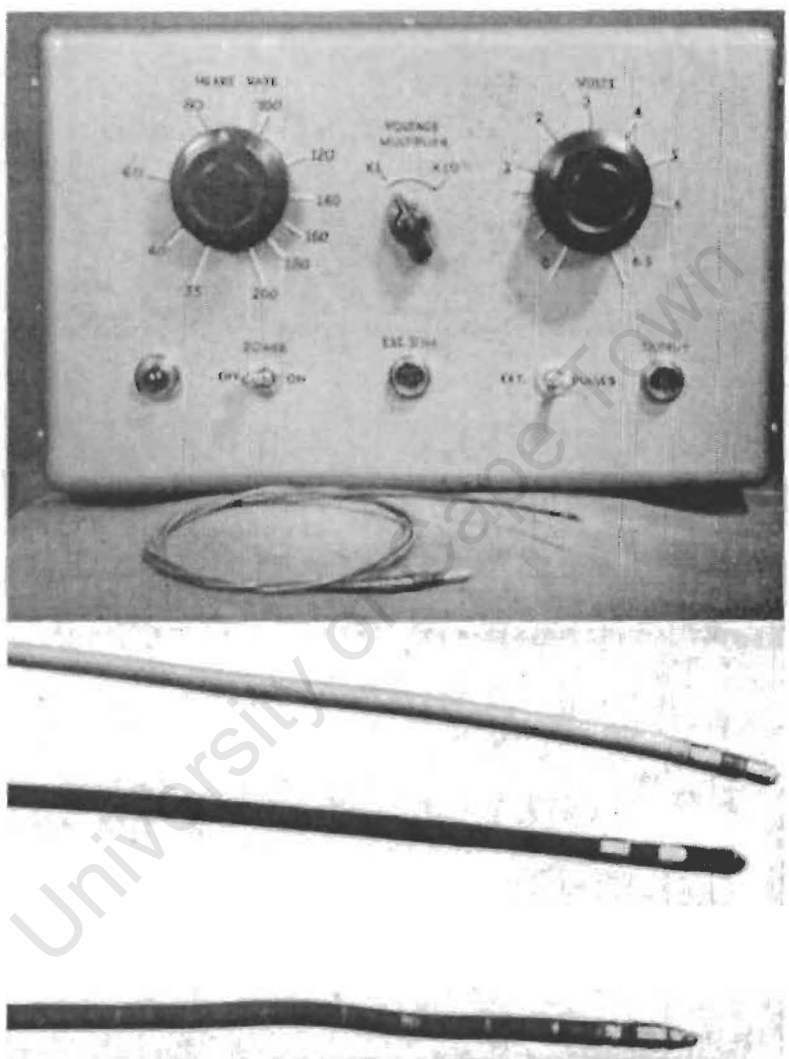


Figure 1.1 The 12 French bipolar pacing leads and temporary pacing generator for stimulation of the canine heart designed by Callaghan and Bigelow in 1951. [11]

Temporary pacing leads remain relatively simple in design compared to more sophisticated and durable permanent pacing leads. Most temporary leads consist of simple wire strands, covered with insulation material, with two electrodes at the tip for bipolar pacing. The relatively rigid woven dacron insulation has been replaced by more flexible plastic coating with a reduced tendency to perforate the right ventricle. Likewise, the diameter of the leads has reduced from 8 French to 5 or 6 French to reduce catheter trauma (recently a 2F active-fixation temporary pacing lead has been introduced). The flexibility of the leads varies substantially with different plastic polymers and, although more flexible leads are less likely to perforate the ventricle, they can be more difficult to manipulate. Most temporary leads do not have a stylet to facilitate positioning but many have a pre-formed curve at the tip to direct the lead across the tricuspid valve. Flotation temporary leads have 1-2 millilitre inflatable balloon at the tip to enable flow-directed manipulation across the tricuspid valve. These leads were designed to be implanted without fluoroscopy, thereby expediting emergency bed-side pacing. Unfortunately 'blind' placement often results in unstable positions and subsequent lead displacement and most operators routinely use fluoroscopic guidance to position the leads. The tips of most temporary leads do not have tines or active fixation mechanisms and lie passively within the trabeculae of the myocardium. This facilitates lead placement and subsequent atraumatic removal but can increase tendency of temporary leads to dislodge, particularly if positioned outside of the right ventricular apex. Most leads have one electrode at the tip and a second within 1cm of the tip, to enable bipolar endocardial pacing. The design of the lead tip has

remained simple and high impedence leads have not been used as battery drain is not problematic in temporary pacing. Temporary atrial leads are occasionally used and will be discussed in more detail later.

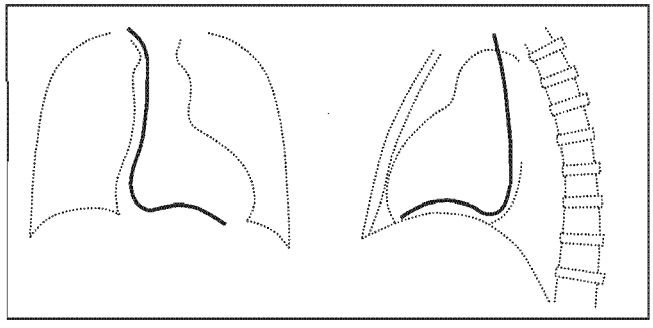
Venous access for temporary pacing

The earliest transvenous pacing leads were inserted via basilic or femoral vein cutdown, a technique which is time consuming, uncomfortable for the patient and can potentially lead to neurovascular injury. The introduction of the Seldinger technique in the 1960's revolutionised both venous and arterial access procedures and allowed rapid and safe introduction of venous sheaths to both central and peripheral veins. [26] Nowadays, most temporary pacing procedures are done via the subclavian or internal jugular route which provide a direct approach to the right heart. Central venous access does carry a small risk of pneumothorax, but this is usually less than 1 percent. [27] In patients with clotting abnormalities, for instance after thrombolysis, the internal jugular, femoral or basilic routes can be considered. Prolonged manual compression is feasible in these sites if haematomas should develop. The femoral route is still commonly used, especially in conjunction with cardiac catheterisation procedures via the femoral artery. The femoral route does however, carry an increased risk of sepsis[28] and small studies have reported and increased risk of venous thrombosis. [29] The basilic approach is seldom used, probably because of previous reports of higher rates of lead dislodgement when using relatively rigid temporary pacing leads.

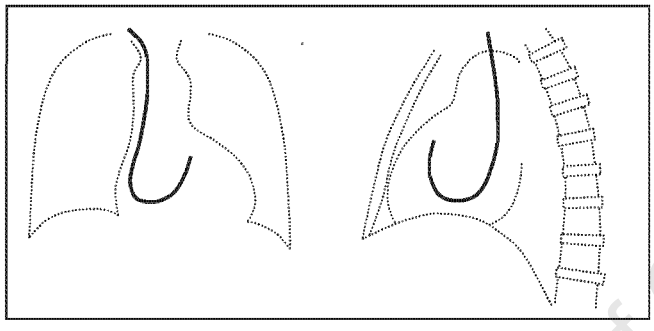
Techniques for implantation of temporary transvenous pacing leads

Transvenous pacing technique is well described and has not changed much in the last four decades. [4,5] Typically, the temporary lead is introduced into the heart via a central vein and advanced into the right atrium, across the tricuspid valve and into the right ventricle, usually under fluoroscopic guidance. In an effort to reduce subsequent lead dislodgement, the tip of the lead should be positioned in the right ventricular apex pointing downwards. The lead should have a generous loop within the right atrium to prevent displacement during deep inspiration and semi-erect posture (see Fig. 1.2). An external temporary pacing generator is then connected to the lead and the ventricular threshold is measured. Lead stability is checked by pacing at outputs just above the capture threshold during deep respiration and cough. The outputs are then typically set to at least twice the capture threshold lead should then be secured into position using a combination of sutures, adhesive dressings and locking haemostatic valves integral with the venous sheath. A post-insertion chest radiograph is needed to exclude pneumothorax and record the lead position. To minimise complications during continuous pacing, the capture threshold should be measured daily and the patients should be closely observed for signs of sepsis or other potential complications.

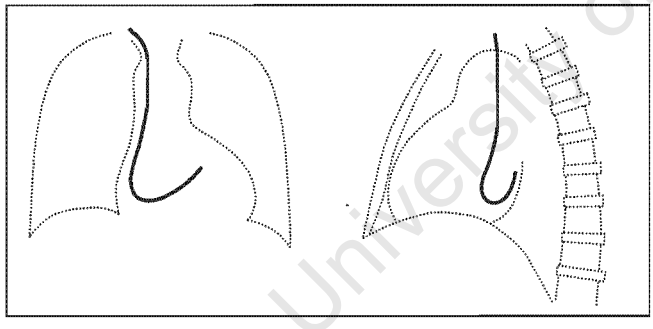
Figure 1.2
Temporary pacing lead positions



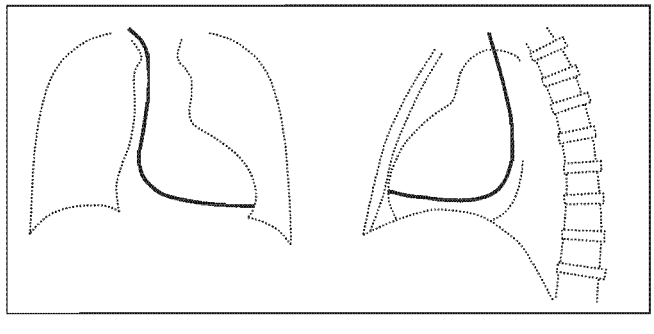
Good position
Note the tip of the lead is well left of the spine within the RV apex and pointing inferiorly. The generous right atrial loop provides stability during deep inspiration.



RV outflow tract
The tip points superiorly and anteriorly and the lead can be passed freely into either right or left pulmonary artery, excluding a coronary sinus position.



Coronary sinus
The tip points superiorly and posteriorly towards the left shoulder



RV perforation
The tip reaches the lateral border of the cardiac contour causing pleuritic pain and unacceptably high thresholds

PROBLEMS WITH TEMPORARY VVI PACING

Complications associated with temporary VVI pacing

Despite the relatively simple and well described transvenous technique, contemporary studies have reported an unacceptably high incidence of related complications. [16,23,24,28] Patients requiring temporary pacing are often sick and have a poor prognosis from the outset but there are a number of factors that may predispose to complications: lack of operator experience and supervision, distressed/confused patients who may be unable to tolerate a prolonged procedure, suboptimal lead positions within the right ventricular apex increasing the risk of lead displacement, clotting abnormalities, inattention to aseptic technique etc. However, as the following study illustrates, complications remain common even when temporary pacing is performed under expert supervision.

In a study from the Mayo Clinic, Hynes et al described the clinical course of 1022 consecutive patients receiving a temporary transvenous pacemaker in the coronary care unit between 1976 and 1981. [23] All were inserted under the direct supervision of the attending cardiologist. Interestingly, antecubital vein cutdown was used in 59% of cases. Pacemaker related complications occurred in 140 (13.7%) patients and pacemaker malfunction occurred in 183 (17.9%) patients. The incidence of complications increased with the duration of pacemaker therapy. Hospital death occurred in 17.6% of cases although none was attributed to a pacemaker related complication. Loss of ventricular capture occurred in 183 (17.9%) patients and

necessitated repositioning in 155 cases. A pericardial friction rub was detected in 5.3%, unequivocal right ventricular perforation occurred in 2.1% with only one patient requiring pericardiocentesis for cardiac tamponade. Ventricular fibrillation/flutter occurred in 2.3%. Local infection or phlebitis was reported in only 18 patients with no cases of systemic sepsis. One pneumothorax was reported after subclavian vein puncture.

In a further study from Oxford, Winner et al reported on the complications of temporary pacing in 145 patients awaiting permanent pacemaker implantation. [24] Many of the temporary pacing leads had been implanted by physicians without formal cardiology training. At least one major complications occurred in 52 (36%) patients, including failure to pace in 44 patients, sepsis in 9, haemothorax in 2, pericarditis in 6, diaphragmatic capture 1, and inadvertant left ventricular pacing in 1 patient. One of the patients died after multiple episodes of loss of capture and numerous attempts to reposition the lead.

An effective strategy to reduce the complication rate of temporary pacing has been to improve access to immediate or early permanent pacing. [4] In many cases, temporary pacing can be avoided altogether but in others, a reduction in the duration of temporary pacing therapy can reduce the incidence of sepsis or complications relating to lead displacement. Although access to permanent pacing lists has improved over recent years, early permanent pacing may not be immediately available in all hospitals. Moreover, permanent pacing is preferably

avoided in patients with a self-limiting bradyarrhythmia or septicaemia and, in some cases, prolonged temporary pacing may be required.

Operator experience

Major complications can occur even when temporary cardiac pacing is performed under expert supervision, as was demonstrated by the Mayo Clinic study. In many countries outside the USA emergency cardiac pacing is often performed by generalists with minimal training in intravenous pacing techniques. [16,18,30] The Oxford experience demonstrated that the incidence of complications appeared inversely proportional to the number of temporary pacing procedures performed in each hospital. Moreover, the total number of temporary pacing procedures being performed in acute medical settings appears to be falling as a result of improved access to permanent pacing in district hospitals and also the widespread use of thrombolysis for acute myocardial infarction. [17,31] Thus, experience in temporary pacing techniques is becoming more difficult to obtain and this may have further discouraged the uptake of emergency DDD pacing.

Deleterious haemodynamic effects of VVI pacing

Temporary VVI pacing increases heart rate without restoring AV synchrony and may not improve cardiac output, [32-36] particularly in patients with abnormal ventricular compliance such as those with acute myocardial infarction (MI), aortic stenosis, or chronic left ventricular dysfunction. The haemodynamic consequences of AV asynchrony include reduced stroke volume, functional mitral regurgitation

and atrial cannon waves. [33,34,37] The resultant fluctuations in atrial pressure may result in over-activation of atrial stretch receptors, leading to inappropriate vaso-dilatation. [38,39] Such potentially deleterious effects may be particularly harmful in critically ill patients. Despite these significant limitations, the VVI mode remains the standard for emergency cardiac pacing.

POTENTIAL BENEFITS OF RELIABLE TEMPORARY DDD PACING

The benefits of AV sequential pacing

Dual chamber (DDD) systems maintain atrioventricular synchrony with clear evidence of improved cardiac performance and patient tolerability[19-22] in a wide range of clinical settings. [40,41] Studies with permanent dual chamber pacemakers have consistently shown that DDD mode results in an immediate increase in stroke volume, cardiac output and mean arterial pressure compared to VVI pacing, [34,42,43] even in haemodynamically stable patients. However, little attention has been paid to the potential haemodynamic benefits of DDD pacing in acute settings. Small studies have shown significant improvements in cardiac output, blood pressure and filling pressures with AV sequential pacing compared to VVI pacing in patients with complete heart block complicating acute MI. [44-48] Other acutely ill patients with impaired diastolic function (eg. aortic stenosis, left ventricular dysfunction

etc.) are also likely to benefit. [32,49-51] Despite these potentially important benefits, temporary DDD pacing is seldom used in the emergency setting.

Effect of AV Delay

The AV delay varies substantially with loading conditions and heart rate, and is especially important in conditions where diastolic filling is critical. Optimising the AV delay will significantly increase cardiac output. [52-54] The programmed AV delay does not accurately correlate with true timing of atrial contraction as significant intra-atrial conduction delays may delay the onset of atrial systole. Measurement of the haemodynamic response to a range of AV delays is thus required to optimise AV synchrony and several studies in permanent pacing have used echocardiography for this purpose. [51,55,56] There are no studies however, on the effect of altering AV delay during emergency DDD pacing.

Technical challenges associated with emergency DDD pacing

Given the high incidence of clinical problems and complications associated with temporary VVI pacing, it is likely that these practical difficulties have precluded the widespread uptake of DDD pacing in acute settings. Introducing two electrodes and achieving a stable atrial position can present a formidable technical challenge in sick, haemodynamically compromised patients. Even then, temporary atrial electrodes exhibit a notoriously high incidence of displacement requiring repositioning (often of both electrodes). The requirement for two central venous punctures as well as prolonged/repeated cardiac instrumentation in acutely ill

patients is inevitably associated with increased risks (sepsis, pulmonary oedema, asystole, cardiac arrest[57,58] etc.).

PATIENT SELECTION

The indications for temporary pacing are poorly defined with little hard evidence on which to base our current practice. [5] In particular, there have been no prospective studies to determine which clinical characteristics identify patients likely to benefit from restoration of AV synchrony. Moreover, there is little data on the absolute magnitude of haemodynamic improvement achieved with emergency DDD pacing in different patient subgroups. Thus, it is hardly surprising that temporary DDD pacing is avoided, particularly considering the potential procedural difficulties out-lined above.

OPTIMISING TEMPORARY CARDIAC PACING

Temporary cardiac pacing remains essential in the management of patients presenting with symptomatic bradyarrhythmias. Considering the unacceptably high incidence of complications relating to temporary transvenous pacing, it is surprising that there has been so little effort to optimise implantation techniques and lead design. New temporary lead designs have been developed but these have

been introduced without proper evaluation of their safety or efficacy and the choice of lead and implantation technique is usually determined simply by operator preference. Furthermore, temporary dual chamber pacing is largely avoided, even in sick patients exhibiting significant haemodynamic instability. Although the technical difficulties of achieving and maintaining temporary DDD pacing in these patients can be formidable, dual chamber pacing is likely to offer significant advantage compared to the VVI mode. New developments to facilitate more simple and reliable DDD pacing would represent a major advance.

THESIS HYPOTHESIS AND OBJECTIVES

Hypothesis: A temporary pacing lead, incorporating electrodes for both atrial and ventricular pacing, that can be easily and rapidly deployed and achieve reliable dual-chamber pacing should benefit patients presenting with bradyarrhythmias and haemodynamic compromise.

To address this hypothesis several studies have been performed.

(i) The first study evaluated a new implantation technique of an existing ventricular temporary pacing lead. A randomised trial of temporary pacing in patients with bradyarrhythmia was performed comparing standard semi-rigid temporary pacing leads to balloon-flotation temporary pacing leads inserted under

fluoroscopic guidance. The study assessed whether this technique could reduce procedure times and achieve stable positions within the right ventricular apex even when inserted by relatively unskilled operators.

(ii) The second study has involved the development and initial evaluation of a single-lead balloon flotation DDD pacing catheter which incorporates Overlapping Biphasic Impulse (OLBI®) stimulation via non-contact atrial electrodes. This lead has been evaluated in patients undergoing electrophysiological studies and in emergency settings. The procedure duration, fluoroscopy time, atrial and ventricular sensing and pacing parameters were measured.

(iii) The third study was a randomised controlled trial of temporary DDD pacing, comparing the single-lead system with standard atrial plus ventricular pacing leads. The procedural and fluoroscopy times, reliability of DDD pacing and lead displacement were compared.

(iv) The fourth study compared the haemodynamic changes of VVI and optimal DDD temporary pacing modes in patients presenting with bradyarrhythmia so as to quantify the haemodynamic benefits of DDD pacing.

CHAPTER 2

Optimising Temporary Ventricular Demand Pacing: A Randomised Trial Of Temporary Cardiac Pacing with Semi-Rigid and Balloon-Flotation Pacing Leads

INTRODUCTION

The incidence of clinical problems related to temporary transvenous VVI pacing remains unacceptably high[23,24] and has been highlighted in the previous chapter. Nevertheless, it is likely that for the foreseeable future this mode of pacing will remain the most commonly utilised mode in patients presenting with symptomatic bradycardias. [4] Many of the clinical problems related to temporary transvenous VVI pacing could be prevented by improved techniques. For instance, (i) more flexible leads may be less traumatic and reduce the risk of arrhythmias or ventricular perforation (ii) improved lead positions within the right ventricular apex may reduce the risk of subsequent displacement (iii) techniques to simplify lead implantation may reduce procedure times (iv) shorter procedure times would reduce exposure to X-rays and also the risk of infection. Currently, the standard insertion technique involves manipulation of semi-rigid electrode catheters under

fluoroscopic guidance into the right ventricle. [5] In this chapter an alternative technique for the implantation of temporary pacing leads is proposed.

In contrast to semi-rigid electrode catheters, balloon-tipped pacing catheters are flow-directed and require minimal manipulation having been designed primarily for introduction at the bedside without fluoroscopy. [59] This technique has been available for over 20 years but has never been widely adopted, partly due to the perception that 'blind' placement will result in unstable catheter positions and an increased risk of displacement. [5] However, balloon-flotation catheters can also be placed under fluoroscopy.

Observational reports suggest that balloon-flotation pacing catheters can be inserted more easily and quickly with fewer complications than semi-rigid catheters, particularly by less experienced operators. [60] Accordingly, a prospective randomised trial of temporary cardiac pacing with semi-rigid and balloon-flotation electrode catheters has been conducted in the coronary care unit. Both leads were inserted using fluoroscopic guidance.

METHODS

Patients

Forty consecutive patients aged ≥ 18 years undergoing emergency or semi-elective temporary ventricular-demand pacing were recruited over a 4 month period in a coronary care unit serving both an acute general hospital and regional cardiac centre. Patients requiring a basilic or femoral venous approach, or atrial/AV sequential pacing were excluded. The study population comprised 20 men and 20 women, mean [SD] age 72(16) years. Indications for temporary cardiac pacing were: high-grade atrioventricular block following acute myocardial infarction (n=15), atrioventricular block without prior myocardial infarction (n=19), sinus arrest (n=1), overdrive termination of ventricular tachycardia (n=5). The study protocol was approved by the Central Oxford Research Ethics Committee and informed consent was obtained in all cases.

Pacing Techniques

The subclavian or internal jugular approach was used for central venous access. Semi-rigid 5F or 6F bipolar pacing catheters (Vygon (UK) Ltd., Cirencester, U.K.) were introduced using standard techniques as previously described. [2] The balloon-flotation pacing catheter (5F PACEL™, Daig Corporation, Minnetonka, MN.) was inserted approximately 10 cm beyond the introducer sheath before inflating the balloon with room air. The catheter could then be advanced across the tricuspid

valve under fluoroscopy and into the right ventricular apex, deflated and the tip wedged into a stable position. If the distal tip passed to the right ventricular outflow tract, it was withdrawn to the tricuspid valve and the balloon deflated before advancing towards the apex. A pacing threshold of ≤ 1.0 V at 2 ms pulse width was considered acceptable. The electrode was secured and a post-insertion chest X-ray was obtained to check the final catheter position.

Protocol

The study design was an open, randomised, parallel group trial with provision for crossover. Eligible patients were randomly allocated to temporary cardiac pacing with either a balloon-flotation or semi-rigid electrode catheter. Procedure duration was measured from insertion of the pacing catheter via the introducer sheath to securing the electrode at the final position (i.e. excluding the time required for central venous cannulation which would be common to both techniques). Fluoroscopy time was also recorded. Pacing threshold was measured at 2 ms pulse width immediately post-insertion, and after 24 and 48 hours. The final catheter position on the post-insertion chest X-ray was classified as 'satisfactory', 'suboptimal' or 'unacceptable' by an independent observer blinded to the randomisation. A satisfactory position was with the electrode tip in the right ventricular apex pointing horizontally or inferiorly, plus an adequate atrial loop (low risk of displacement). A suboptimal but acceptable position was with the electrode tip at the apex but either pointing superiorly and/or with an inadequate

atrial loop. A position was considered unacceptable if the electrode tip had been placed outside the right ventricular apex (high risk of displacement).

Crossover was permitted at the discretion of the operator if cardiac pacing had not been established using the initial catheter after 5 minutes of fluoroscopy, and was required by the protocol after 10 minutes of fluoroscopy.

Statistics

Data are expressed as mean (SD) unless otherwise indicated. Continuous variables have been compared between the two groups by the Mann-Witney U test for non-parametric data and unpaired t test for normally distributed series. Chi-square testing was used for discrete variables. P values less than 0.05 were considered significant. With regard to crossovers, all data has been analysed on intention-to-treat basis except for final catheter positions.

RESULTS

Table 2.1 Patient characteristics

	Semirigid	**Balloon-flotation**
	n=20	*n=20*
Age (yrs) Mean±SD	74±15	70±18
Male:female	11:9	9:11
Indication		
Acute MI	9	6
Chronic AVB	9	10
VT	1	4
Sinus arrest	1	0
Operators		
Cardiology	6	8
GIM	10	9
Resident	4	3

There was no significant difference in any of these variables. Acute MI – Within 72 hours of an acute myocardial infarction; AVB – Atrioventricular heart block; VT – ventricular tachycardia; Cardiology – cardiology registrar; GIM – general internal medicine registrar.

There were no significant differences between the groups with respect to demographic characteristics, pacing indications or operator experience (see Table 2.1). Most of the operators were registrars in general medicine or cardiology. The pacing catheters were left *in situ* for a median duration of 36 hours (range 8 to 118 hours) and 27/40 were removed within 72 hours of insertion. There was no significant difference in duration *in situ* between the balloon-flotation and semi-rigid groups. Cardiac pacing was successfully established with diastolic threshold ≤ 1.0 V in all 40 patients, but crossover was required in 1 patient initially allocated to a semi-rigid catheter and in 2 patients randomised to a balloon-flotation catheter. Both mean procedure duration (867 vs. 427 seconds; $p<0.002$) and fluoroscopy time (328 vs. 153 seconds; $p<0.01$) were substantially longer for the semi-rigid group compared to the balloon-flotation group (see Table 2.2). However, there was no difference in pacing threshold between the groups at implant, 24 hours or 48 hours. Final catheter positions were significantly better in the balloon-flotation group with 14 satisfactory , 5 suboptimal and no unacceptable positions, compared to the semi-rigid group with 1 satisfactory, 12 suboptimal and 7 unacceptable positions ($p<0.0001$).

During follow-up, there were 3 patients in the semi-rigid group who required repositioning of the pacing catheter because of displacement and failure to capture but only 1 patient in the balloon-flotation group. There were no instances of subclinical displacement as evidenced by a sudden rise in pacing threshold of ≥ 2.0 V within 24 hours. There was 1 case of right ventricular perforation in the semi-

rigid group which was successfully managed by removal of the pacing catheter. There were 2 deaths in the semi-rigid group but none in the balloon-flotation group. One death was due to cardiogenic shock and unrelated to pacing. The other death was possibly procedure-related as it occurred during attempted repositioning of a displaced pacing catheter. This patient developed loss of ventricular capture, hypotension and ventricular fibrillation with a prolonged and ultimately unsuccessful attempt at resuscitation.

Table 2.2 Comparison of semirigid and balloon-flotation pacing catheters

	Semirigid *n=20*	**Balloon-flotation** *n=20*
Procedure duration Median(range) seconds	540 (270-3900)	264 (90-2100)*
Fluoroscopy time Median(range) seconds	189 (48-1020)	87 (10-690)‡
Catheter Position		
Satisfactory	2	14
Suboptimum	12	5
Unacceptable	7	0†
Diastolic threshold Mean(SD) Volts		
During implantation	0.6 (0.3)	0.6 (0.2)
Day 2	0.5 (0.3)	0.6 (0.4)
Day 3	0.5 (0.3)	0.6 (0.1)

*p<0.002 vs semirigid catheters. ‡p<0.01 vs semirigid catheters. †P< 0.0001 vs semirigid catheters.

DISCUSSION

This study is the first randomised comparison of the two approaches for temporary transvenous cardiac pacing and it demonstrates that balloon-flotation electrode catheters are significantly easier for junior medical staff to insert than the more

widely used semi-rigid electrode catheters. Procedures with the balloon-flotation pacing catheters were shorter, required less fluoroscopy and were more likely to result in placement of the catheter at a satisfactory final position. One might have expected a corresponding reduction in the risk of catheter tip displacement during follow-up, but this complication only occurred in 4 patients (in 3 cases with semi-rigid catheters and in 1 case with a balloon-flotation catheter). These small numbers precluded statistical analysis and may reflect the relatively short time that the pacing catheters were left *in situ* (approximately 70% were removed within 72 hrs of insertion).

Balloon-flotation pacing catheters were originally designed for insertion at the bedside without X-ray screening. As this 'blind placement' may result in unstable catheter positions[5], this method of temporary pacing has not been generally accepted. Accordingly, fluoroscopic guidance was used in this study to optimise placement of both the flow-directed and semi-rigid wires. Satisfactory placement of the balloon-flotation pacing catheters was achieved rapidly with minimal manipulation in the majority of patients and the use of fluoroscopy allowed immediate identification of 2/20 cases in which pacing could not be established with a balloon-flotation catheter due to persistent passage of the tip into the right ventricular outflow tract. These patients were then successfully paced with a semi-rigid catheter.

Previous Studies

Lang *et al* compared temporary pacing with balloon-flotation and semi-rigid catheters in 111 patients. [60] In their study, although the patient groups were similar in terms of clinical characteristics, treatment was not randomised and the balloon-flotation catheters were introduced via the subclavian or jugular vein whereas the femoral or basilic route was used for semi-rigid wires. As in the present study, placement of a balloon-flotation catheter was successful in most cases (64/67) and the insertion time was significantly shorter than for semi-rigid catheters (405 vs. 810 seconds). Furthermore, catheter tip displacement occurred less frequently with the balloon-flotation catheters (13.4 vs 32.0%) during a mean follow-up of over 4 days. Taken in conjunction with the results of the present study, this suggests that the risk of displacement following fluoroscopically guided placement of balloon-flotation catheters is at least comparable to and probably lower than with conventional temporary pacing using semi-rigid catheters.

Clinical Implications

Most temporary pacing procedures are performed in district hospitals rather than regional centres. Three recent surveys have drawn attention to the unacceptably high incidence of complications and problems that are currently associated with this procedure. Two series looked at patients transferred to a tertiary centre following temporary transvenous pacing in another hospital and reported major problems among 52/145 (36%) and 21/40 (52.5%) of the referrals respectively. [24,61] A prospective study of 194 temporary pacing procedures over a 6 month

period at 18 hospitals within a single region[62] revealed complications or problems affecting 68 patients (35.1%) including catheter displacement in 19.6% and septicaemia in 5.6% of cases. Although some of these problems were related to vascular access, the high incidence of displacement, suboptimal catheter positions and septicaemia may well reflect difficulties encountered at the time of insertion. No data were provided about the proportion of cases that involved prolonged/difficult insertion procedures, but a survey of temporary pacing by general medical senior house officers and registrars demonstrated that 50% of operators had 'failed to position a lead' at least once in the preceding 12 months. [30]

In common with other invasive procedures, there is a learning curve associated with the techniques involved in temporary cardiac pacing. To achieve competence, adequate training and supervision of operators is essential, [62 30] but this can be difficult to implement in smaller district hospitals where temporary pacing procedures occur relatively infrequently and there is a rapid turnover of junior medical staff. Since most of these hospitals do not have the facilities for permanent pacing, temporary pacing catheters are often left *in situ* for longer (pending transfer to a tertiary centre) which adds to the risk of sepsis and lead displacement. Thus, it is even more important that the insertion procedure is as rapid, safe and sterile as possible.

The findings of the this study suggest that routine use of balloon-flotation catheters in conjunction with fluoroscopy may avoid some of the problems associated with

temporary cardiac pacing using conventional semi-rigid electrode catheters. Mean procedure time was reduced by approximately 50% and more catheters were placed in satisfactory positions. This technique may be particularly valuable for operators with no formal training in invasive cardiology. However, further studies would be required to establish whether similar benefits can also be obtained with 'blind' insertion of balloon-flotation pacing catheters.

CHAPTER 3

A Simplified Approach to Temporary DDD Pacing using a Single-Lead, Balloon-Tip Catheter with OLBI® (Overlapping Biphasic Impulse) Stimulation

INTRODUCTION

The first chapter of this thesis included a detailed discussion of how temporary DDD pacing is underutilised in emergency settings, despite the potential clinical benefits in haemodynamically compromised patients. It is likely that the poor uptake of temporary DDD pacing has been partly due to the perceived technical challenge associated with introducing/positioning two electrodes and achieving stable atrial pacing, particularly in very sick patients. In an attempt to overcome these practical difficulties, a single-lead system has been developed for temporary DDD pacing incorporating floating ring electrodes for atrial sensing and overlapping biphasic impulse (OLBI®) pacing. Given the results of Chapter 2, a balloon-tip was included for flow-directed catheter placement in an attempt to reduce procedure times and optimise lead position. This chapter describes the initial experience with these pacing catheters.

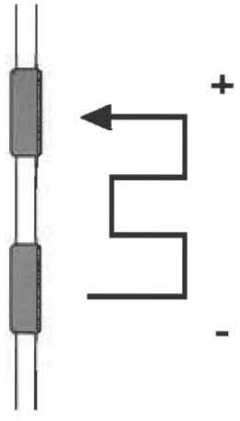
METHODS

Development of the single-lead DDD pacing catheter

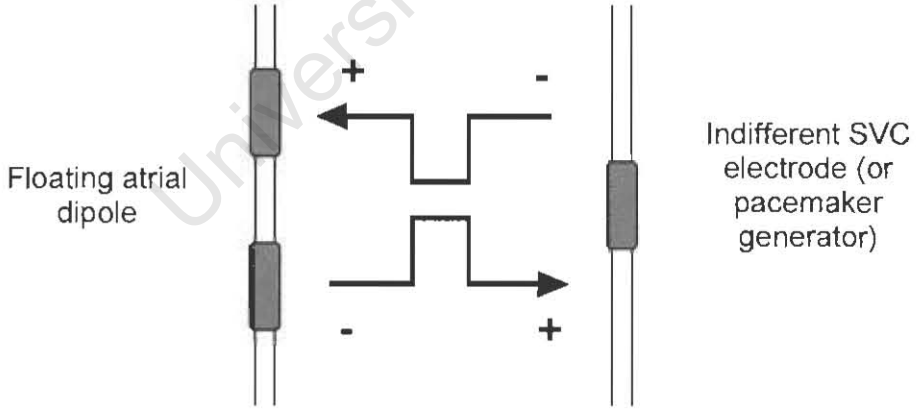
In recent years, efforts have been made to develop a single-lead catheter system for permanent DDD pacing. [63-66] One of the most promising designs is the Biotronik OLBI® system, the key features of which are: (i) reliable sensing of atrial depolarisation via floating electrodes (> 98% of sinus beats), [67] (ii) atrial capture with overlapping biphasic impulses (OLBI®), that is two sequential monophasic impulses of opposite polarity, [68,69] to reduce atrial pacing threshold [69,70] (see Fig. 3.1). As with other single-lead DDD systems, the major restrictions are unreliable atrial capture and/or high thresholds with consequent battery depletion, and inadvertent phrenic nerve stimulation. However, these limitations are less important for temporary DDD pacing because an external generator is used, and one can alter and maintain atrial output at just above capture threshold to minimise the possibility of phrenic nerve stimulation. Accordingly, a temporary single-lead system was developed for use in conjunction with OLBI® pacing, comprising a soft polyurethane, 5F multipolar pacing catheter with one superior vena cava electrode (indifferent), three floating atrial electrodes and two distal ventricular electrodes (see Fig. 3.2). An earlier randomised trial described in Chapter 2, [71] demonstrated that balloon-flotation pacing catheters allow temporary ventricular (VVI) pacing to be established more quickly and reliably compared to conventional semi-rigid catheters with fewer cases of lead displacement or

perforation. Therefore the balloon-tip design (balloon volume 1 ml) was incorporated to facilitate flow-directed placement from either central or peripheral venous access and minimise the risk of right ventricular perforation (see Fig. 3.3 and 3.4). In the first 47 consecutive cases, the pacing catheter was only available with a 14.5 cm spacing between the ventricular and atrial electrodes (see Fig. 3.2). Thereafter, operators had a choice of catheters with a 14.5 or 17.5 cm spacing. The 17.5 cm version was produced to facilitate optimal placement of the atrial electrodes against the lateral right atrial wall in patients with cardiomegaly.

Figure 3.1
Standard Bipolar and Overlapping Biphasic Impulse (OLBI®) Stimulation



Bipolar mode



OLBI® mode

Figure 3.2
Design of the Single-lead, Balloon-Tip Catheter

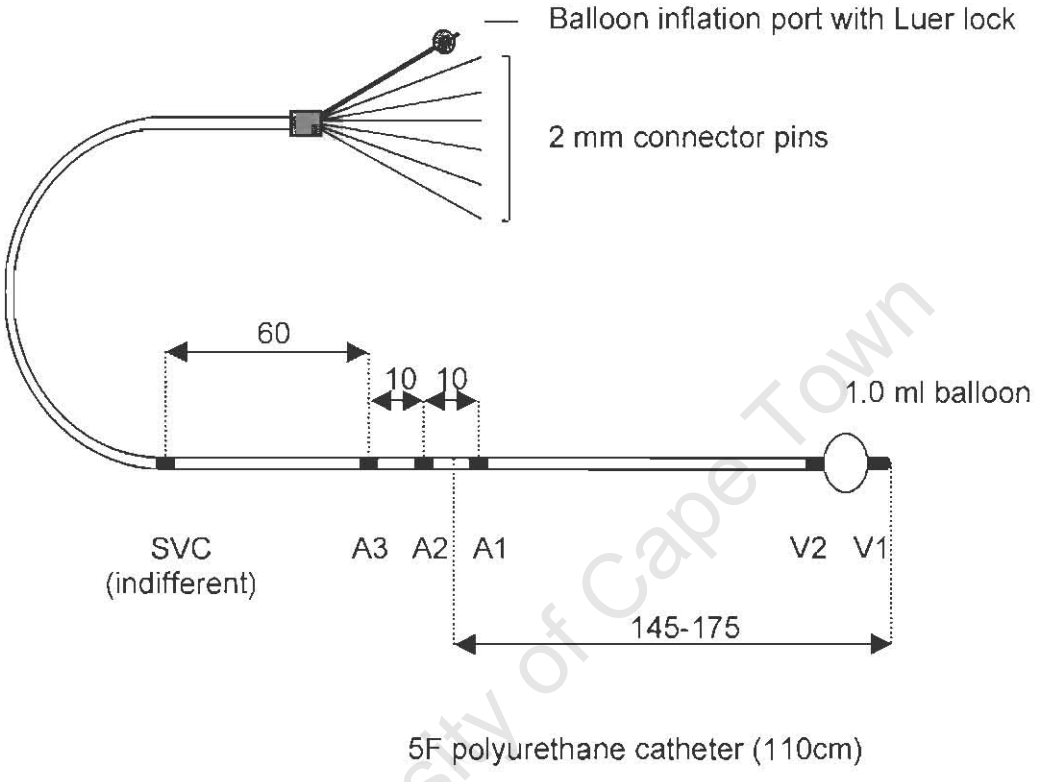


Figure 3.2 Ventricular (V1 and V2), atrial (A1 and A2) and superior vena cava (indifferent) electrodes are labelled. Either proximal (A2+A3) or distal (A1+A2) electrode pairs were used for atrial pacing. Dimensions are in millimetres. Note that there were 2 available electrode catheters with either a 145mm or 175mm spacing between atrial and ventricular electrodes. The drawing is not to scale.

Figure 3.3
Single-Lead, Balloon-Tip Catheter for OLBI® (Overlapping Biphasic Impulse) Stimulation

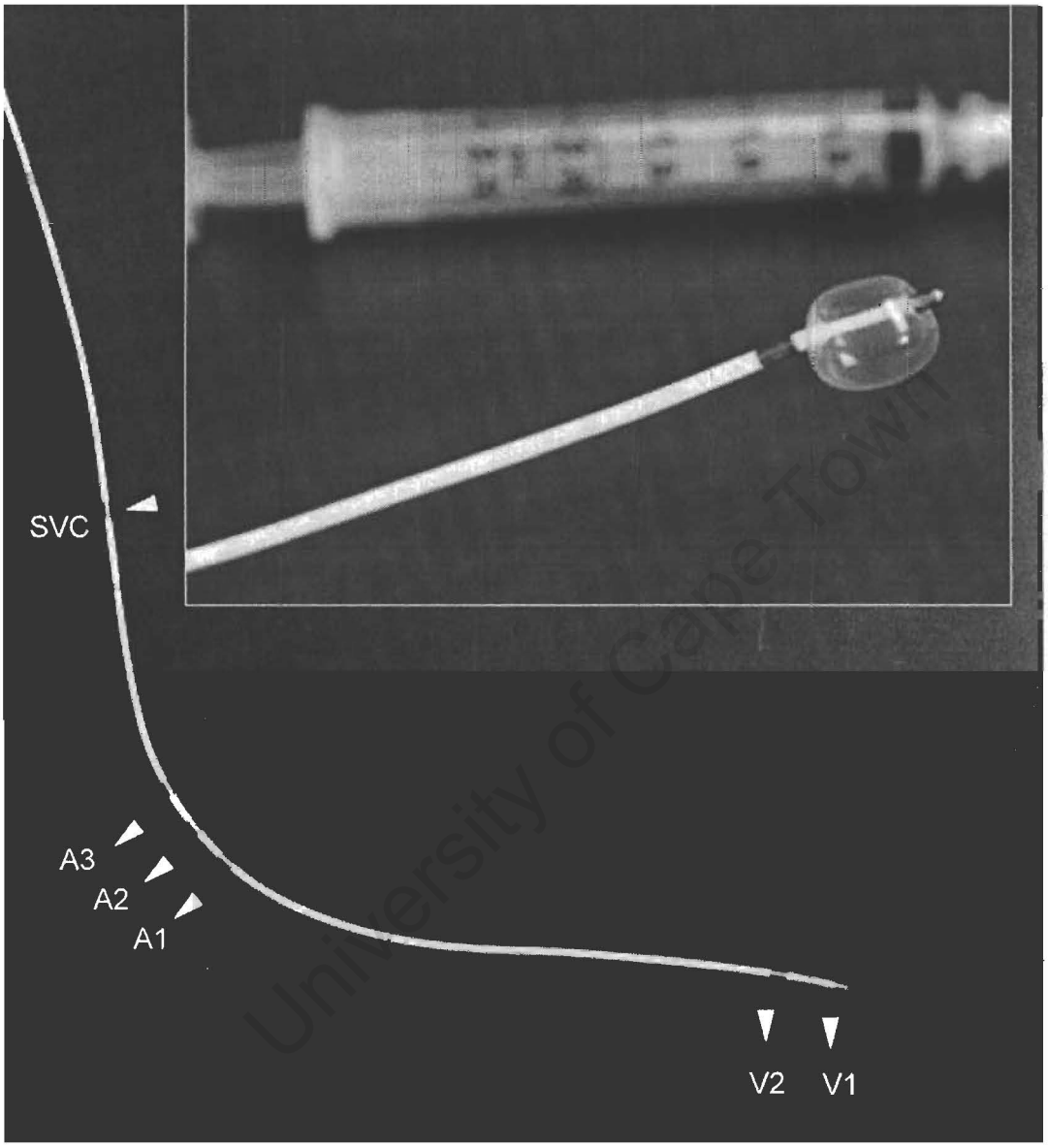


Figure 3.3 Explanted single-lead catheter with inflated 1.0 ml balloon (inset). The balloon tip facilitates flow-directed placement within the right ventricle and the soft polurethane material reduces the risk of ventricular perforation.

Figure 3.4
Chest Radiograph of the Single-Lead, Balloon-Tip Catheter

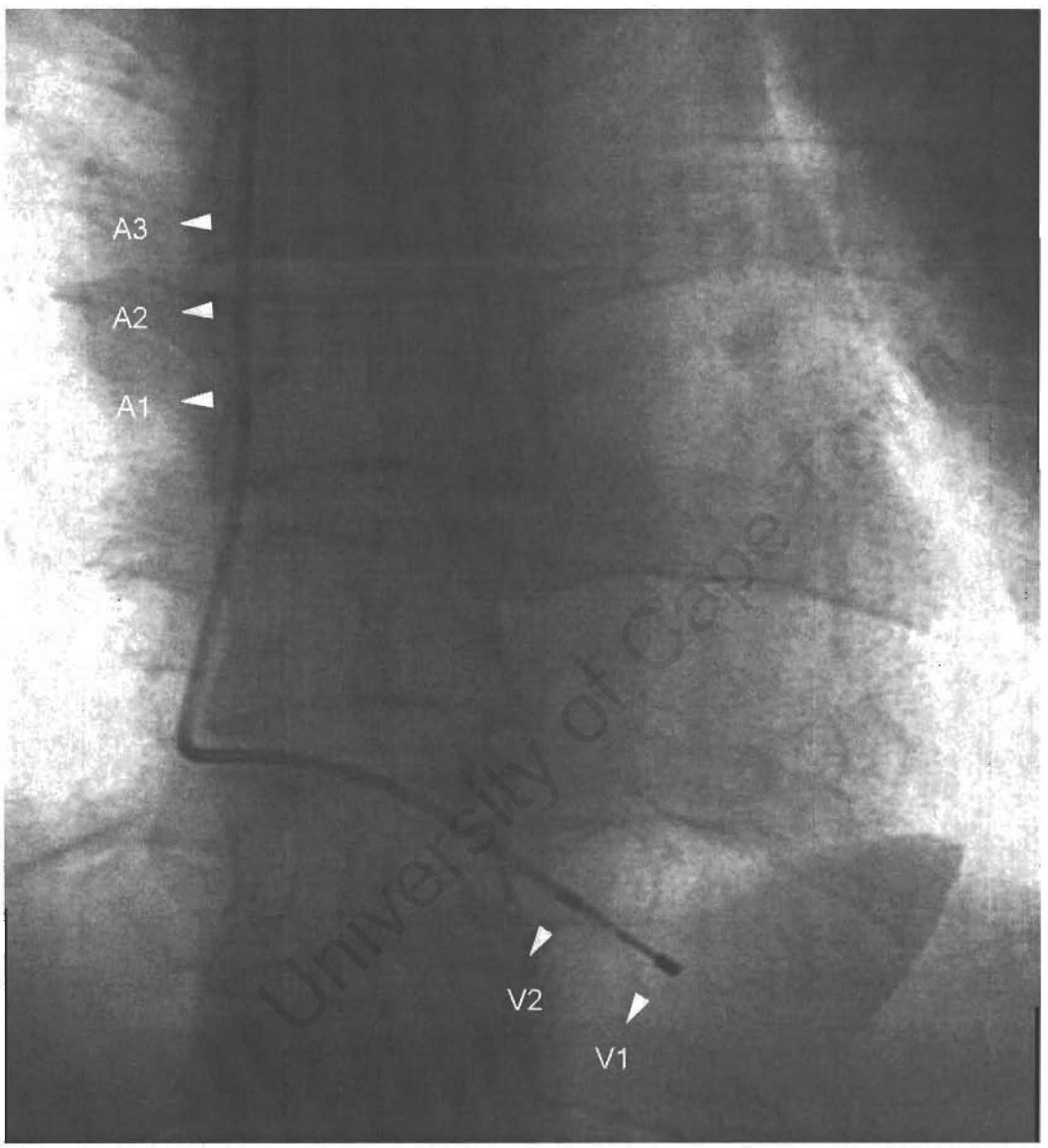


Figure 3.4 Chest radiograph showing the single-lead catheter in-situ. Note the atrial electrodes (A1, A2 and A3) in the high right atrium.

Intellectual property and funding of the study

The concept of incorporating OLBI® stimulation into a temporary pacing catheter for DDD pacing was the idea of Dr Yaver Bashir. The subsequent design and production of our catheter was achieved in collaboration with Dr Keith Channon, Dr Nigel Lever and myself. The intellectual property rights belong to the University of Oxford. The leads were produced to our specification by APC Cardiovascular Products at the cost of two hundred GBP per lead. The costs of this study were met by the Gibson Fund, the research fund of the John Radcliffe Hospital. The specifications and manufacturing process were in accordance with European Union regulations and the catheters were 'CE' marked. Biotronik gave us access to the specifications of their permanent OLBI® leads but were not involved in the initial design or testing of our temporary lead. After our initial reports Biotronik did show interest in the potential utility of this catheter and helped fund the second half of the experiments described in this thesis. To date they have not chosen to take on production of the temporary lead. Neither I nor any of my colleagues mentioned above hold financial interests which conflict with the work published in this thesis.

Adaptation of the Eikos® SLD pacemaker generator for temporary pacing

Electrical parameters were checked at implantation using a pacing system analyser (ERA 300, Biotronik, Berlin, Germany). Currently, there is no commercially available portable generator for temporary OLBI® pacing. Continuous temporary

cardiac pacing was achieved adapting a permanent pacemaker generator (Eikos® SLD, Biotronik, Berlin, Germany). This generator was designed to deliver OLBI® stimulation via a single-pass permanent pacemaker lead. The header has two IS-1 ports, one for ventricular and one for OLBI® atrial pacing. Simultaneous unipolar pulses are delivered via both poles of the atrial ring electrodes. The pacemaker casing forms the opposite pole in each case (see Fig. 3.1). A negative pulse is emitted from the proximal atrial pole and a positive pulse from the distal pole. The resulting electric field concentrates in the right atrium. The Eikos® SLD was adapted for use with the temporary pacing catheter. An adaptor bifurcating cable with an IS-1 pin at one end, was inserted into the pacemaker header. On the other end, were two plugs for attachment to the 2mm connector pins of the catheter shown in Fig. 3.2. The indifferent electrode connector pin was connected to a plug attached to the pacemaker can to complete the OLBI® configuration. A similar bifurcating cable was used for bipolar ventricular pacing.

Both the pacing system analyser and the Eikos® SLD are capable of constant voltage stimulation and all thresholds were measured by lowering the voltage amplitude during constant voltage stimulation at a fixed pulse width.

Study Design

This was an observational study in 74 patients over the age of 18 years. Two groups of patients were included (i) 46 patients undergoing electrophysiological studies/ablation who were in sinus rhythm at baseline (ii) 28 patients who had a clinical indication for temporary pacing. The protocol was approved by the Central Oxford Research Ethics Committee and written, informed consent was obtained in all cases.

Protocol

Venous access was via the subclavian or jugular route using a 5F introducer with a 'locking' haemostatic valve and sterile external protective sheath (Fast-Cath, Daig Corp., Minnetonka, MN). The catheter was introduced and advanced 20 cm before inflating the balloon. The catheter could then be easily advanced across the tricuspid valve and into the right ventricular apex using fluoroscopic guidance. With the balloon deflated, the catheter was further advanced to achieve a stable right ventricular position and to fashion a proximal loop with the atrial electrodes against the lateral wall of the right atrium. Electrical parameters were checked at implantation using a pacing system analyser (ERA 300, Biotronik, Berlin, Germany). After optimising the lead position, the catheter was secured using the locking haemostatic valve, and the external protective sheath was drawn back to cover at least 20-30 cm of the body of the catheter externally, to facilitate later re-positioning of the atrial loop if required. Ambulant patients were allowed to

mobilise if they wished, but assessment of pacing parameters was always performed in the semi-recumbent or supine position.

End-points

(i) Procedure duration including measurement of electrical parameters. (ii) Fluoroscopy time. (iii) Atrial and ventricular sensing parameters (electrogram amplitude) (iii) Atrial and ventricular capture threshold measured at implantation, after 12 hours and then daily until the lead was explanted. Voltage threshold was measured at 0.5 ms pulse width for bipolar stimulation and 1.0 ms for OLBI® stimulation (two simultaneous unipolar pulses of 0.5ms, ie. 1.0ms total). For the atrial electrodes, parameters were assessed via both the proximal and distal pairings and the more favourable measurement was used. Atrial pacing threshold was determined in both bipolar and OLBI® modes. (iv) Threshold of phrenic nerve stimulation in both bipolar and OLBI® modes. Phrenic nerve stimulation was defined as palpable diaphragmatic stimulation.

Statistical Analysis

Results were expressed as mean(SD) or median(range). Comparisons between pacing modes were performed using χ^2 and Fisher's Exact tests. Analysis of variance was used to compare repeated measurements of continuous variables during follow-up. A p value of <0.05 was regarded as significant.

RESULTS

Patient characteristics

The single-lead system was deployed and tested in 74 consecutive patients, 43 male/31 female, mean(SD) age 56.9(17.0) years. 22 patients had atrioventricular conduction abnormalities, 6 had sino-atrial disease, 16 had ventricular tachycardia and 30 patients had paroxysmal supraventricular tachycardia and were in sinus rhythm at implantation. In patients undergoing electrophysiological procedures and/or radiofrequency ablation, temporary cardiac pacing was discontinued 6-8 hours after the procedure unless a standard indication for temporary cardiac pacing persisted (7/16 patients with ventricular tachycardia required continuous overdrive suppression of their ventricular tachycardia). 23 patients had impaired left ventricular function secondary to ischaemic heart disease, 8 patients had recent myocardial infarctions, 7 patients had non-ischaemic cardiomyopathy, 6 patients had significant valvular heart disease and 30 patients had structurally normal hearts.

Procedural times and electrical parameters

The median(range) procedure duration was 6.7(1.2-25) mins, and fluoroscopy time 1.9(0.2-7.8) mins. Electrical parameters are summarised in Table 3.1. The changes in individual patients between implantation and 12 hour follow-up are shown in Figure 3.6. As expected, the voltage threshold for atrial capture in OLBI® mode was approximately 50% of threshold in bipolar mode. The leads remained in-situ for a median duration of 53(6-168) hours. Atrial sensing and pacing were found to be reasonably stable over the follow-up period (see Fig. 3.7).

Table 3.1 Electrical parameters

	Implantation	**Follow-up**	*Significance*
R wave amplitude (mV)	10.3(0.9-37.0)	9.2(2.2-22.3)	*NS*
Ventricular threshold (V)	0.8(0.3-1.6)	1.1(0.4-3.0)	*NS*
Ventricular impedance (Ω)	436(264-504)	473(286-724	*NS*
P wave amplitude (mV)	1.6(0.4-4.5)	1.3(0.3-3.6)	*NS*
Atrial threshold (OLBI®)	2.1(0.7-5+)	2.6(1.0-3.8)	*NS*
Atrial threshold (Bipolar)	3.6(1.6-10+)	4.0(1.5-7.3)	*NS*
Atrial impedance (Ω)	332(309-358)	366(278-420)	*NS*

Parameters are expressed as median(range)

Pacing thresholds and phrenic nerve stimulation

Stable VDD pacing (i.e. atrial sensing) could be obtained in all cases throughout the study period. Phrenic nerve stimulation was the main limitation on atrial and DDD pacing. Atrial capture could be achieved in 73/74 of cases with both modes at maximum output but was precluded by phrenic nerve stimulation at outputs below atrial capture threshold in 3/74 patients with OLBI® and 10/74 patients with bipolar mode ($p = 0.04$). In addition, whenever PNS was detected at outputs of <1.0V above atrial capture threshold at implantation, changes in posture (such as sitting upright, or deep inspiration) would frequently result in troublesome PNS

during follow-up, even if outputs were kept just above capture threshold. This phenomenon of clinically important PNS at <1.0V above atrial capture threshold was observed in another 3 patients in OLBI® mode and another 9 patients in bipolar mode. Thus, at outputs at least 1.0 V above atrial threshold, reliable DDD pacing without clinically significant PNS could be achieved in 67/74 (91%) patients with OLBI® stimulation compared to 53/74 (72%) patients in standard bipolar mode ($p = 0.003$).

Far-field Sensing

In 3 patients with the 14.5 cm spacing between atrial and ventricular electrodes we detected far-field sensing of ventricular depolarisation via the atrial electrodes during implantation. In 2/3 cases this effect could be eliminated by changing the atrial sensitivity. In one case the amplitude of the atrial electrogram was less than that of the far-field ventricular signal and the lead needed to be repositioned with the tip of the lead in a more proximal inflow tract position. There were no cases of far-field sensing of the atrial signal via the ventricular electrodes with inappropriate inhibition of ventricular pacing even at maximal outputs.

Repositioning of the atrial loop

Minor adjustment of the atrial loop without fluoroscopy (usually advancing the lead body 2-3cm within the protective sheath) was required in 15 cases during follow-up either for suboptimal atrial electrical parameters or phrenic nerve stimulation. These problems most commonly arose when the patient sat up. In 3

cases, 'blind' repositioning was insufficient to prevent PNS and fluoroscopic guidance was required to improve parameters.

Complications

There were no major complications either at implantation or during follow-up. Specifically, there were no cases of ventricular perforation or acute ventricular lead displacement (although 3 patients required repositioning of the catheter because of rising ventricular thresholds). There were no definite cases of systemic sepsis although one patient developed an unexplained pyrexia which resolved within 24 hours of removing the pacing catheter (multiple blood cultures negative).

DISCUSSION

This study demonstrates that a flow-directed, single-lead pacing catheter with floating atrial electrodes can be rapidly, easily and safely deployed to establish reliable temporary VDD pacing in almost all patients, and DDD pacing in the majority. Moreover, stable atrial sensing and pacing were sustained over a median follow-up period of 53 hours. Although repositioning of the atrial loop was required in approximately 25 percent of cases to maintain optimum atrial electrical parameters or to avoid phrenic nerve stimulation, in most patients this was achieved by minor adjustment of the lead body within its protective sheath at the bedside – fluoroscopically guided repositioning was only required in 3 cases. Failure of DDD pacing, either due to high atrial threshold or intolerable phrenic nerve stimulation at or below atrial threshold, was commoner with standard bipolar stimulation. At atrial outputs at least 1.0 V above PNS threshold (to avoid clinically significant phrenic nerve stimulation during follow-up) atrial pacing could be achieved in 67/74 (91%) of patients using OLBI® mode but in only 53/74 (72%) using bipolar stimulation.

OLBI® Stimulation for Single-Lead DDD Pacing

Several studies have demonstrated the efficacy of permanent VDD(R) pacing with single lead systems for treatment of patients with AV block but preserved sinus

node function. [63,72,73] By contrast, single-lead DDD pacing via floating atrial electrodes is often limited by high atrial thresholds or phrenic nerve stimulation using standard bipolar or unipolar stimulation. Recently, a new stimulation mode employing two sequential unipolar pulses of opposite polarity (OLBI®) has been shown to reduce atrial pacing threshold in experimental animals, possibly by concentrating current density at the endocardial surface, but without changing the threshold for phrenic nerve stimulation. [70] Clinical studies in patients undergoing permanent pacemaker implantation with a single lead have confirmed that OLBI® mode can reduce atrial threshold with a wider safety margin for phrenic nerve stimulation. [68,69] However, the technique is still limited by unreliable atrial capture during long-term follow-up in ≥ 25% of patients, the effects of changes in posture on atrial sensing/pacing, an unacceptable incidence of phrenic nerve stimulation with output set at twice atrial threshold, and high current drain (3-6 times greater than pacing via conventional atrial leads). Given that permanent DDD pacing can be achieved so reliably and easily using standard techniques with two electrodes, single lead permanent DDD pacing could be characterised as a partial solution to a non-existent problem. By contrast, these limitations are less important for temporary DDD pacing. (i) Current drain is not an issue. (ii) If necessary the output can be maintained at just above atrial threshold to limit phrenic nerve stimulation, even if this requires adjustment from time to time. (iii) Most patients requiring emergency DDD are restricted to bed and maintained in the supine or semi-recumbent position. (iv) It is easy to make minor adjustments to the atrial loop at the bedside (without fluoroscopy) by advancing or withdrawing

the catheter within its protective sheath if the patient manifests loss of atrial capture or diaphragmatic pacing.

Previous Studies

There have been no other published reports of temporay DDD pacing via a single-lead system. However, Voiglander et al[74] evaluated temporary transvenous VDD pacing in 22 patients with high-grade AV block using a semi-rigid, single-lead pacing catheter with the atrial dipole 13 cm proximal to tip. As in our study, VDD pacing could be achieved in all cases and maintained over mean follow-up of 14.1 hours with just transient loss of AV synchrony in 4/22 cases due intermittent undersensing. DDD pacing was not assessed. Newby et al[75] evaluated a single-lead multipolar pacing catheter in 15 patients during intracardiac electrophysiology studies. The catheter incorporated four pairs of atrial electrodes at 11.5-14.5 separation from the tip. Atrial capture could be achieved in 12 cases using conventional bipolar and unipolar stimulation but there was no follow-up.

Clinical Implications

Temporary DDD pacing is much less commonly used in the emergency setting than ventricular-demand (VVI) pacing, despite the potential haemodynamic benefits. VVI pacing increases heart rate without restoring AV synchrony and may not improve cardiac output, [32-36] particularly in patients with abnormal ventricular compliance such as those with acute myocardial infarction (MI), aortic

stenosis, or chronic left ventricular dysfunction. Studies with permanent dual chamber pacemakers have consistently shown that DDD mode results in an immediate increase in stroke volume, cardiac output and mean arterial pressure compared to VVI mode, [34,42,43] even in haemodynamically stable patients. Several groups have reported significant improvements in cardiac output, blood pressure and filling pressures with temporary AV sequential pacing compared to VVI pacing in complete heart block complicating acute MI, [44-48] although the number of patients studied was small. Other acutely ill patients with impaired diastolic function are also likely to benefit. [32,49-51]

It is likely that practical difficulties have precluded widespread uptake of emergency DDD pacing. Introducing two electrodes and achieving a stable atrial position can present a formidable technical challenge in sick patients, who are frequently shocked and/or requiring artificial ventilation on the intensive care unit. Even then, temporary atrial electrodes exhibit a notoriously high incidence of displacement requiring repositioning (often of both leads). Moreover, the requirement for prolonged/repeated cardiac instrumentation inevitably leads to increased risks of sepsis, pulmonary oedema, asystole, cardiac arrest[57,58] etc.).

Such practical issues could be addressed and minimised by the use of single-lead systems for emergency DDD pacing. The balloon-tip design facilitates flow-directed/assisted placement of the ventricular electrodes at the right ventricular apex with minimal risk of perforation , even in the context of acute infarction. The

protective repositioning sheath allows minor adjustments of the atrial loop position at the bedside without fluoroscopy and while maintaining asepsis. Although VDD mode may be adequate for restoring AV synchrony in patients with heart block and normal sinus node function, the ability to achieve DDD pacing is essential for cases involving asystole or sinus/junctional bradycardia, and some patients with cardiogenic shock may even require AV sequential pacing at supraphysiological rates. In one recent study of emergency DDD pacing[49] in a heterogeneous population of patients admitted to the intensive care unit or coronary care unit of a university hospital, fewer than 50% would have been suitable for VDD pacing alone.

Future Research

This was only a preliminary investigation to establish the feasibility of temporary transvenous DDD pacing using the single-lead system. Nevertheless, our encouraging results suggest that the technique could simplify and transform the practice of emergency cardiac pacing, offering significant clinical benefits to haemodynamically compromised patients with bradyarrhythmias. However, the potential advantages of the single-lead approach need to be established by a prospective randomised comparison with conventional techniques for temporary DDD pacing.

CHAPTER 4

A Randomised Trial of Temporary DDD Pacing using Conventional (Atrial plus Ventricular) Pacing Leads or a Single-Lead Catheter Incorporating Atrial Dipoles for Overlapping Biphasic Impulse (OLBI®) Stimulation.

INTRODUCTION

The conventional technique for temporary DDD pacing currently involves the implantation of separate atrial and ventricular leads using fluoroscopic guidance (see Chapter 1). An alternative technique for temporary DDD pacing using a single-lead, balloon-flotation system was described in Chapter 3. This system can be inserted quickly with minimal fluoroscopy and achieve stable atrial capture in 91 percent of patients. [76] Following these encouraging results, a randomised controlled trial was performed comparing this single-lead system with conventional (atrial plus ventricular) pacing leads for temporary DDD pacing. It was our hypothesis that emergency DDD pacing with the single-lead system is (i)

quicker and easier to achieve, and (ii) at least as reliable as the conventional technique for emergency DDD pacing with separate atrial plus ventricular leads.

METHODS

Study design

This was a prospective, randomised controlled, open-labelled trial. Eligible patients included consecutive patients over 18 years who presented with symptomatic bradycardia (sinus or atrioventricular node disease) or recurrent ventricular tachycardia and in addition, had an indication for temporary DDD pacing including: (i) hypotension (systolic BP<90mmHg), (ii) congestive cardiac failure (clinical and radiological), (iii) myocardial infarction <72 hours prior to pacing, (iv) severe valvular heart disease. Patients with atrial tachyarrhythmia, severe electrolyte abnormalities or drug intoxication which could effect capture thresholds were excluded from the study. The protocol was approved by the Central Oxford Research Ethics Committee.

The pacing group was allocated using sealed unmarked envelopes. Patients were randomised to receive either the single-lead catheter or conventional (atrial and ventricular) pacing leads. Accordingly, one or two introducer sheaths were inserted via either the subclavian or supraclavicular route. In the conventional group a single venous puncture with a retained guide wire was used in the majority of

cases to minimise the complications of venous access. Both the single-lead balloon flotation catheter and the conventional (atrial and ventricular) leads were inserted under fluoroscopic guidance.

Implantation techniques

A 6 French introducer sheath with a 'locking' haemostatic valve and sterile external protective sheath (Fast-Cath, Daig Corp., Minnetonka, MN) was used for all leads.

(i) The single-lead balloon flotation system was introduced and advanced 20 cm before inflating the balloon. The catheter could then be advanced across the tricuspid valve and into the right ventricular apex using fluoroscopic guidance. The balloon was then deflated and the catheter advanced further into the apex of the right ventricle. A loop was fashioned in the right atrium to position the atrial electrodes in the mid or high right atrium close to the lateral wall.

(ii) The conventional leads included a 5 French balloon-flotation ventricular lead (PACEL™, Daig Corporation, Minnetonka, MN) implanted using the balloon flotation method described above to cross the tricuspid valve and fluoroscopy to optimise the position within the right ventricular apex. [77] A 5 French atrial temporary pacing lead with a preformed J-curve (Sulzer Osypka, Grenzach-Wyhlen, Germany) was introduced into the mid right atrium with the straight stylet advanced to the tip of the lead. The stylet was then withdrawn 5-8cm to allow the 'J-curve' to form and the tip was then positioned within the right atrial appendage.

Electrical parameters were checked at implantation using a pacing system analyser (ERA 300, Biotronik, Berlin, Germany). After optimising the lead position and checking stability during deep respiration and cough, the catheter was secured using the locking haemostatic valve, and the external protective sheath was drawn back to cover at least 20-30 cm of the body of the catheter externally, to facilitate later re-positioning if required.

Pacing protocol

After assessing the initial electrical parameters, patients were paced continuously in DDD mode at a minimum rate of 80bpm and a maximum tracking rate of 120bpm. The single lead system was attached to an explanted adapted pacemaker generator (Eikos SLD, Biotronik, Berlin, Germany) to enable continuous OLBI® atrial and bipolar ventricular pacing. The conventional leads were attached to a temporary dual chamber pacing generator (ERA 300B, Biotronik, Berlin, Germany) to provide standard bipolar DDD pacing. The outputs were set at 2.0 V above capture threshold or at maximum output of 5.0 V at a pulse width of 1.0 ms (total for both pulses) for OLBI® and of 10.0 V at 0.5ms for the bipolar mode. If phrenic nerve stimulation was detected the output was carefully reduced to minimise phrenic nerve stimulation but still maintain atrial capture. Patients were allowed to move to a semi-recumbent position if they wished, but assessment of pacing parameters was always performed in the supine position. In patients who moved from supine to semi-recumbent position, atrial pacing parameters could be

optimised by minor adjustment of the lead within the sterile sheath at the bedside without fluoroscopic guidance.

Major end-points

(i) Procedure duration, measured from introduction of the lead into the venous sheath to securing it after insertion including catheter positioning and baseline electrical testing. (ii) Fluoroscopy time. (iii) Atrial and ventricular diastolic threshold and sensing parameters measured at implantation. Voltage threshold was measured at 0.5 ms pulse width for bipolar stimulation and 1.0 ms (total) for OLBI® stimulation. For the atrial electrodes of the single-lead system, parameters were assessed via both the proximal and distal pairings and the more favourable measurement was used. (iv) Incidence of lead displacement and repositioning. Lead displacement was defined as a loss of AV synchrony requiring fluoroscopic re-positioning of the lead.

Minor end-points

(i) Venous cannulation time, measured from insertion of the introducing needle into the skin to completed insertion of either one or two venous sheaths. (ii) Assessment of appropriate AV synchrony ('subclinical' atrial lead malfunction) on continuous ECG telemetry performed in the first hour after implantation. (iv) Incidence and threshold of phrenic nerve stimulation in both bipolar and OLBI®

modes. (i) Incidence of adverse events including: myocardial perforation, septicaemia, cardiac arrest etc.

Statistical analysis

All variables were expressed as median (range). Continuous variables have been compared between the two groups by the Mann-Witney U test for non-parametric data and unpaired *t* test for normally distributed series. χ^2 testing was used for discrete variables. Comparison of procedure times was performed using the unpaired *t* test. A *p* value of less than 0.05 was considered significant.

RESULTS

Patient characteristics

Temporary DDD pacing was performed in 40 consecutive patients, 25 male and 15 female, median(range) age of 73(48-96) years. The indication for temporary pacing was atrio-ventricular block in 21 patients, sino-atrial disease in 8 patients and recurrent ventricular tachycardia in 11 patients. All patients had at least 1 definite indication for temporary DDD pacing (see Table 4.1). Twenty patients were allocated to each of the conventional and single-lead groups. Baseline clinical characteristics were similar in the two groups although there were more patients with hypotension, heart failure and myocardial infarction in the single-lead group.

Table 4.1 Patient characteristics

	Conventional *n=20*	**Single-lead** *n=20*	**Total** *n=40*
Age (Years)	75(48-92)	71(46-96)	73(46-96)
F:M	7:13	8:12	15:25
Hypotension	7	12	19
CCF	7	14	21
Oliguria	8	9	17
Confusion	3	4	7
Diabetic	1	0	1
MI	5	10	15
Valve disease	1	2	3
Ventricular arrhythmia	5	6	11
Rhythm			
Sinus	5	6	11
SA disease	4	4	8
Heart block	11	10	21

Hypotension - Systolic blood pressure <90mmHg; CCF - Congestive cardiac failure; MI - Myocardial infarction < 72hours prior to pacing; Oliguria - Urine output of < 30ml/hr; SA - sino-atrial disease.

Procedure times

Catheter manipulation and fluoroscopy times in the single-lead group were less than half of those in the conventional group (see Table 4.2). The insertion of a single venous sheath for the single-lead group was more rapid than for two sheaths for the conventional group. The internal jugular route was used in 2 patients in the single-lead group and the subclavian route was used in all other patients. There were no complications of venous access in either group.

Table 4.2 Procedure times (minutes)

	Conventional *n=20*	**Single-lead** *n=20*	*Significance*
Venous Access	6.9(2-35)	4.4(0.5-12)	*0.04*
Catheter manipulation	31.8(16-50)	7.2(2.1-12)	*< 0.001*
Fluoroscopy	7.5(2.7-19)	1.4(0.2-5.8)	*< 0.001*
Total Procedure Time	37.2(20-70)	11.6(6-20)	*< 0.001*

Electrical parameters at implantation

Reliable atrial capture could not be achieved even at maximum output in 1 patient in the single-lead group and 2 patients in the conventional group. The median atrial capture threshold with the conventional bipolar mode was much less than the OLBI® mode (1.6[0.3-8.6] vs. 3.8[1.4-5.7] Volts, p=0.009). Atrial electrogram amplitude sensed via the conventional lead was greater than via single-lead system

(2.5[0.3-3.2] vs. 1.0[0.3-3.9] mV) although this difference did not reach significance. In all cases a stable atrial electrogram of >0.3mV was achieved at implantation. There was no difference in the ventricular sensing or capture thresholds between the two groups (see Table 4.4). Phrenic nerve stimulation could be demonstrated at outputs >1 Volt above diastolic threshold in 2 patients in the single-lead group but could be avoided by keeping outputs just above threshold.

Table 4.3 Pacing achieved

	Conventional *n=20*	**Single-lead** *n=20*	*Significance*
Implantation			
Atrial capture	19	18	*NS*
Ventricular capture	20	20	*NS*
AV synchrony* (%)	95.3 (78-100)	96.2 (80-99)	*NS*
Follow-up			
Pacing duration (hours)	120 (24-192)	108 (8-192)	*NS*
Lead displacement**	7	1	*0.04*

AV synchrony* was defined as the percentage of beats exhibiting appropriate AV synchrony observed on continuous telemetry during the first hour after temporary lead insertion. Patients in whom atrial capture had not been achieved were excluded from this analysis.

Lead displacement** was defined as loss of AV synchrony requiring fluoroscopic repositioning/re-siting

Table 4.4 Electrical parameters at implantation.

	Conventional *n=20*	**OLBI®** *n=20*	*Significance*
R wave	8.7(7-19)	8.4(3.5-18)	*NS*
V thresh	1.2(0.6-2.1)	1.0(0.4-1.6)	*NS*
P wave	2.5(0.3-3.2)	1.0(0.3-3.9)	*NS*
A thresh (bipolar)	1.6(0.3-8.6)	3.8(1.4-5.7)	*0.009*
A thresh (OLBI®)	-	1.2(0.8-3.8)	-

Telemetry

Analysis of continuous ECG telemetry in the first hour following implantation demonstrated appropriate AV synchrony in 95.3 (78-100) and 96.2 (80-99) percent of recorded beats in the conventional and single-lead groups respectively (p=NS). The 3 patients in whom atrial capture was not achieved were excluded from this analysis. Ventricular pacing and sensing was completely reliable in both groups during this same period.

Lead displacement

Lead displacement with loss of either atrial or ventricular capture occurred in 7 patients in the conventional group and 1 patient in the single-lead group (p=0.02). In 6/8 cases the displacement occurred within 24 hours of implantation. In the

conventional group displacement of the atrial lead alone occurred in 3 cases, both atrial and ventricular leads in 2 cases and ventricular leads alone in 2 cases. The lead displacement in the single-lead group involved loss of both atrial and ventricular capture. Repositioning of the conventional atrial lead failed in 2/3 cases and new atrial leads were implanted. Repositioning of the single-lead system was successful and a new lead was not required. The time to reposition the conventional leads required an average of 29 minutes and 4.5 minutes of fluoroscopy. In all 3 of these cases both atrial and ventricular leads required repositioning. The time required to reposition one of the single-lead system was 4 minutes with 1.2 minutes of fluoroscopy.

Complications

The median duration of pacing therapy in the conventional group was 120(12-192) hours compared to 108(8-192) hours in the single-lead group (p=NS). In the conventional group, 1 patient had a VF arrest and was successfully resuscitated during insertion of the ventricular lead, 1 patient developed septicaemia 5 days following temporary pacing, 1 patient lost consciousness during prolonged ventricular standstill when the ventricular lead displaced and 1 patient developed atrial fibrillation 6 hours after pacing. In the single-lead group, 1 patient required external pacing after dislodgement of the lead, 1 patient developed atrial fibrillation 12 hours after pacing lead insertion and no patients developed fever or sepsis.

DISCUSSION

Over the last two decades many new temporary pacing leads have been designed but none of them have been rigorously tested against conventional techniques. This is the first prospective randomised controlled trial comparing two techniques for temporary DDD pacing. The study was performed in an emergency clinical setting in which patients with an indication for temporary pacing and evidence of haemodynamic instability underwent temporary DDD pacing using either the single-lead system or conventional atrial and ventricular leads. The single-lead system could be inserted more quickly and with less fluoroscopy than the conventional leads, it was equally effective in achieving AV synchrony at implantation but was less likely to subsequently displace.

This study illustrates how the implantation of conventional atrial and ventricular leads can present a formidable challenge. Insertion of the ventricular lead was not usually problematic but positioning the atrial lead into the right atrial appendage was considerably more difficult. Even if a stable position within the right atrial appendage was achieved, the temporary atrial leads had a high incidence of displacement. There are a number of factors which might explain this. [4] (i) Unlike permanent atrial leads, temporary leads do not have tines to maintain the position of the lead tip. (ii) When temporary leads warm up in the circulation, they tend to loose 'memory' of the preformed J-curve further reducing the stability of the lead. (iii) Too much torque on the semi-rigid lead body whilst securing the lead

externally can rotate the tip out of the atrial appendage. When the atrial leads displaced, reliable atrial sensing and capture was lost. Not only did this result in loss of the haemodynamic benefit of AV synchrony but atrial undersensing or intermittent loss of capture also provoked arrhythmia. One patient with a displaced atrial lead developed atrial fibrillation and in another patient the atrial lead prolapsed out of the atrial appendage and into right ventricle causing inappropriate ventricular pacing and runs of non-sustained ventricular tachycardia.

In contrast to conventional atrial leads, the single-lead system appears to be much less prone to displacement. This lead has a floating dipole for atrial pacing using the OLBI® mode and does not require contact with the atrial wall. Providing the ventricular tip did not displace, the atrial dipole remained remarkedly stable in the body of the right atrium as the lead traversed from the superior vena cava through the tricuspid valve to the right ventricle. There appear to be small changes in the position of the dipole relative to the atrial wall during normal respiration or changes in posture but the pacing output could be adjusted to maintain reliable atrial capture without phrenic nerve stimulation in 19/20 patients. In this study only one single-lead system displaced when the lead was inadvertently pulled back by the patient.

There was an obvious difference in repositioning the displaced conventional leads and the single-lead system. Repositioning of the displaced conventional leads typically required a prolonged procedure. The atrial and ventricular leads

commonly interfered with each other during repositioning. It invariably required manipulation of both atrial and ventricular leads with fluoroscopic guidance and usually required the introduction of a new atrial lead to achieve a stable atrial position. In contrast, the single–lead system exhibited a high degree of reliability during follow-up and repositioning of the displaced temporary lead was relatively simple.

Compared with the initial evaluation of the single-lead system described in Chapter 3, the patients in this study had more haemodynamic instability and yet the performance of the single-lead system compared favourably in the two patient populations. Procedure times of 6.7(1.2-25) vs. 7.2(2.1-12) minutes and fluoroscopy times of 1.9(0.2-7.8) vs. 1.4(0.2-5.8) minutes were very similar in the Chapter 3 and 4 studies respectively. In the previous study, reliable atrial capture without phrenic nerve stimulation was achieved in 67/74 (91%) patients. In this study, atrial capture was achieved in 19/20 (95%) patients and appropriate AV synchrony was maintained in 96 percent of recorded heartbeats immediately after implantation.

In patients with heart failure the effects of different procedure times was striking. The single-lead system was inserted and tested very quickly and the implantation procedure was well tolerated in all patients, including those with heart failure. In contrast, many patients with heart failure did not tolerate the implantation of the conventional leads. Several of them developed significant hypoxia after prolonged

periods of lying supine and one patient had ventricular fibrillation during a prolonged and difficult procedure. Furthermore, prolonged procedures are more likely to be associated with sepsis and other complications.

Only a single venous puncture was required for insertion of the single-lead system which was preferable to the two punctures required for conventional leads, particularly in patients with recent myocardial infarction treated with thrombolytic therapy or antiplatelet agents. The single-lead system was inserted via the antecubital vein in 8 patients not included in this trial and successfully positioned in the right ventricular apex in 7/8 patients. This route could further reduce the risk of venous puncture in patients with abnormal clotting who require temporary DDD pacing.

Clinical Implications

This study has demonstrated some of the difficulties that may be encountered with temporary DDD pacing using conventional atrial and ventricular leads. Implantation procedures are long, difficult and poorly tolerated by some patients. Even if a stable atrial position is achieved, temporary atrial leads still exhibit a high incidence of displacement and are subsequently difficult to reposition. Considering these difficulties, it is not surprising that many physicians do not attempt temporary DDD pacing but elect to use VVI pacing exclusively, even in patients with haemodynamically instability.

By comparison, the single lead system provides a simple and rapid technique for temporary DDD pacing and can maintain reliable AV synchrony for several days. The clinical implications of these findings are interesting. In patients with bradycardia and haemodynamic instability temporary DDD pacing is likely to offer greater benefit than VVI pacing alone and it appears from this study that these patients would tolerate implantation of the single-lead system. As the single-lead technique is comparable to the insertion of a ventricular lead for VVI pacing, even physicians with relatively little experience in positioning atrial pacing leads would be able to achieve temporary DDD pacing. Pacing the atrium at rates of 80-90 bpm is helpful in suppressing ventricular tachycardia in some patients refractory to initial medical therapy. The single-lead system is well suited to maintaining reliable atrial capture and also to overdrive pacing for termination of monomorphic ventricular tachycardia in such patients.

This study has examined the differences in two different techniques for temporary DDD pacing but has not looked at the clinical effects of DDD pacing in these patients. There is currently little data available describing the haemodynamic effects of temporary DDD pacing in acute settings and we do not know which patients we should select for this procedure. More trials are required and the single-lead system could facilitate temporary DDD pacing in a wide range of clinical settings without exposing patients to prolonged procedures or unnecessary venous puncture.

CHAPTER 5

A Comparison of the Effects of VVI and Optimal DDD Pacing Modes on the Cardiovascular Function of Patients Requiring Temporary Cardiac Pacing.

INTRODUCTION

Recent advances in temporary pacing lead design, including our own single-lead system, allow temporary DDD pacing to be achieved relatively simply and quickly. It is now possible to study the effects of AV sequential pacing in a wide range of acute clinical settings without subjecting patients to additional venous puncture or to prolonged implantation procedures. A better understanding of the effects of temporary DDD pacing in different clinical settings may help physicians to identify patients who are likely to benefit from this more sophisticated mode of temporary pacing. A prospective study was performed to quantify the effects of different pacing modes on the cardiovascular function of consecutive patients requiring temporary cardiac pacing.

METHODS

Study design

This was a prospective observational study of patients undergoing temporary cardiac pacing at the John Radcliffe Hospital. The decision to perform temporary cardiac pacing was made by the admitting physician and standard temporary cardiac pacing indications were observed. All patients underwent temporary DDD pacemaker implantation of either the single-lead system described in chapters 3 and 4, or conventional atrial plus ventricular leads. 'Within' patient comparison of VVI and DDD pacing modes could then be performed. The protocol was approved by the Central Oxford Research Ethics Committee and informed consent was sought in all cases.

Objectives

(i) To compare the effects of VVI and optimal DDD pacing on cardiovascular function. (ii) To test the hypothesis that optimising the AV delay will improve cardiovascular function during emergency DDD pacing. (iii) To examine the effect of a number of clinical variables on these changes in cardiovascular function. These variables included age, initial heart rate, left ventricular end diastolic dimension and ejection fraction. Markers of haemodynamic instability included recent myocardial infarction (within 72 hours of pacing), hypotension (systolic BP<90mmHg), congestive cardiac failure (clinical and radiological) and severe valvular heart disease.

Protocol

After reliable DDD pacing was achieved, measurements of cardiovascular function including transthoracic Doppler echocardiography were performed. Measurements were taken at baseline (pacing switched off or VVI mode at 40 bpm if pacing dependent), in VVI mode and DDD mode at three AV delay settings (50, 100 and 150 ms). The order of the pacing modes was randomised. Measurements were obtained after at least 2 minutes of continuous pacing in each mode to allow for stabilisation. Thereafter, patients were left pacing in DDD mode at the AV delay resulting the highest cardiac power output.

Doppler echocardiographic methods

Transthoracic echocardiography was performed using a Hewlett-Packard 5500 Sonos and 2.5MHz transducer in left lateral decubitus position. A full transthoracic echocardiographic examination was performed and included quantification of LV dimensions and ejection fraction (Simpson's rule), LV wall thickness and identification of any major valvular disease or shunt. Calculation of cardiac output using the velocity time integral of aortic outflow velocities[34,42,43] and mitral inflow velocities were recorded in each pacing mode.

Measurements of cardiovascular function

(i) Phasic and mean arterial pressure (MAP). Arterial pressure monitoring was performed either via intra-arterial cannula or non-invasively via sphygmomanometer (if invasive monitoring was contraindicated). (ii) Doppler

cardiac output (CO)(l/min). (iii) Cardiac power output (CPO)(Watts)[78] = CO x [mean arterial pressure - mean right atrial pressure] x 2.2167 x 10^{-3}. CPO was used as a measure which reflects a change in both MAP and CO. [78] Baseline indices were defined as the CO, MAP and CPO measured prior to pacing or with VVI pacing at 40 bpm if patients were unstable and pacing dependent (6 patients). ΔCPO was defined as the relative change in cardiac power output from baseline (CPO in VVI *or* optDDD mode ÷ CPO at baseline). Rigt atrial pressure was measured by manometry of the central venous pressure at the time of insertion of the temporary pacing leads.

Statistical analysis

Variables will be expressed as median(range), mean(SD) or proportions. Discrete variables will be compared between groups by χ^2 test. Data for normally distributed variables will be compared using paired t-test for comparison of different pacing modes in individual patients and unpaired t-test for comparisons between groups. Skewed data will be compared using Mann-Witney U tests. To identify 'independent' clinical predictors of haemodynamic benefit from DDD pacing, multivariate linear regression analyses were performed. Significant independent predictors were selected by the use of a backward stepwise elimination that began with all analysed factors and then incrementally discarded factors with the highest *p* values and terminated when remaining variables were

significant at the $p<0.20$ level. All analyses were performed using Statview® 4.5 software (Abacus Concepts, Berkley, CA).

RESULTS

Evaluation of cardiovascular function was performed in forty-four patients who presented with an urgent indication for temporary cardiac pacing. The characteristics of their presentation are detailed in Table 5.1. Their median age was 71(43-96) years, 26 were male and 18 female, 33 had symptomatic bradyarrhythmia and 11 had sustained or recurrent ventricular tachycardia refractory to initial medical management. Twenty-four patients had evidence of haemodynamic instability.

Pacing achieved

All patients underwent successful implantation of temporary dual chamber pacing leads prior to entry into the haemodynamic study. The single-lead system was deployed in 36 patients and 7 patients had implantation of separate atrial and ventricular leads. VA conduction was demonstrated in 25 patients including 7/20 patients with AV block. The optimal dual chamber mode was 'AAI' in 16 patients and DDD in 28 patients.

Table 5.1 Patient Characteristics

	n=44
Age (years)	71(43-96)
Sex (M:F)	26:18
Initial ventricular rate (bpm)	56 (20-95)
Rhythm	
AV block	26
Sinus node disease	7
Ventricular tachycardia	11
VA conduction	25
LV ejection fraction (%)	37 (14)
LV end diastolic dimension (cm)	5.5 (0.76)
LV end systolic dimension (cm)	4.6 (0.97)
LA diameter (cm)	4.0 (0.78)
Hypotension	17
Heart failure	18
Valve disease	4
Recent myocardial infarction	16

General effects of VVI and DDD pacing on cardiovascular function

VVI pacing. Ventricular demand pacing had no overall effect on the baseline indices of this group of patients (see Figure 5.1). MAP changed from 75.6(15.7) to 74.3 (15.5) mmHg, p=NS; CO changed from 4.03 (1.48) to 4.21 (1.56) l/min, p=NS; and the CPO changed from 654.2 (319.9) to 660.4 (371.1) Watts, p=NS. The line plots in Figure 5.1 illustrate the varied individual responses to VVI pacing showing that 22/44 patients had little or no change but 19 patients had a reduction in both mean arterial pressure and cardiac output.

DDD pacing. Compared with baseline indices, optimal DDD pacing improved MAP by 12 percent (75.6[15.7] to 84.5 [14.4] mmHg, $p<0.001$), CO by 40 percent (4.03 [1.48] to 5.7 [1.60] l/min; $p<0.001$) and CPO by 54 percent (654.2 [319.9] to 1010.5 [384.1]; $p<0.001$). There were 8 patients who had no increase in MAP with optimal DDD pacing but 6 of these had an increase in CO and CPO.

Paired comparison of the effects of VVI and optimal DDD modes showed there was a 14 percent difference in mean arterial pressure, a 34 percent difference in cardiac output and a 54 percent difference in cardiac power (see Table 5.2).

Figure 5.1
Changes in cardiovascular function of all patients

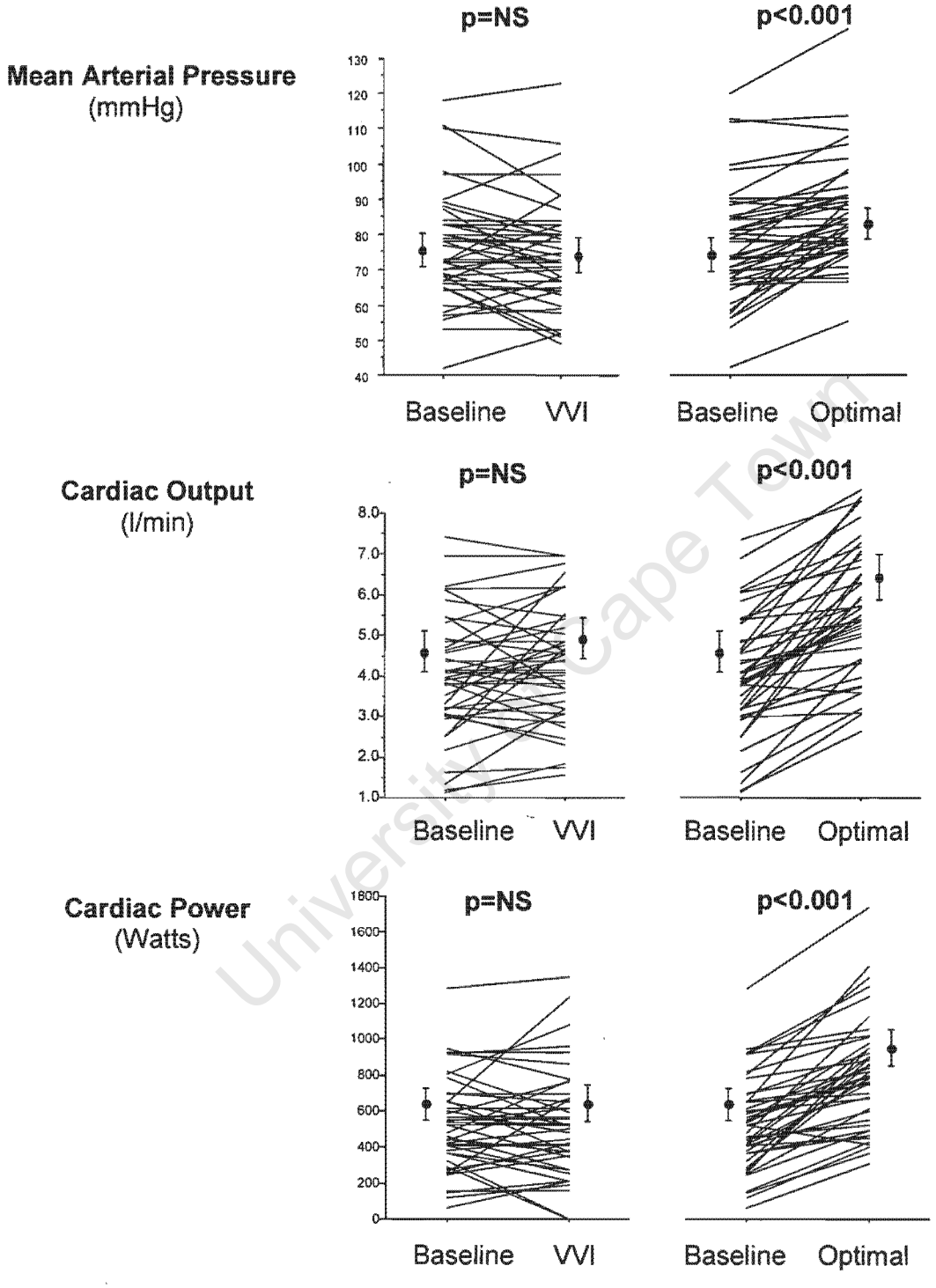


Table 5.2 Paired comparison of VVI and optimal DDD modes

	VVI *n=44*	**Optimal DDD** *n=44*	*Significance*
MAP (mmHg)	74.3 (15.5)	84.5 (14.4)	*<0.001*
CO (l/min)	4.21 (1.56)	5.67 (1.60)	*<0.001*
CPO (Watts)	660.4 (371.1)	1010.5 (384.1)	*<0.001*

Effect of AV delay

An AV delay of 50, 100 and 150 ms could be tested in all 26 patients with AV block but not in the patients with isolated sinus node dysfunction. The optimal AVD varied from 50 to 150 ms. The mean difference between the worst AV delay and the optimal AV delay are illustrated in Table 5.3. There was not a significant increase in MAP between the VVI and 'worst' DDD modes (DDD mode at the AV delay which resulted in the lowest indices of cardiac function). The 'worst' DDD mode was superior to the VVI mode by increasing the CO by 17 percent (4.8 [3.0] to 5.6 [2.9] l/min; p=0.006) and CPO by 21 percent (779 [501] to 959 [481] Watts; p=0.048).

The optimal DDD mode was superior to the 'worst' DDD mode by increasing the CO by 14 percent (5.6 [2.9] to 6.4 [3.1] l/min; p=0.013) and CPO by 13 percent (959 [481] to 1088 [467] Watts; p=0.028). Similarly, there was not a significant increase in MAP between the 'worst' DDD and optimal DDD modes.

In 16/18 patients with isolated sinus node dysfunction long AV delays allowed intrinsic AV node conduction in a manor analogous to AAI pacing mode. Comparison of the 'AAI' and optimal DDD mode were performed. For this comparison care was taken to find AV delays which allowed complete right ventricular pre-excitation during optimal DDD pacing. The AAI mode was superior to the optimal DDD mode by increasing MAP by 8 percent (76 [10.6] to

82 [11.5] mmHg; p=0.008), the CO by 34 percent (4.1 [1.5] to 5.5 [1.5] l/min; p=0.005) and the CPO by 47 percent (640 [227] to 940 [303] watts; p=0.004).

Table 5.3 Effects of AV delay on cardiac function

	VVI	**Worst DDD**	*Significance*
MAP (mmHg)	73 (13.7)	76 (12.7)	*NS*
CO (l/min)	4.83 (3.0)	5.6 (2.9)	*0.006*
CPO (Watts)	779 (501)	959 (481)	*0.048*
	Worst DDD	**Optimal DDD**	*Significance*
MAP (mmHg)	76 (12.7)	78 (8.1)	*NS*
CO (l/min)	5.6 (2.9)	6.4 (3.1)	*0.013*
CPO (Watts)	959 (481)	1088 (467)	*0.028*
	Optimal DDD	**AAI**	*Significance*
MAP (mmHg)	76 (10.6)	82 (11.5)	*<0.001*
CO (l/min)	4.1 (1.5)	5.5 (1.5)	*0.005*
CPO (W)	640 (227)	940 (303)	*0.004*

VVI - cardiac function during VVI mode; Worst and Optimal DDD - lowest and highest indices of cardiac function obtained by varying the AV delay during DDD pacing; AAI - indices of cardiac function obtained by prolonging the AV delay during DDD pacing to allow intrinsic AV nodal conduction.

Predictors of change in cardiovascular function

Univariate analysis

There was no clinical variable that predicted a change in cardiovascular function during VVI pacing but a number of variables affected CPO during optimal DDD pacing (see Table 5.4). There was a correlation in initial heart rate and age with CPO (see Figure 5.2 and 5.3) but the difference was not significant when these variables were dichotomised (age ≥/< 70 years, initial heart rate ≥/< 50 bpm) (see Table 5.4). No correlation of LV ejection fraction or LV end diastolic diameter with CPO was detected (see Figure 5.4). In optimal DDD mode there was a 125 and 46 percent increase in baseline CPO in patients with and without heart failure respectively (p=0.002); a 120 and 50 percent increase in baseline CPO in patients with and without hypotension (p=0.005); and a 126 and 55 percent increase in baseline CPO in patients with and without recent myocardial infarction (p=0.005) (see Table 5.4).

The differences between patients with and without one or more marker of haemodynamic instability were also analysed (see Figure 5.5). With optimal DDD pacing the relative increase in baseline MAP, CO and CPO was significantly greater in patients with haemodynamic instability than in those without (see Table 5.5). There was no difference in the relative change of baseline cardiac indices between groups with VVI pacing.

Table 5.4 Univariate analysis of the effect of clinical variables on cardiac power output during VVI and optimal DDD pacing

		VVI pacing		Optimal DDD pacing	
Variable	**No.**	**ΔCPO**	*p value*	**ΔCPO**	*p value*
All patients	44	1.09(0.56)		1.81(0.84)	<0.001
Age					
< 70 years	23	0.99(0.24)	*p=NS*	1.85(0.79)	*p=NS*
≥ 70 years	21	1.19(0.39)		2.07(0.64)	
Initial heart rate					
< 50 bpm	26	1.24(0.40)	*p=NS*	2.07(0.82)	*p=NS*
≥ 50 bpm	18	0.89(0.15)		1.79(0.26)	
LV EF					
< 0.40	24	1.03(0.47)	*p=NS*	2.19(0.81)	*p=NS*
≥ 0.40	20	1.15(0.20)		1.76(0.33)	
CCF					
Yes	24	1.16(0.78)	*p=NS*	2.25 (1.02)	*p=0.002*
No	20	1.04(0.32)		1.46 (0.44)	
Hypotension					
Yes	19	1.15 (0.78)	*p=NS*	2.20 (1.0)	*p=0.005*
No	25	1.05 (0.32)		1.50 (0.18)	
Recent MI					
Yes	16	1.24 (0.77)	*p=NS*	2.26 (1.09)	*p=0.006*
No	28	1.00 (0.39)		1.55 (0.51)	

ΔCPO – Change in cardiac power output from baseline (CPO in VVI or optDDD mode ÷ CPO at baseline); Initial heart rate – initial ventricular rate; LV EF – left ventricular ejection fraction; CCF – clinical and radiological pulmonary oedema; Hypotesion – systolic blood pressure < 90mmHg; Recent MI – documented myocardial infarction <72 hours prior to pacing

Figure 5.2
Correlation of cardiac power and initial heart rate

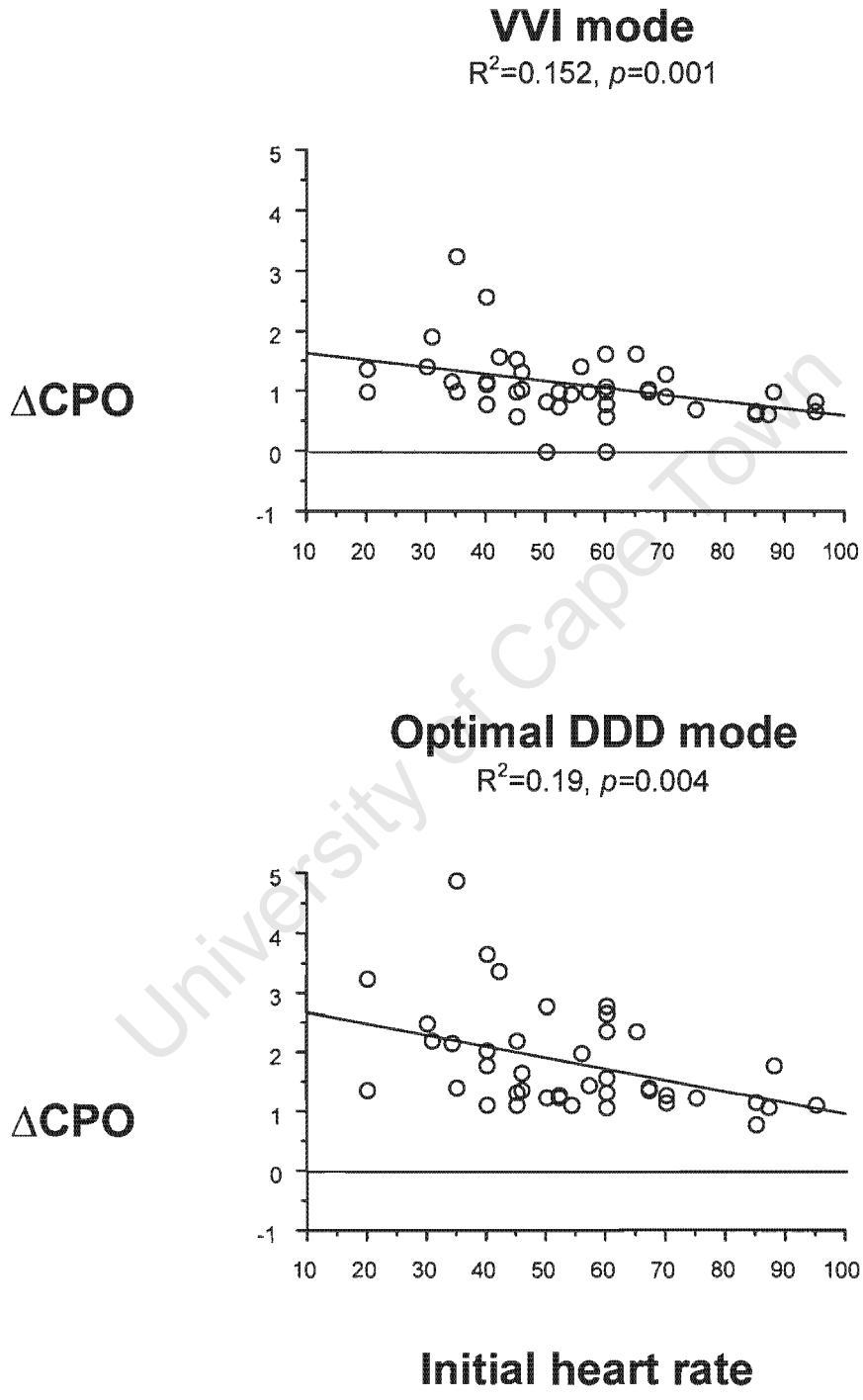


Figure 5.3
Correlation of changes in cardiac power and age

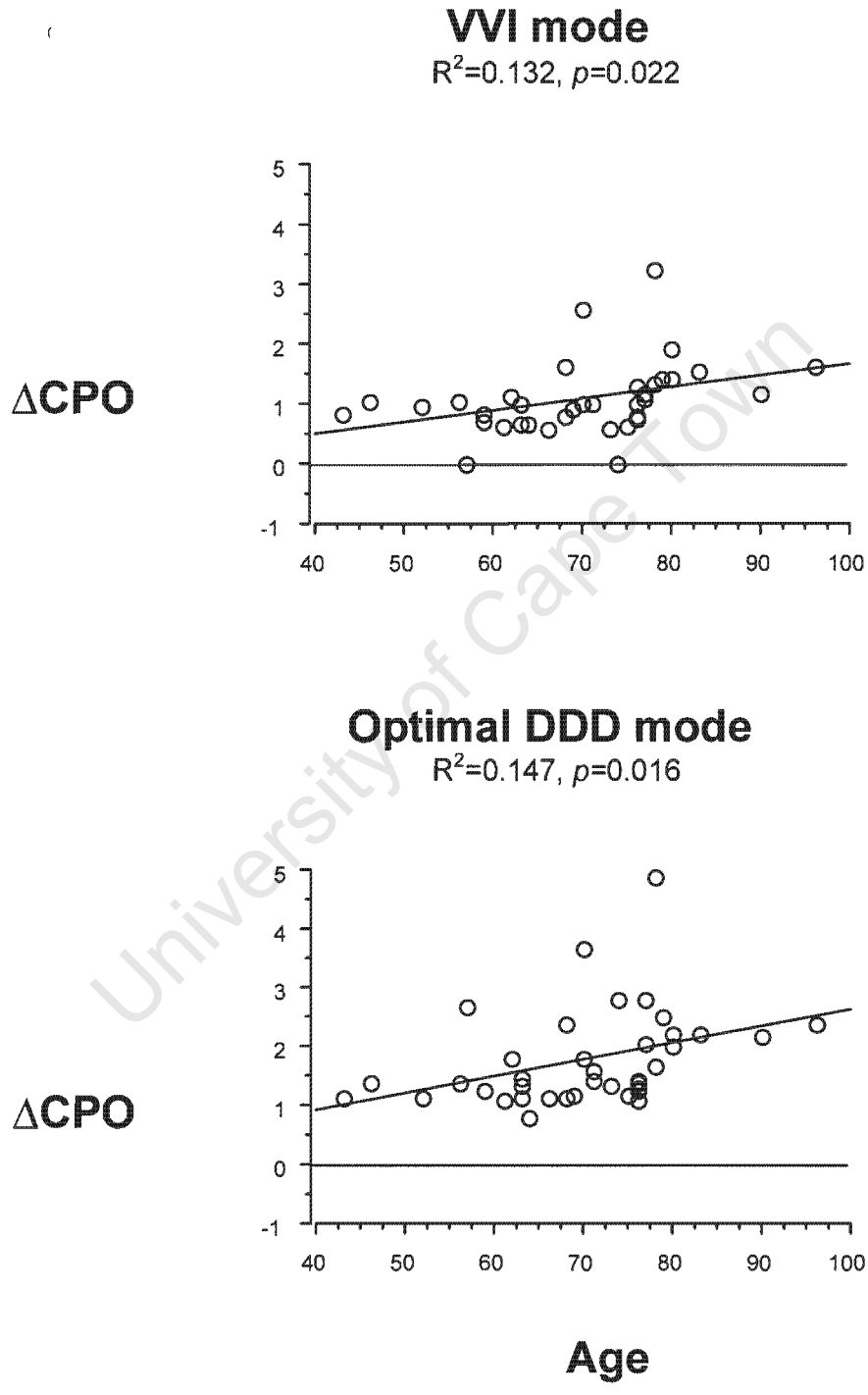
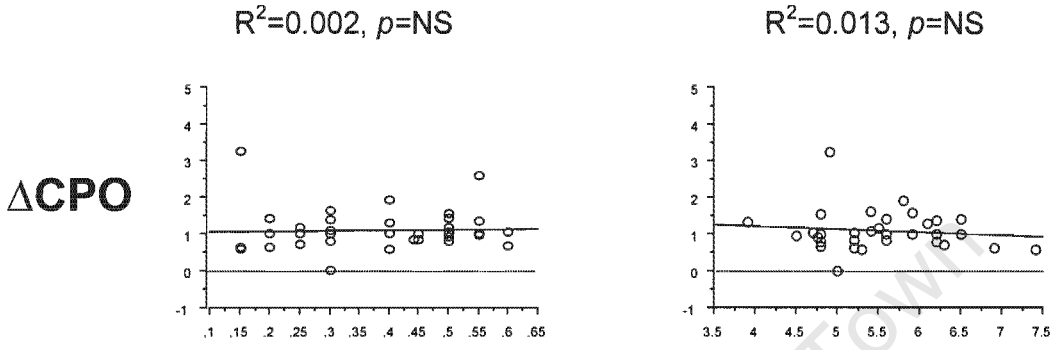
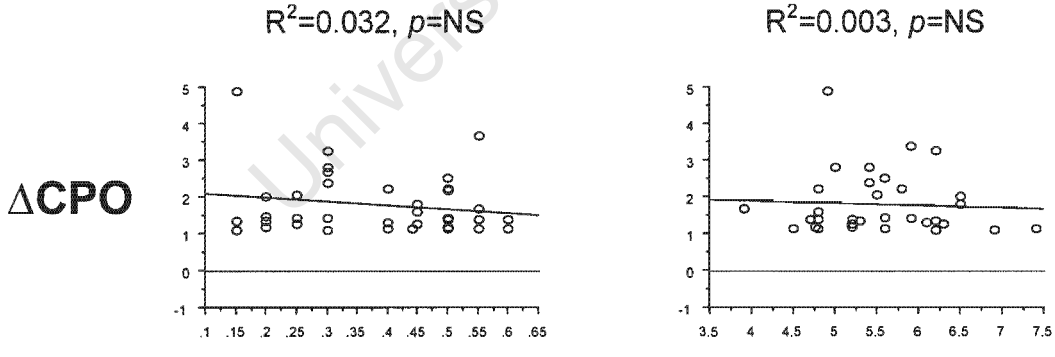


Figure 5.4
Correlation of cardiac power output with ejection fraction and LV end diastolic diameter

VVI mode



Optimal DDD mode



Ejection fraction **LV end diastolic diameter**

Table 5.5 Change in baseline indices of cardiac function during optimal DDD pacing in patients with and without haemodynamic instability

	'Stable' *n=20*	**'Unstable'** *n=24*	*Significance*
ΔMAP	1.05 (0.97-1.19)	1.19 (0.98-1.43)	*<0.001*
ΔCO	1.28(0.95-2.15)	1.71(1.1-3.29)	*0.003*
ΔCPO	1.4(0.80-2.2)	2.1(1.2-4.8)	*<0.001*

'Stable' and 'Unstable' patients were those with and without one or more marker of haemodynamic instability (hypotension, heart failure, recent myocardial infarction or significant valvular heart disease).

Multivariate analysis

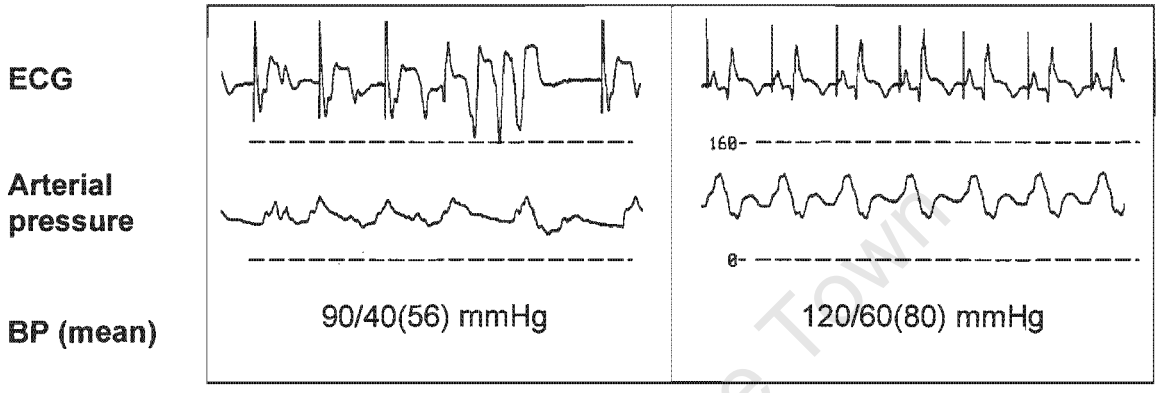
The only clinical variable that could independently predict significant increase in CPO between VVI and optimal DDD pacing was the presence of clinical and radiological heart failure (see Table 5.6).

Table 5.6 Results from a multiple regression model for predicting change in cardiac power output* between VVI and optimal DDD modes

Variable	**Coefficient**	**Standard Error**	*Significance*
Intercept	2.23	0.19	
Ejection fraction <0.40	-0.17	0.11	*0.12*
Heart failure	-0.25	0.11	*0.02*

*ΔCPO: Change in cardiac power output from VVI to optDDD mode (CPO in optDDD mode ÷ CPO in VVI mode)

Figure 5.5
A case report illustrating the dramatic effect of DDD pacing on cardiovascular function



A 74 year old woman, presented with cardiogenic shock and a ventricular septal defect (VSD), 4 days following an undiagnosed inferior myocardial infarction. An infero-apical VSD was repaired using a 4 x 3 cm Dacron patch during emergency cardiopulmonary bypass. Despite postoperative ventilation, balloon pump and inotropic support she remained hypotensive and oliguric on the third post-operative day. In addition, inappropriate sinus bradycardia resulted in frequent ectopy and 8 episodes of ventricular tachycardia/fibrillation, requiring DC cardioversion. Ventricular demand (VVI) pacing via epicardial temporary pacing leads increased heart rate, but did not improve blood-pressure or urine output. Neither VVI pacing, nor intravenous loading with amiodarone, suppressed the ventricular arrhythmia.

Dual chamber (DDD) temporary pacing was achieved using a single-lead balloon flotation catheter Fluoroscopic screening was used to optimise electrode position. Reliable DDD pacing using an external generator (Eikos SLD, Biotronik) was maintained at 100bpm for 5 days with dramatic clinical improvement. There was a 24 mmHg rise in mean arterial pressure enabling withdrawal of inotropic support, recovery of renal function and a steady clinical improvement. In addition, the ventricular arrhythmia was completely suppressed apart from 2 further episodes of ventricular tachycardia provoked by testing ventricular thresholds in VVI mode.

DISCUSSION

Comparison on the effects of permanent VVI and DDD pacing on cardiovascular function have mostly been studied in stable patients. These studies may be applicable to some patients undergoing temporary cardiac pacing who have isolated bradyarrhythmia and little structural heart disease. However, patients presenting acutely will more commonly have impaired systolic function and/or stiff, non-compliant ventricles (eg. following acute myocardial infarction); elevated ventricular filling pressures (eg. in patients with pulmonary oedema); and significant comorbidity (eg. intensive care and post-operative patients). The effects of different pacing modes on the cardiovascular function of such patients is not well documented.

This study was performed on a typical population of patients requiring emergency temporary cardiac pacing. They either had symptomatic bradyarrhythmias or ventricular tachycardia refractory to initial medical management. Half of them had clinical markers of haemodynamic instability. The single-lead pacing system gave the unique advantage of being able to study the effects of temporary DDD pacing on both 'stable' patients and those with haemodynamic instability without exposing them to additional venous puncture or prolonged procedures. Temporary DDD pacing was achieved in sick patients with haemodynamic instability who may not have tolerated prolonged procedures typical of implantation of conventional atrial and ventricular temporary leads. These studies have

demonstrated a significant difference in the effects of VVI and DDD pacing on cardiovascular function.

The potential deleterious effects of VVI pacing

This study has shown that the overall effect of temporary VVI pacing on cardiovascular function was neutral. In most haemodynamically stable patients, the VVI mode was well tolerated and was useful to prevent and/or treat profound bradycardia. However, in certain patients, temporary VVI pacing increased heart rate but adversely effect cardiovascular function. Analysis of individual patients in our study showed that 19/44 patients had a reduction in both MAP and CO. The maximum reduction in MAP was 25 percent (68 to 49 mmHg). This adverse effect may be particularly important in patients with haemodynamic instability and/or myocardial ischaemia.

The physiology of asynchronous ventricular demand pacing is complex. The associated loss of AV synchrony means that atrial contraction occurs during ventricular systole against closed mitral and tricuspid valves. The subsequent loss of the atrial contribution to ventricular filling reduces stroke volume. [4,34] The extent of this reduction depends on both atrial mechanical function but also on ventricular compliance. A further consequence of the loss of AV synchrony is stimulation of atrial and pulmonary baroreceptors resulting in peripheral vasodilatation and hypotension. [79,80] Pacing from the right ventricular apex causes asynchrony of the left and right ventricles and this effect alone can cause a

reduction in cardiac output, particularly in patients with impaired left ventricular function. The interaction of all these factors is complex and varies considerably in individual patients. Given this complex interaction, it is difficult to predict the ultimate effect of VVI pacing from the right ventricular apex. In this study there was no clinical factor that predicted either a positive or negative effect of VVI pacing on cardiovascular function. However, it is likely that many physicians have underestimated the potential for VVI pacing to produce significant deleterious effects in acute settings.

Changes in cardiovascular function with temporary DDD pacing

Restoration of AV synchrony can significantly improve cardiovascular function but the magnitude of this effect in acute clinical settings has not been clearly documented. In this study, analysis of the entire group of patients demonstrated that optimal DDD pacing increased baseline MAP by 12 percent, CO by 40 percent and CPO by 54 percent. Optimal DDD pacing consistently improved cardiovascular function and only 2/44 patients had a reduction in both MAP and CO.

Optimising AV interval

Previous studies in haemodynamically stable permanent pacemaker patients using plethysmography and echocardiography have demonstrated that AV interval has an important effect on left ventricular filling and cardiac output. [53,55,81] Stroke volumes were highly dependent on AV delay but the optimal AV delay varied

considerably between individual patients. These studies illustrated that optimisation of the AV interval resulted in a 5 to 10 percent increase in cardiac output. In this study, optimisation of the AV delay resulted in a 14 percent increase in cardiac output. It is possible that the atrial contribution to left ventricular filling plays an even more important role in patients with haemodynamic instability than in 'stable' patients. In patients with intact AV nodal conduction, there was an even greater increase in cardiac output if the AV delay could be adjusted to avoid ventricular pacing.

Clinical predictors of change in cardiovascular function

A number of clinical factors are reported to affect cardiovascular function during cardiac pacing including: sinus node function and heart rate, AV node function and paced /sensed AV delay, regularity of rhythm, the presence and severity of underlying structural heart disease, atrial electrical and mechanical function, autonomic tone and vasomotor reflexes, release of atrial natriuretic factors and other neurohormones, body posture, fluid and electrolyte balance, oxygenation, drugs and age.

This study of temporary cardiac pacing has examined whether certain clinical factors can predict benefit with optimal DDD pacing compared to VVI mode. Patients with heart failure, hypotension, and recent myocardial infarction had a greater relative benefit from optimal DDD pacing than patients without these clinical variables. Age and initial heart rate correlated weakly with cardiac output

but left ventricular dimensions, ejection fraction and left atrial dimensions did not correlate with cardiac output from temporary DDD pacing.

Heart rate

Although cardiac output is the product of heart rate and stroke volume, correction of bradycardia with temporary VVI pacing does not usually increase cardiac output. In this study there was no significant increase in MAP or CO with temporary VVI pacing despite an increase in heart rate from a mean of 52 to 78 bpm. In another study of 12 patients with complete heart block following myocardial infarction, Murphy et al showed that temporary VVI pacing did not significantly change MAP (76.4 [15.1] vs. 84.0[16.3] mmHg; *p*=NS) or CO (3.33 [1.9] vs. 3.49 [1.7] l/min; *p*=NS) despite an increase in mean heart rate from 41.8 (16.6) to 92.7 (18.5) bpm. [48] This effect is well documented in permanent pacing[4] and can be attributed to both lack of AV synchrony and the induced interventricular asynchrony caused by VVI pacing.

Left ventricular function

Left ventricular size and function did not correlate with the relative change in cardiac output both in this and other studies. These findings have been confirmed in several other Doppler and radionuclide studies. [32,81,82]

Left atrial size

Permanent pacemaker studies have found that patients with normal left atrial size were more sensitive to the loss of AV synchrony and thus left atrial dimensions may be a useful predictor of who might benefit from DDD pacing. [37] There was no correlation with left atrial size and relative change in cardiac output.

Heart failure

Patients with clinical and radiographic heart failure typically have an elevated left ventricular end diastolic pressure (LVEDP) and pulmonary capillary wedge pressure (PCWP). The atrial contribution to ventricular filling in these patients depends on atrial mechanical function, the timing of the AV delay and ventricular filling pressures. Small studies have indicated that the atrial contribution may be low in some patients with elevated LV end diastolic pressures. [55] However, this may be true for patients with impaired atrial mechanical function but, in patients with intact atrial mechanical function, AV synchrony can make a crucial contribution to ventricular filling.

The effect of pacing mode on left ventricular end diastolic pressure and pulmonary capillary wedge pressure is important. Several studies have illustrated that LVEDP and PCWP will be significantly lower in the DDD mode compared to the VVI mode. [55,56] In addition, VVI pacing can even elevate left ventricular end diastolic

pressure and pulmonary capillary wedge pressure and exacerbate the heart failure of some patients. [55]

The timing of atrial systole is also important. In some patients with a long PR interval, ventricular end-diastolic pressures can exceed those in the atrium causing flow reversal and pre-systolic mitral regurgitation. [83] In the 1980s, patients paced for bradyarrrhythmia who also had heart failure had greater symptomatic benefit with dual-chamber pacing than with ventricular pacing alone. [84] Direct application of dual-chamber pacing to the management of heart failure in patients with no bradyarrhythmic indication for pacing was introduced in the early 1990s, [85] in an uncontrolled, non-randomised study of 16 patients in sinus rhythm. Dual-chamber pacing led to a reduction in New York Heart Association class (from a mean at baseline of 3·6 to 2·1 with pacing) and a fall in the cardiothoracic ratio and to significant increases in blood pressure. The proposed mechanism of benefit was elimination of pre-systolic regurgitation by shortening of the atrioventricular interval and improvement of the filling pattern of the left ventricle.

These findings have not been confirmed by other investigators and it is likely that the benefits of optimising the AV delay are partially offset by the asynchrony produced by right ventricular pacing. Currently there is much interest in permanent biventricular pacing to resynchronise the ventricular function of patients with symptomatic heart failure, impaired left ventricular function and interventricular

conduction delay (QRS >130ms). [86] Permanent biventricular pacing is achieved by conventional positioning of a right ventricular apex lead and using the coronary sinus tributaries to position a lead on the posterolateral surface of the left ventricle. This procedure is time consuming and complex and is unlikely to be employed for temporary pacing. Left ventricular leads can also be placed on the epicardium and this approach is used when coronary sinus lead placement fails. It would simple to attach temporary left and right ventricualr epicardial leads at the time of coronary artery bypass surgery and temporary biventricular pacing could have a role to play in the early post-operative phase.

Hypotension

Cardiac pacing has direct effects on cardiac output and peripheral vascular resistance, both of which are important in the regulation of blood pressure. The effects of atrioventricular and interventricular asynchrony have been discussed above and the potential deleterious effects of VVI pacing on blood pressure have been highlighted. In addition, asynchronous atrial contraction during VVI pacing can cause stimulation of atrial baroreceptors and the release of atrial natriuretic peptide resulting in inappropriate peripheral vasodilatation and hypotension. [80] In this study patients with hypotension had a greater relative increase in CPO than those without hypotension during DDD pacing. This may in part reflect the fact that those with normal blood pressure are unlikely to have a further increase in blood pressure during cardiac pacing. However, in patients with a systolic blood pressure of < 90 mmHg, increasing heart rate, restoring AV synchrony and

optimising AV delay can improve mean arterial pressure by 20 percent. Correction of significant hypotension is a major therapeutic goal in haemodynamically compromised patients and even small increases in blood pressure may substantially improve the clinical state of the patient.

Myocardial infarction

The management of patients with bradyarrhythmia following recent myocardial infarction presents specific challenges. Although many patients with asymptomatic heart block can be managed without transvenous temporary pacing, patients with bradycardia and haemodynamic instability invariably require transvenous pacing. These patients are often sick with hypotension and heart failure and poorly able to tolerate invasive procedures. In addition, the early management of myocardial infarction usually involves the administration of thrombolytic therapy or antiplatelet agents which increase the risk of bleeding complications from transvenous pacemaker insertion.

Myocardial infarction decreases ventricular compliance making the atrial contribution to ventricular filling of greater importance. Small studies have compared the effects of VVI and DDD pacing in patients with myocardial infarction. Restoring AV synchrony can significantly improve cardiovascular function in patients with complete heart block following right ventricular infarction in whom VVI pacing had failed to improve haemodynamic status. [44,87,88]

Clinical Implications

Currently, most patients requiring temporary cardiac pacing are managed with the simple VVI mode for the correction of bradycardia. Although temporary VVI pacing may be appropriate for patients with intermittent or stable bradycardias, it is apparent that asynchronous VVI pacing can result in a fall in MAP and CO and a rise in PCWP in some patients. These negative effects can be poorly tolerated and even exacerbate the clinical condition in some cases. It is difficult to justify the continued use of VVI pacing in patients with symptomatic bradycardias and haemodynamic instability.

By contrast, achieving reliable temporary DDD pacing will improve cardiovascular function in the vast majority of cases and only very rarely will it cause any deterioration in MAP or CO. However, this improvement is dependent on careful adjustment of the AV delay to optimise cardiovascular function. Clinical heart failure is the strongest predictor of benefit from optimal DDD pacing although hypotension is also likely to benefit. Paradoxically, heart failure is frequently a strong deterrent for physicians to undertake temporary pacing procedures and emphasises the need for a quick implantation technique.

Patients with bradycardia and haemodynamic instability are often critically ill and have a high mortality. Our study has demonstrated a significant improvement in

cardiovascular function with optimal DDD pacing compared to VVI pacing. It is likely that these haemodynamic improvements could ultimately affect clinical outcomes but large trials would be required to determine the effects of temporary DDD pacing on mortality. At present it seems unlikely that such trials would be performed and that clinical decisions will need to be based on the haemodynamic data that are available. Providing temporary DDD pacing can be rapidly and safely achieved, it appears that its effect on cardiovascular function is significantly greater than the VVI mode.

Study limitations

This study illustrates some of the challenges of performing assessment of cardiovascular function in patients requiring temporary cardiac pacing. Typically there is a heterogeneous population of patients with different heart rates, different conduction abnormalities and varying degrees of haemodynamic instability and their response to temporary pacing is not predictable. To overcome some of these difficulties, this study assessed the effects of different pacing modes on individual patients rather than perform comparisons between patients. Noninvasive Doppler measurements of cardiac output were used rather than right heart catheterisation to obtain more precise measurements of cardiovascular function. Additional venous puncture and the potential risk of Swann-Ganz catheter insertion could not be justified in most patients, particularly in stable post-infarction patients who had recently received thrombolytic therapy. Doppler derived cardiac outputs have been well validated and extensively used in haemodynamic pacemaker studies.

Although the quantitative assessment of cardiac output is less accurate than right heart catheterisation, the qualitative changes in cardiac output in individual patients can be reasonably accurately derived with Doppler echocardiography. Also, echocardiography is more likely to be used to optimise DDD pacing in routine clinical practice. Cardiac power output (CPO) was used as measure cardiac function that included both cardiac output and mean arterial pressure. CPO has been validated in patients with heart failure and, unlike left ventricular stroke work index it does not require measurement of pulmonary capillary wedge pressure. [78] The multivariate analysis showed heart failure to be the only independent predictor of response to DDD pacing. Hypotension and recent myocardial infarction were significant univariate predictors and it is likely that this study was underpowered to detect these factors in a multivariate analysis.

CHAPTER 6

Conclusions

The rationale for developing temporary DDD pacing

Temporary transvenous cardiac pacing remains an essential component in the management of many patients with symptomatic bradyarrhythmia. [4,5] These patients are often sick with hypotension, heart failure and confusion and both the initial implantation procedure and subsequent maintenance of pacing therapy can present a significant challenge. Major clinical problems (lead displacement, loss of capture, sepsis, pericarditis, death) are reported in up to a third of cases[23,24] and are more prevalent with operators who are not skilled in invasive cardiac procedures. [16,17,89] Alternatives to transvenous pacing can be deployed in some patients. External transcutaneous pacing has evolved into a useful therapy for the immediate management of asystolic cardiac arrest and also for the prophylaxis of patients at risk of developing bradycardia (eg. Bifasicular block following anterior infarction and thrombolytic therapy) but is not usually tolerated for more than a few hours. [4] More widespread access to immediate permanent pacing has reduced the number of patients who need temporary pacing to facilitate safe transfer to another center. Nevertheless, these alternatives can only be considered in a proportion of patients

and temporary transvenous pacing should be available in most hospitals which offer emergency care. Considering the unacceptably high incidence of complications associated with this procedure, there has been very little published on strategies to improve the technique.

From our clinical experience, both the number and type of patients requiring temporary transvenous pacing has changed over the last two decades. Patients with acute myocardial infarction frequently required temporary pacing in the past but recent efforts to minimize the delay to definitive treatment and the widespread availability of reperfusion therapy appears to have reduced the incidence of bradyarrhythmia in these patients. Also, the recent administration of thrombolytic or antiplatelet therapy has raised the threshold to undertake invasive procedures such as transvenous pacing. The more widespread availability of permanent pacing and external transcutaneous pacing has reduced the number of patients requiring temporary pacing for conduction disease and prophylactic indications. It is our impression that most patients with well-tolerated or intermittent bradyarrhythmia are managed with either prophylactic transcutaneous pacing or immediate permanent pacing. A large number (and possibly the majority) of patients now requiring temporary transvenous pacing are those who exhibit significant haemodynamic compromise associated with the bradyarrhythmia. These patients may be better managed with temporary DDD pacing.

The hypothesis of this thesis was that a temporary pacing lead, incorporating electrodes for both atrial and ventricular pacing, that can be easily and rapidly deployed and achieve reliable dual-chamber pacing should benefit patients presenting with bradyarrhythmias and haemodynamic compromise. To test this hypothesis a single-lead system for temporary DDD pacing was developed, evaluated and subsequently compared with the conventional technique for temporary DDD pacing. The effects of optimal DDD pacing on cardiovascular function were then compared with those of the simple VVI mode.

Summary of the findings

The first study was an open-labelled, randomised controlled trial of temporary cardiac pacing comparing standard semi-rigid and balloon-flotation temporary pacing leads. [71] Both were inserted under fluoroscopic guidance. The study found that procedure and fluoroscopy times were significantly reduced and that stable positions within the right ventricular apex were more often achieved with the balloon-flotation catheter even when inserted by relatively unskilled operators.

The second study has involved the development and initial evaluation of a single-lead DDD pacing catheter which incorporates OLBI® stimulation via non-contact atrial electrodes. [76] The design included a balloon-tip to facilitate lead placement. This lead has been evaluated in patients undergoing electrophysiological studies and in emergency settings. The lead can be inserted very quickly with minimal

fluoroscopy and achieve reliable atrial capture in over 91 percent of patients. Phrenic nerve stimulation can usually be avoided by adjusting the atrial output.

The third study was a randomised controlled trial of temporary DDD pacing in patients with haemodynamic instability, comparing the single-lead system with standard atrial plus ventricular pacing leads. [90] The single-lead system was inserted much more quickly with significantly shorter fluoroscopy times. Reliability of DDD pacing at the time of implantation was equivalent in the two groups but the conventional leads were much more prone to displacement during follow-up (35 vs. 5 percent, p=0.02). Repositioning of displaced conventional leads took much longer and usually required implantation of a new atrial lead and manipulation of both atrial and ventricular leads.

The fourth study compared the effects of VVI and optimal DDD temporary pacing modes on the cardiovascular function of patients requiring temporary cardiac pacing. [91] Overall VVI pacing had a neutral effect on baseline mean arterial pressure (MAP) and cardiac output (CO). However, analysis of individual patients showed that both MAP and CO were reduced in 19/44 patients. In comparison, optimal DDD pacing reliably increased both MAP and CO in the majority of patients. Adjustment of the AV delay was required to optimise DDD pacing and increased the CO by a mean of 14 percent. In a univariate analysis, hypotension and recent myocardial infarction were predictors of benefit from DDD pacing. Heart failure was the only significant predictor in a multivariate analysis.

Final comments

Although many new temporary pacing leads have been developed over recent years, they have not been rigorously evaluated or formally compared with standard clinical practice. By contrast, the studies described in this thesis have been designed to test a new single-lead temporary pacing system in randomised controlled trials using simple clinical end-points. I have endeavoured to make these trials clinically relevant by studying a typical patient population and using physicians with differing levels of invasive cardiology skills.

The single-lead system performed better than was expected and it does appear to offer a genuine alternative to the conventional technique now used for temporary DDD pacing. The single-lead system could be inserted more quickly and easily than conventional atrial and ventricular leads and appeared to perform at least as reliably as them during follow-up. Moreover, it appears that temporary DDD pacing can be achieved in the majority of patients and that optimal DDD pacing can offer a substantial improvement in cardiovascular function compared with simple VVI mode. In particular, patients with heart failure and hypotension are likely to receive considerable benefit. Given the potential advantages of the single-lead system, it is interesting to consider its role in modern cardiology practice.

Although the single-lead system is quick and easy to implant, achieving dual chamber pacing remains more complex and time consuming than VVI pacing.

Physicians would require a working understanding of dual-chamber pacemaker programming and should be able to alter heart rate, pacing mode, outputs, sensitivities and AV delay appropriately. In addition, the AV delay should be adjusted to optimise the cardiac output by using either Doppler or invasive measurements of cardiac function. This added complexity and time burden, albeit in a small number of patients, is significant and frequently entails 'out of hours' patient care. It is unlikely that junior doctors alone would have the necessary expertise and the provision of this sort of temporary pacing service would require the commitment of experienced physicians to assist with these cases. However, to expect this level of commitment from cardiological services does not seem unreasonable. After all, when patients are sick with bradycardia and haemodynamic compromise, meticulous attention to all details of patient care can save lives.

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91. Ferguson JD, Lever N, Channon KM, Bashir Y. Temporary dual chamber pacing in patients with heart failure and hypotension: Is there significant haemodynamic benefit? *Heart* 2001;**85**(Suppl I):P45.

Publications arising from this thesis

Papers

1. JD Ferguson, N Lever, KM Channon, Y Bashir. A Simplified Approach To Temporary DDD Pacing Using a Single-Lead, Balloon-Tip Catheter with Overlapping Biphasic Impulse Stimulation. *PACE* 2001; **24**: 939-44

2. Ferguson JD, Lever N, Bashir Y, Channon KM. A Novel Approach to Emergency DDD Pacing using a Single-Lead, Balloon-Tip Catheter. *Heart* 2000; **84**: 210

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Abstracts

1. JD Ferguson, N Lever, KM Channon, Y Bashir. A randomised trial of temporary dual chamber pacing using conventional atrial and ventricular leads or a single-lead system. *PACE* 2002; **25**: 597

2. JD Ferguson, N Lever, KM Channon, Y Bashir. Temporary dual chamber pacing in patients with heart failure and hypotension: Is there significant haemodynamic benefit? *Heart* 2001; **85** (Suppl I): P45

3. JD Ferguson, N Lever, KM Channon, Y Bashir. Single-lead dual chamber pacing via floating atrial dipoles: overlapping biphasic impulse (OLBI®) stimulation reduces phrenic nerve stimulation. *PACE* 2001; **24**: 583

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5. Ferguson JD, Banning AP, Bashir Y.
Temporary Cardiac Pacing in CCU using Balloon-Flotation Electrode Catheters: a randomised comparison with conventional semi-rigid electrode catheters
JACC 1997; **29** (2) suppl:147A