Epicardial Pacing in New Zealand (1977 – 2002)

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Abstract

Reviews of clinical practice for paediatric pacemaker implantation and follow-up are necessary to provide an evidence-base for future policy and practice in this field. Epicardial pacing data available through Green Lane Hospital, New Zealand's (NZ) primary referral centre for paediatric cardiac surgery and pacemaker implantation, was reviewed with the following aims:

- Assessment of pacemaker lead performance over time in relation to the type of epicardial lead implanted - steroid-eluting (SE) and non steroid-eluting (NSE).
- Determination of the survival rate of epicardial leads.
- Identifying factors predicting or associated with lead failure.

A database of pacing and sensing thresholds and lead impedance data at implant, 2, 6 and 18 weeks and 6 monthly intervals thereafter, was compiled and the prevalence and timing of complications in relation to lead type, location and implant route determined. In total 192 leads (155 SE, 37 NSE) were implanted in 96 patients (52 male) aged 3 days to 71 years (y) (median 1.7y), 74 patients were < 17 years of age at implant. Congenital heart defects were present in 82% of patients. Follow-up (f/u) was possible for 180 leads. Mean f/u duration for the 150 SE leads was 3.1y (2 weeks – 8.8y) and for the 30 NSE leads was 4.5y (2 weeks – 27y).

SE and NSE pacing thresholds were similar at implant. NSE pacing thresholds peaked at 6 weeks post implant and remained significantly higher than SE leads throughout f/u in surviving leads, although the difference was small at 2 and 4 y. SE and NSE leads had similar ventricular sensing thresholds and lead impedances throughout the study period.

Survival at 5 years for all leads was 61% (66% for SE leads and 41% for NSE leads). Primary causes of failure in the leads receiving f/u were exit block and lead fracture. The occurrence of exit block was significantly higher ($p<0.0001$) in NSE leads (57%) compared to SE leads (5%). Lead fracture occurred in 15% of leads with the highest fracture rate at 2-3 y post implant. Patient age and weight at implant, gender, previous cardiac surgery, lead polarity, indication for pacing and implant route were not predictors of lead failure. NSE leads were 6 times more likely to fail compared to SE leads ($p <0.0001$).

The main study findings were: SE leads maintain lower pacing thresholds and a reduced incidence of exit block compared to NSE leads. It is therefore recommended that SE leads be developed which can penetrate fibrosed, scarred or fatty epicardial surfaces. Where SE lead use is contraindicated, alternative surgical techniques for SE lead placement should be attempted rather than implanting NSE leads. Lead fracture is a significant complication of epicardial pacing in paediatric patients. Using stronger bipolar leads implanted by the subxiphoid route may reduce the risk of fracture.

Medium term survival (5 y) of SE epicardial leads is acceptable and therefore the continued use of these leads is recommended, particularly in young patients, allowing their veins to be saved for transvenous leads later in their life.

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Statement of Originality

'I hearby declare that this submission is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person nor any material which to a substantial extent has been accepted for the award of any other degree or diploma of a university or other institution of higher learning, except where due acknowledgement is made in the acknowledgements'.

…….. (signed)

…….. (date)

Abbreviations

Throughout this thesis standard international units and standard abbreviations have been used. Where applicable units used for measurements are stated.

AA	Atrial arrhythmia
AAI	Atrial paced, atrial sensed, inhibit in response to sensing
ACH	Auckland City Hospital
ACHD	Adult congenital heart disease
AMS	Abdominal muscle stimulation
AS	Atrial sense marker
AUTEC	Auckland University of Technology Ethics Committee
AV	Atrio-ventricular
AVB	Atrio-ventricular block
AVN	Atrio-ventricular node
Calc V_B	Calculated voltage B
CCAVB	Congenital complete atrio-ventricular block
CPI	Cardiac Pacemakers Incorporated
CRT	Cardiac resynchronisation therapy
CS	Coronary sinus
DDD	Dual paced, dual sensed, dual response to sensing
DS	Diaphragmatic stimulation
DTGA	Dextrotransposition of the great arteries
EB	Exit block
ECG	Electrocardiography
Echo	Echocardiography
GA	General anaesthetic
GLH	Green Lane Hospital
HT	High threshold
LA	Left atrium

LQT	Long QT
LQTS	Long QT syndrome
LTGA	Levotransposition of the great arteries
LV	Left ventricle
Meas V_B	Measured voltage B
msec	Millisecond
mV	Millivolts
NSE	Non steroid-eluting lead
NZ	New Zealand
%	Parts per hundred, percent
PDA	Patent ductus arteriosus
PPM	Pulses per minute
PV	P wave to ventricular pace
PWT	Pulse width threshold
RA	Right atrium
RPA	Right pulmonary artery
RV	Right ventricle
SAVD	Sensed atrio-ventricular delay
SE	Steroid-eluting
SSS	Sick sinus syndrome
SVC	Superior vena cava
ToF	Tetralogy of Fallot
US	United States
V	Volt
VSD	Ventricular septal defect
VT	Voltage threshold
VVI	Ventricular paced, ventricular sensed, inhibit in response to sensing

Glossary

Abdominal muscle stimulation	Activation of the abdominal muscle by the pacing stimulus.
Active fixation	Method of pacing lead attachment to the heart where the lead tip contains a corkscrew or barb (epicardial leads only) mechanism which is screwed or pushed into the myocardium to hold the lead in place.
Bi-directional Glenn	See Glenn shunt.
Bipolar pacing	Current flows from the pacemaker through a conductor to the lead tip (cathode) electrode and from there to the more proximal ring electrode (anode) located approximately 1cm away and returns to the pacemaker through the second conductor.
Bi-ventricular pacing	Pacing therapy where the stimulus is delivered to the right ventricular lead and the left ventricular (LV) lead simultaneously or within a short interval of each other. The LV lead is typically placed into an LV branch of the coronary sinus.
Diaphragmatic stimulation	Activation of the diaphragm due to conduction of the pacing stimulus to the muscle or the phrenic nerve.
Dislodgement (lead)	The location of the lead tip moves from the implant location.
Dual site atrial pacing	One lead is placed within the right atrium (RA) and a second atrial lead is placed within the coronary sinus to activate the left atrium (LA). The atrial stimulus is delivered to the RA and LA lead simultaneously in an attempt to suppress atrial arrhythmias.
Epi-myocardial	The myocardial layer immediately beneath the epicardium.
Escape rhythm	Electrocardiograph rhythm caused by impulses arising from an ectopic pacemaker as a result of undue delay in normal impulse formation or conduction.
Exit block	Failure of the pacemaker output to cause myocardial depolarisation because the pacing threshold exceeds the output capacity of the pacemaker.
Fontan	Surgical procedure performed post bi-directional Glenn where an extra or intra-cardiac pathway (tunnel) is formed to connect IVC to the pulmonary artery.

Glenn shunt	Surgical procedure involving ligation of any previous aorto-pulmonary shunt, anastomosis of SVC to RPA, the cardiac end of the SVC is over-sewn and the main pulmonary artery is over-sewn. This is also known as a bi-directional Glen (BDG) or hemi-Fontan.
Hemi-Fontan	See Glenn shunt.
High threshold	An elevated pacing threshold resulting in intervention due to the inability to programme adequate safety margin for capture.
Impedance (pacing)	The opposition to current flow in a pacing circuit, including the electrode tissue interface, lead conductor and the polarisation resistance.
Loss of sensing	Failure of the pacemaker sensing circuit to detect intrinsic depolarisation signals, at the maximum programmable sensitivity, causing inappropriate delivery of a pacemaker stimulus.
Measured data	Real time measurements performed at the time of pacemaker interrogation, transmitted by telemetry to the programmer. Measurements include battery data such as: voltage, current and impedance and lead data such as: energy, current, impedance and amplitude.
Muscle inhibition	Detection by the pacemaker sensing circuit of skeletal muscle signals resulting in failure of the pacemaker to deliver a stimulus at the appropriate time. This may also be referred to as myopotential inhibition.
Myopotential inhibition	See muscle inhibition
Oversensing	Detection by the pacemaker sensing circuit of cardiac, skeletal or external signals resulting in failure of the pacemaker to deliver a stimulus at the appropriate time.
Pacing threshold	The minimum amount of energy required to consistently achieve myocardial depolarisation outside the hearts refractory period.
Passive fixation	Method of pacing lead attachment to the heart where the lead tip lies against the myocardial surface and is held in position using sutures (epicardial leads) or tines (transvenous leads).
Polarisation	A build-up of charge on or near the electrode following a pacing stimulus, which opposes the flow of current from the lead tip to the myocardium.

Rate responsive pacing	Pacing function where the pacemaker rate changes in response to the signals from a sensor which is within the pacemaker. The sensor may detect activity level, minute ventilation or other parameters.
Safety margin (capture)	The difference between the programmed voltage and measured voltage pacing threshold or the difference between the programmed pulse width and the measured pulse width pacing threshold.
Sensing threshold	The minimum signal strength (highest sensitivity setting) that allows continuous sensing of the intrinsic depolarization.
Sensitivity	The responsiveness of a pacemaker's sensing amplifiers to electrical activity which is usually from the heart.
Steroid-eluting	The lead electrode contains a small reservoir of steroid (such as dexamethasone sodium phosphate) which is eluted into the local tissue when the lead tip contacts body fluid.
Strength duration curve	A graph of the pacing threshold (voltage) as a function of the pulse duration (milliseconds).
Stylet	A temporary guide wire that is inserted into the core of a transvenous lead during implantation to aid in lead manipulation.
Telemetry	The use of radiofrequency waves to transmit programmed parameters, measured and diagnostic data from the pacemaker to the programmer.
Twitch	Stimulation of the diaphragm or stimulation of skeletal muscle in the location of the pacemaker by the pacemaker output.
Unipolar	Current flows from the pacemaker through a conductor to the lead tip (cathode) electrode and from there via the body tissues to the metal case of the pacemaker (anode).
Uni-ventricular heart	Congenital cardiac anatomy where one of the ventricles is hypoplastic.

1 Introduction

Cardiac pacing is for some patients a life saving procedure while for others pacing dramatically improves their quality of life. Patients may be completely dependant on the reliable performance of the artificial pacemaker and the pacing leads, which are both required in order to achieve cardiac pacing.

Cardiac pacing in adults typically uses transvenous lead placement which is described in section 1.5.1, with the pacemaker located subcutaneously in the pectoral region. Pacing in adults is relatively common with approximately 1700 endocardial leads sold in New Zealand (NZ) per year (personal communication with Rosemary White). A significant amount of literature has been produced on the practice and outcome of pacing in this group with the conclusion that cardiac pacing in adults has a relatively low risk of complications (Helguera, *et al*. 1994; Kazama, *et al*. 1993; Arnsbo and Moller. 2000). Pacing hardware manufacturers have invested considerable time and money into research and development in order to improve pacemakers and leads for this group of patients.

Cardiac pacing in the paediatric age group and in a small proportion of adults may require the use of epicardial lead placement, which is described in section 1.5.2. There is limited experience and relatively little published data in this specialty group of the cardiac pacing population. The Danish pacemaker registry contains data on approximately 33,000 transvenous pacing leads and only 159 epicardial leads (Arnsbo and Moller, 2000). In NZ an average of 16 epicardial lead implants were performed each year between 1992 and 2002.

Cardiac pacing in paediatric patients using epicardial lead placement has specific challenges which make this pacing subgroup complex. The implanting surgeon, pacemaker technologist, cardiologist, child and parents face many difficulties. Four such difficulties are described below:

1. The small patient size at the time of implantation means there is limited space for placement of the electrodes on the epicardium and limited area within the pericardial cavity and abdomen for containing the lead body and pacemaker unit.
2. Leads implanted in infants and children will be required to sustain pacing through to adulthood, thus requiring continual assessment of lead length with regard to patient growth and determination of the appropriate time for lead revision.
3. Patients may have had multiple complex cardiac surgical procedures which can result in the myocardium becoming fibrotic, being covered in adhesions or having poor contractile function.
4. Patients are looking at a lifetime of pacing including multiple pacemaker related surgical procedures, with an ongoing requirement to attend outpatient pacemaker clinics on a regular basis to ensure adequate pacing function is maintained.

Green Lane Hospital (GLH) has a relatively extensive experience in implantation and follow-up of epicardial pacing leads for three main reasons. Firstly, GLH was the paediatric cardiothoracic specialist hospital for NZ until this service transferred to the Starship hospital in 2003. Ninety nine percent of NZ epicardial lead implants were performed there. Also GLH received referrals for paediatric patients from the Pacific Islands. Secondly, while follow-up of these patients is performed through out NZ and the Pacific, the GLH pacing and cardiology service maintained an advisory role to these centers and therefore receives information on the performance of the leads and patient outcomes. Thirdly, steroid-eluting (SE) epicardial leads were first used in NZ in 1993 which is 3 years earlier then the United States (US) due to the lengthy approval process of the Food and Drug Administration in the US.

In the field of epicardial pacing, the relatively low number of patients and leads reported in international publications reflects the limited data available. Four of the largest and most recent studies on epicardial pacing leads were: Thomson in 2004 who reported on 96 leads implanted in 59 patients, Horenstein in 2003 who reported on 62 patients with 79 leads implanted, Cohen in 2001 who reports the findings from 123 patients with 207 epicardial leads implanted and Noiseux in 2004 who reported 122 patients with 260 epicardial leads.

The collation of the GLH experience serves to add to the international body of knowledge on epicardial pacing and to improve the outcome for current and future patients receiving these leads. It will assist the pacing service in deciding the best techniques to deal with this complex group of patients.

1.1 History of cardiac pacing

Permanent cardiac pacing is a relatively recent medical achievement. The first cardiac pacemaker to be implanted was developed by Senning and Elmqvist and implanted in 1958 with an epicardial pacing lead (Elmqvist, *et al*. 1963). From this time onwards, cardiac pacemaker development underwent rapid improvement along with a growing application for use.

In 1959 the first fully battery powered pacemaker, developed by Greatbach, was implanted (Varriale and Naclerio, 1979). Lithium batteries were invented in the 1970s and the lithium-iodine version was soon applied to cardiac pacemakers due to the small size, stability and longevity properties of this technology. Lithium-iodine batteries have a proven record of reliability and are therefore still used today (Ellenbogen, *et al*. 1995).

Developments in electronic circuitry have expanded the therapeutic and diagnostic capabilities of modern pacemakers. Telemetry was initially introduced in 1978, and is now considered an essential pacemaker feature. Telemetry allows non-invasive parameter interrogation, real time diagnostic battery and lead measurements to be performed, diagnostic data retrieval and transmission of the information from the pacemaker to the programmer for interpretation.

Early pacemaker implants used epi-myocardial leads which were implanted by a thoracotomy incision. In the early 1960's transvenous leads were successfully implanted and following design improvements to ensure dependable fixation this method of lead placement rapidly became the norm, thus simplifying the implantation procedure (Varriale and Naclerio, 1979). Specific atrial transvenous leads were developed in 1978, allowing dual chamber pacing. The first dual chamber rate responsive pacemaker was implanted as recently as 1986 (Nelson, 1993).

The innovations in pacing technology in the 1970's and 1980's have resulted in smaller pacemaker units and leads making them applicable to children. Around this time there was also advancement of paediatric surgical techniques, which resulted in increased survival of children with congenital heart defects. Along with the development of surgical techniques came an increase in the incidence of surgically-induced conduction system problems. The use of pacing in the prevention of atrial arrhythmias and treatment of conditions such as Long QT syndrome has also expanded over recent decades. These factors have resulted in an overall increase in the use of permanent pacing in paediatric patients, although numbers remain small in comparison to permanent pacing in the adult population.

1.2 Green Lane Hospital history

Cardiac congenital bypass surgery was first performed at GLH in 1958 and this service expanded significantly over the next decade. In the late 1960's Sir Brian Barratt-Boyes refined a technique which used profound hypothermia with circulatory arrest during open heart surgery on infants with dramatic improvements seen in patient outcome. This method was quickly adopted internationally which resulted in GLH achieving widespread international recognition in this specialty. Many overseas patients were referred to the hospital for treatment and a number of surgeons visited to observe the techniques first hand (Hutchinson, 1990).

The first pacemaker implantation at GLH was performed in 1961 using an epicardial lead (Mond and Whitlock, 2001). By 1964 the total number of implants had reached double figures and in 1969 the first endocardial lead was implanted. By 1977 GLH was implanting one hundred pacemakers a year with the first programmable unit implanted in 1981.

1.3 Pacing indications

Pacemakers are required in paediatric patients where there are cardiac conduction system abnormalities such as second or third degree atrio-ventricular block (AVB) or sick sinus syndrome (SSS). Conduction system abnormalities may be either acquired or congenital conditions. These abnormalities may result in a loss of atrio-ventricular synchrony and / or an inadequate ventricular rate resulting in a reduced or no cardiac output. A patient in this abnormal haemodynamic state has the potential for syncope, pre-syncope, lethargy, poor growth, poor exercise tolerance and death.

The American Mid West pacing registry with over a thousand paediatric patients registered, reports that the most common indications for pacemaker implantation in 2002 were surgical SSS followed by congenital AVB (**Table 1**) (Mid West pediatric pacemaker registry, 2002).

Table 1 Mid West paediatric pacemaker registry, indications for pacing in 2002

Pacing indication	**% patients**
Surgical sick sinus syndrome	38%
Congenital atrio-ventricular block	36%
Surgical atrio-ventricular block	18%
Congenital sick sinus syndrome	8%

Other less common indications for pacing are prevention of atrial arrhythmias and long QT syndrome.

1.3.1 Acquired conduction system abnormalities

Surgery for complex congenital heart disease has undergone significant improvements over recent years and these techniques are applied to a wider group of paediatric patients. This has resulted in an improved quality of life and increased longevity for a greater number of children with congenital heart disease. These surgical procedures may involve the intervention in the location of the sinus or atrio-ventricular node with the potential for sinus node dysfunction (**Figure 1**) or varying degrees of atrio-ventricular block (**Figure 2**) respectively, therefore resulting in the requirement for permanent pacing.

Figure 1 Electrocardiograph recording of a sinus pause due to sinus node dysfunction

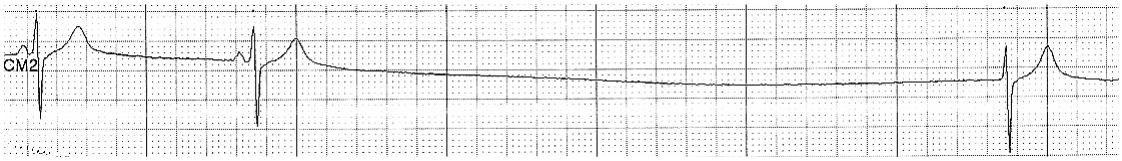
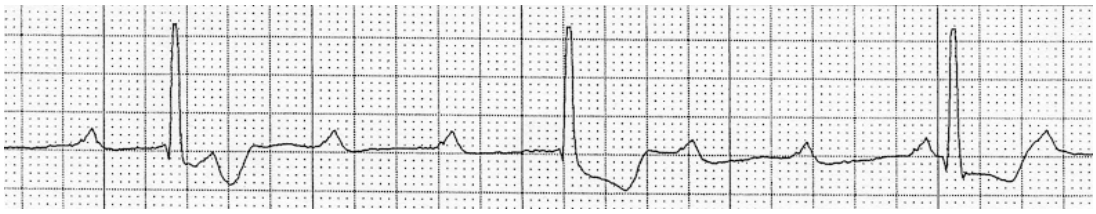


Figure 2 Electrocardiograph recording of complete atrio-ventricular block



Review of the last 6 years statistics from the Mid West pacing registry shows that surgical AV block used to be the most common indication for pacing in the late 1990's but has reduced over recent years, which may be due to improved surgical techniques. In recent years there has been an increased incidence of pacing for surgical SSS, which is likely to be due to the increased application of surgical corrections involving the atria such as the Fontan procedure (Mid West pediatric pacemaker registry, 2002).

Surgical procedures such as the Fontan operation for palliative treatment of valvular atresia or univentricular heart have a 16 to 44% incidence of sinus node dysfunction (Manning and Mayer, 1996; Cohen, *et al*. 1998). This is due to damage to the sinus node or its vascular supply by the extensive atrial suturing involved in this region during the Fontan procedure. Late atrial arrhythmias occurring post Fontan may even involve excision of the sinus node with atrial reduction, when an atrio-pulmonary connection is changed to an external cardiac conduit (Mavroudis, *et al.* 2001).

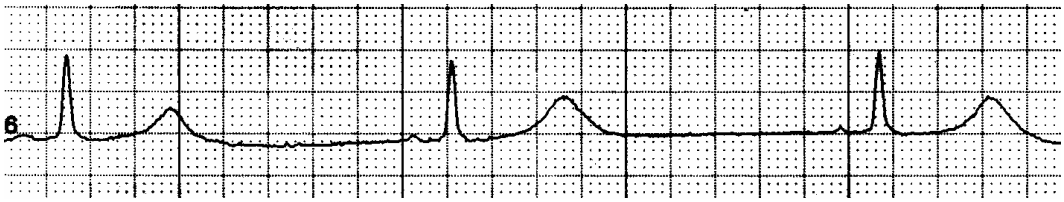
Acquired conduction system abnormalities may also be exacerbated by anti-arrhythmic medications, which may suppress the automaticity or the conductive properties of the neuromyocardium to a point where permanent pacing is required.

1.3.2 Congenital conduction system abnormalities

The most significant congenital conduction system abnormality is congenital atrio-ventricular block (**Figure 2**) which has an incidence of approximately 1/20,000 births (Hamilton. 2002). Michaelsson, *et al*. (1997) reported the mortality rate of infants and children with untreated congenital complete AV block (CCAVB) and a normal heart to be 8 to 16%. Several studies have indicated that the majority of patients with CCAVB eventually require pacing (Jaeggi, *et al*. 2002; Michaelsson, *et al*. 1995). Published guidelines on the indications for pacing indicate that pacing is required for congenital third degree AV block when there is a wide QRS escape rhythm, complex ventricular ectopy, ventricular dysfunction and for infants, a ventricular rate less than 50-55bpm with a normal heart or less then 70bpm with congenital heart disease (Gregoratos *et al*. 2002).

Another congenital conduction system abnormality is long QT (LQT) syndrome (**Figure 3**). In this condition there is abnormal sodium and potassium ion movement across the cell membrane resulting in delayed repolarisation which may result in torsade de pointes and sudden cardiac death. Some genetically inherited forms of LQT have been treated with beta blockade and permanent pacing, although implantable pacemaker-defibrillators are used more commonly now.

Figure 3 Electrocardiograph recording of sinus rhythm with a long QT interval



1.4 Pacing hardware

1.4.1 Pacemakers

Pacemakers contain a battery, microprocessor and circuitry, which are housed within a titanium case. The epoxy header block provides a sealed connection port between the lead(s) and the rest of the pacemaker. The casing is hermetically sealed so that fluids do not enter the device and to prevent corrosive battery materials leaking out of the unit. Titanium, as well as being an inert material, helps to shield the internal components to reduce the effect of external interferences (Handbook of materials for medical devices, 2003).

A significant amount of research and development has been carried out by pacemaker manufacturers over recent decades. Pacemakers implanted in the 1970's did not have telemetry features and therefore were non programmable. These devices were single chamber, fixed rate and had a fixed output of approximately 5 volts at 0.5 milliseconds (msecs). Pacemakers implanted today may have over 50 programmable parameters, algorithms to alter pacing modality and diagnostic features. The diagnostic data acquired by the device enables interpretation of the day to day pacemaker function and the patient's intrinsic rhythm.

Modern pacemakers contain a solid state, lithium-iodine battery and the longevity depends on the battery size and current drain. The current drain is affected by the programmed pulse amplitude, pulse width and lead impedance. Ohms law (I = V/R) shows that the lower the programmed voltage and the higher the impedance, the lower the battery current drain. One of the relatively new features of current pacemakers is automatic capture detection with automatic output adjustment to values just above the pacing threshold which minimizes battery drain and therefore increases battery longevity.

Pacemakers implanted in paediatric patients are the same models available for use in adult patients although the criteria for device selection may be quite different for young patients. Some of the considerations which must be taken into account when choosing the pacemaker for a paediatric patient include the maximum programmable upper rate, the availability of automatic output detection to increase device longevity and device size particularly in infants.

The production of smaller and lighter pacemakers is a significant factor in the evolution of paediatric pacing today compared to the 1970's. Devices implanted in the late 1970s were 85 mm high, 55 mm in length, 16 mm wide and weighed 130gms (Telectronics 120B, Pacer identification reference, 1993). The smallest single chamber rate responsive pacemaker currently available is the Microny™, produced by St Jude Medical. This device is only 33mm high, 33 mm in length and 6mm wide and weighs 12.8 grams (St Jude Medical bradycardia devices reference manual, 2003). **Figure 4** shows the size difference between the Telectronics 150L pacemaker which was implanted in 1979 compared to the St Jude Microny which is currently implanted.

Figure 4 Telectronics 150L and St Jude Microny pacemakers

1.4.1.1 Pacemaker replacement

Pacemaker replacement is a relatively straight forward procedure which is required approximately every 5 to 10 years due to battery depletion. The procedure involves an incision over the existing pacemaker and removal of the old device. In paediatric patients the pacemaker is generally placed subcutaneously in the abdominal region although in some cases the device is implanted sub-muscularly. The lead(s) are tested and if acceptable function is confirmed the new pacemaker is then connected to the existing lead(s) and placed back into the same pocket as the previous pacemaker.

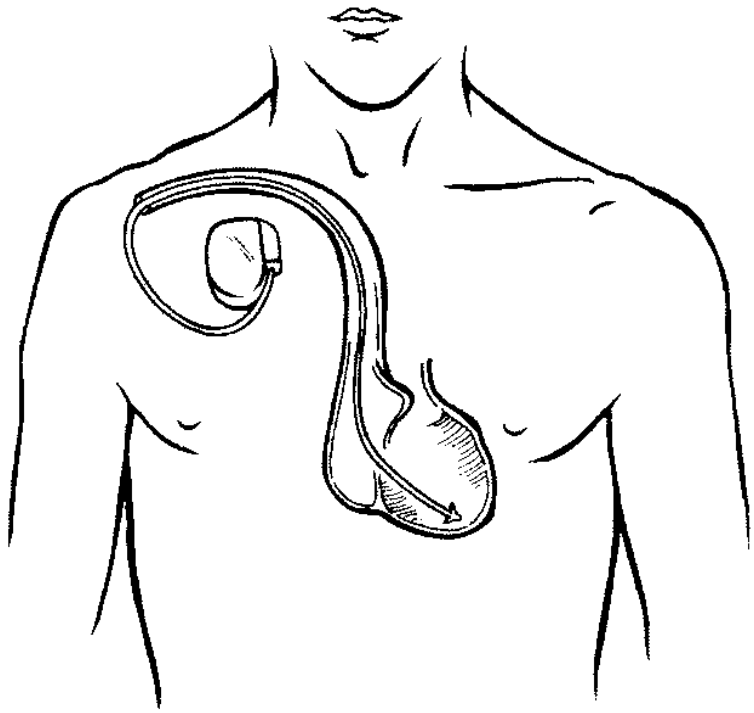
1.4.2 Pacing leads

Pacing leads are composed of inner coils of conductive wire covered with an outer insulation material of silicone or polyurethane. At the tip of the lead are one or two electrode(s) through which the energy is delivered to the myocardium.

1.4.2.1 Transvenous pacing leads

Transvenous pacing leads may be attached to the endocardium by passive fixation which uses tines, located at the lead tip (**Figure 5**) or by active fixation which uses a screw-in mechanism. Lead access to the heart is usually via the cephalic or subclavian veins, with the pacemaker commonly placed in the pectoral region. Both active and passive fixation transvenous leads have been available with steroid-elution since the 1980's.

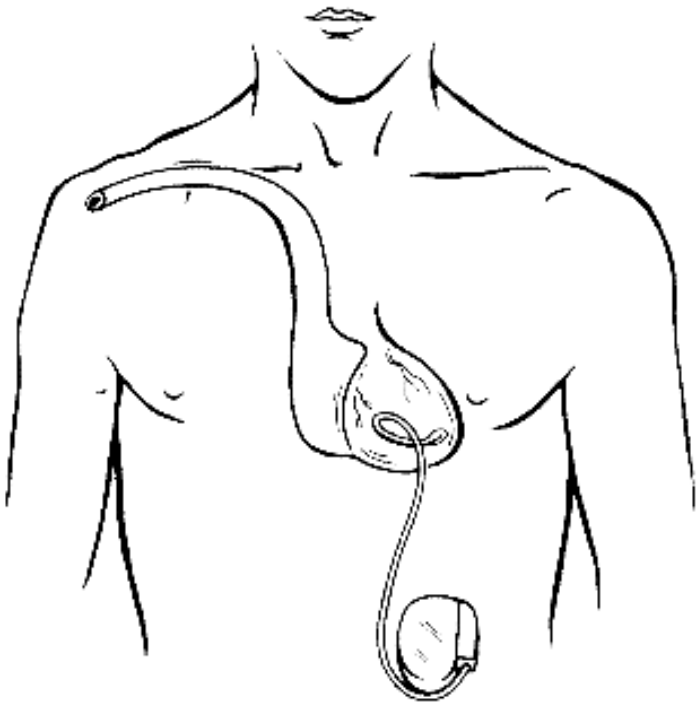
Figure 5 Transvenous lead placed within the heart



1.4.2.2 Epicardial pacing leads

Epicardial leads use either passive fixation, where the electrode lies against the surface of the heart and stay sutures hold the lead in place (**Figure 6**), or active fixation. Active fixation leads are more accurately referred to as epi-myocardial leads which may use a fishhook or screw in mechanism to anchor the lead to the myocardium. Steroid-eluting passive fixation epicardial leads became available in New Zealand in 1992. Active fixation epi-myocardial leads are not manufactured with a steroid-eluting tip.

Figure 6 Epicardial lead attached to the heart



1.4.2.3 Epicardial lead specifications

The epicardial leads most commonly implanted are the Medtronic 4965 and 4951M models described below. The major difference between these two lead models is the presence or absence of steroid at the tip and the passive suture versus the active fishhook barb fixation methods. The bipolar equivalent of the 4965 lead is the Medtronic 4968 lead which is also described.

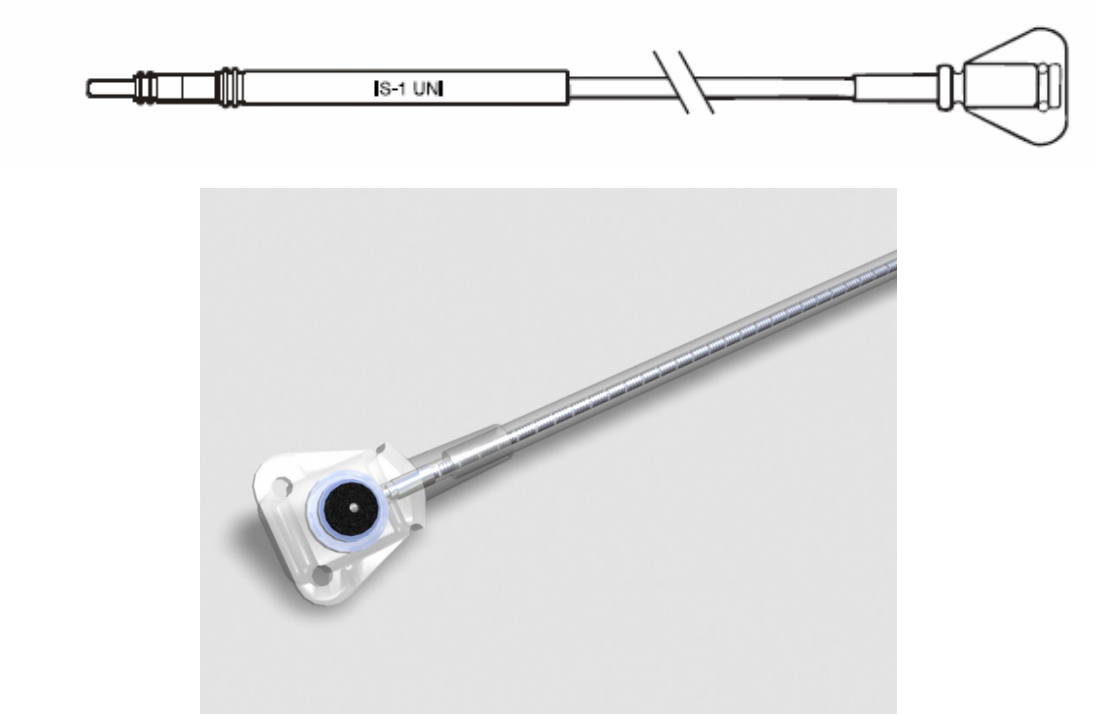
1.4.2.4 Medtronic 4965 epicardial lead

The Medtronic 4965 lead is a steroid-eluting, unipolar, epicardial pacing lead with the specifications outlined in **Table 2** (Medtronic 4965 Technical Manual, 1992) and the lead tip appearance shown in **Figure 7**.

Table 2 Specifications of the Medtronic 4965 epicardial lead

Parameter	Specification
Electrode material	platinum alloy, porous, platinized with platinum black
Surface area	14mm^2
Steroid	1 mg of dexamethasone sodium phosphate at the tip
Diameter	4.5 French (1.5 mm)
Length	110cm
Fixation	sutures
Placement	atrial or ventricular epicardium
Conductor	MP35N nickel-alloy
Insulator	silicone rubber

Figure 7 Medtronic 4965 lead appearance



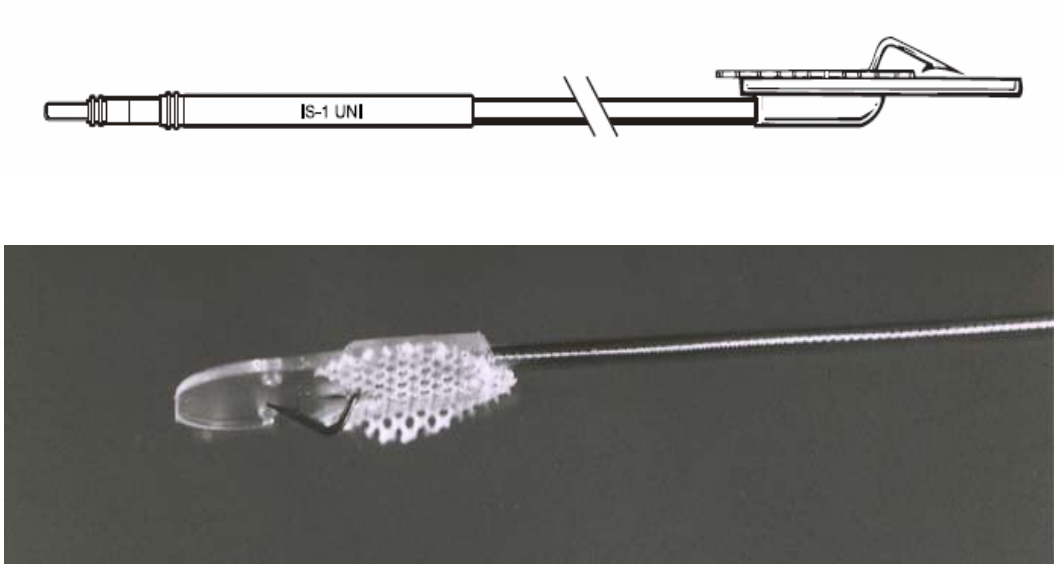
1.4.2.5 Medtronic 4951-M epicardial lead

The Medtronic 4951-M lead is a myocardial, unipolar lead with the specifications outlined in **Table 3** (Medtronic 4951-M Technical Manual, 1991) and the lead tip appearance shown in **Figure 8**.

Table 3 Specifications of the Medtronic 4951-M epicardial lead

Parameter	Specification
Electrode material	platinized platinum alloy
Surface area	$10mm^2$
Steroid	none
Diameter	4.3 French (1.4 mm)
Length	110cm
Fixation	fishhook barb $\pm$ sutures
Penetration depth	2mm
Placement	atrial or ventricular epicardium
Conductor	MP35N nickel-alloy
Insulator	polyurethane

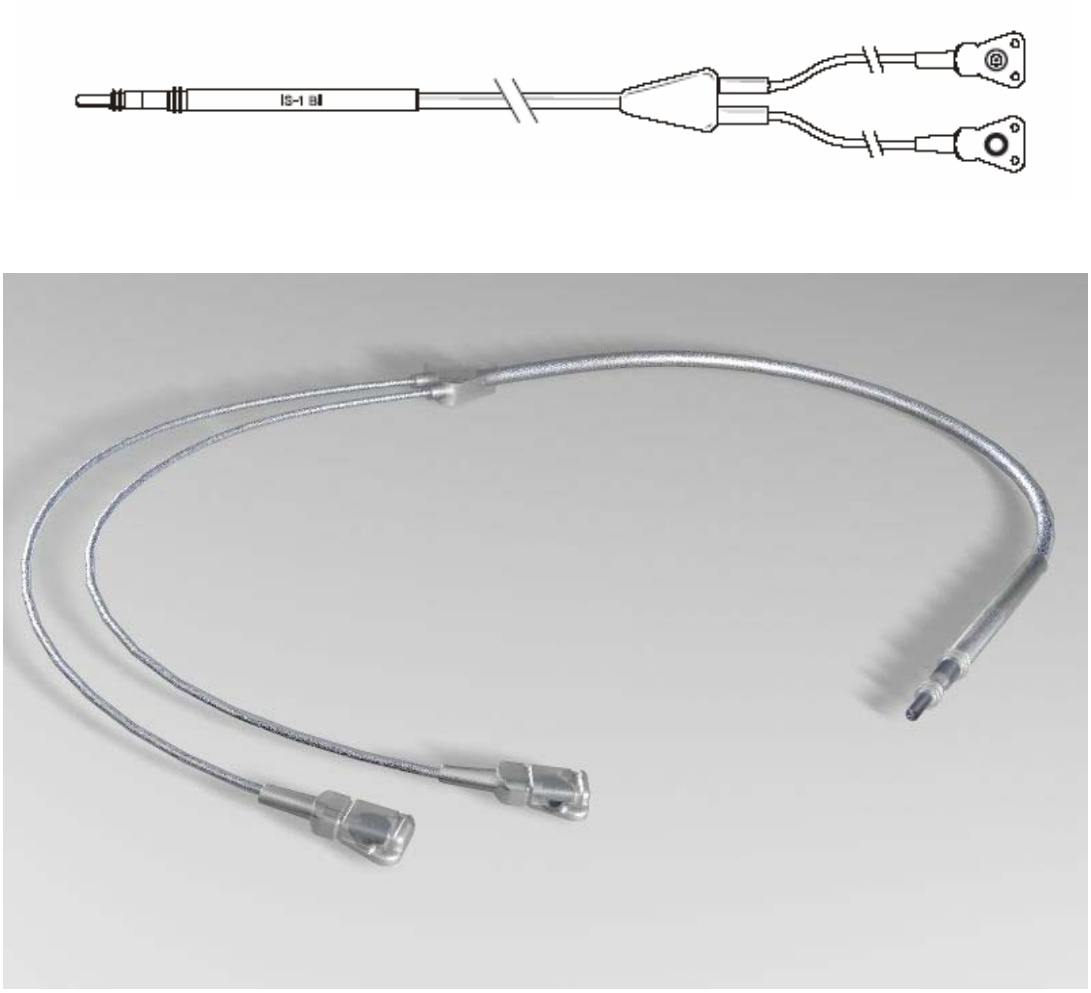
Figure 8 Medtronic 4951-M lead appearance



1.4.2.6 Medtronic 4968 epicardial lead

The Medtronic 4968 lead is a bipolar model of the 4965 lead and has similar specifications, including steroid-elution although the lead diameter after the junction is 8 Fr (2.7 mm) (Medtronic capsure® epi 4968 technical manual, 2003). The appearance is shown in **Figure 9**. This lead became available in NZ in 1992 and in the US in September 1999. The 4968 lead was also identified by the engineering code number 10366 when it was first released.

Figure 9 Medtronic 4968 lead appearance



1.4.2.7 Steroid-eluting epicardial leads

Pacing leads have undergone important technological improvements over the past two decades with the most significant recent advancement being the introduction of steroid to the tip of the pacing lead. The presence of steroid is described in the Medtronic 4965 technical manual as follows: “Each electrode contains a maximum of 1.0mg of dexamethasone sodium phosphate, a portion of which is in a silicone rubber binder. Upon exposure to body fluids, the steroid elutes from the electrode. Steroid suppresses the inflammatory response that is believed to cause threshold rises.” (Medtronic 4965 technical manual, 1992).

The Medtronic 4965 technical manual also states the following contraindication to the use of this lead: “The lead should not be used on a patient with a heavily infarcted or fibrotic myocardium. It is also contraindicated for the patient whose myocardium is suffused with fat”.

1.5 Implant techniques

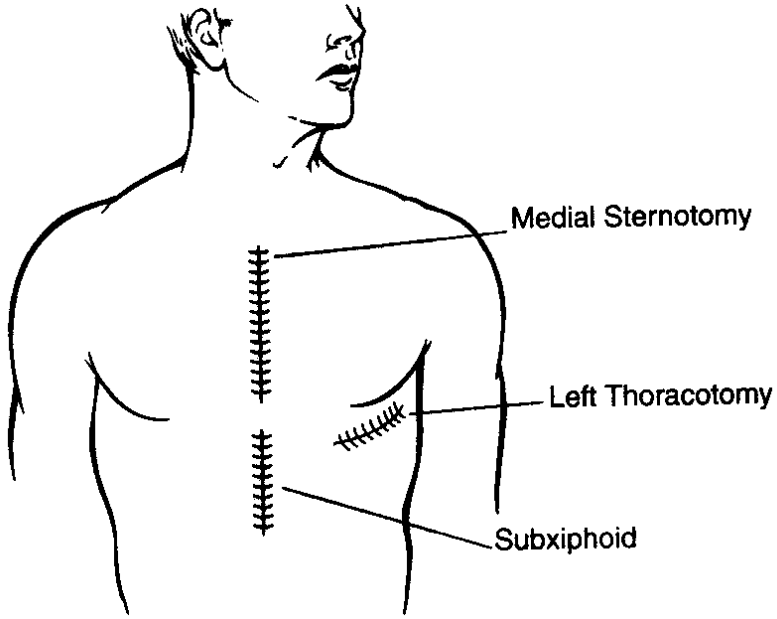
1.5.1 Transvenous lead placement

Transvenous lead placement is normally performed by a cut down to the cephalic vein or a percutaneous puncture of the subclavian vein both within the pectoral region. Once venous access has been obtained the transvenous lead(s) are passed through the vein and positioned in the required intra-cardiac location(s), which are typically the right atrium and right ventricle, with the assistance of a temporary guiding stylet. Lead measurements are performed to ensure the position is acceptable for normal lead function and then the lead(s) are connected to the pacemaker header block using a screw in mechanism. The transvenous method of lead placement is used in adult patients with rare exceptions. This approach is minimally invasive as it only requires a local anaesthetic (for adult implants) in the region where the vein is accessed and the pacemaker is placed.

1.5.2 Epicardial lead placement

Epicardial lead electrodes may be affixed to the surface of the heart by either sutures or a fishhook or corkscrew mechanism. Visual access to the epicardium is required for this method of lead placement necessitating a lateral thoracotomy, median sternotomy or subxiphoid incision (**Figure 10**). These significantly invasive surgical procedures require the patient to have a general anaesthetic (GA).

Figure 10 Surgical incisions used for epicardial lead implantation



(Medtronic capsure® epi 4968 technical manual)

The implantation procedures suggested in the technical manuals for the Medtronic 4951(M) and 4965 leads are as follows: "For atrial application: Use a thoracotomy or median sternotomy to expose the atrium." "For ventricular application: A variety of surgical approaches can be used, including limited thoracotomy, subxiphoid, transxiphoid, and transmediastinal." (Medtronic 4951(M) and 4965 technical manual, 1991 and 1992). However, recent experience with lead implantation in young children is that the subxiphoid approach can also be used for atrial leads.

Steroid starts to be eluted when the electrode comes in contact with fluid so movement of the electrode should be kept to a minimum. The electrode must be securely sutured to ensure good long term lead performance.

1.6 Lead selection

In the last decade the type of lead selected for implant has significantly altered due to the technological improvements in lead design, specifically the introduction of steroid to the tip of the lead. The following factors must be taken in to consideration when selecting the appropriate lead(s) for a patient.

1.6.1 Atrial, ventricular or both

Placement of both atrial and ventricular leads allows physiological (AV synchronous) pacing and is therefore preferable although not always possible. Placement of atrial leads can be difficult when the subxiphoid route is used due to limited access to the atria. In general, the bigger the child, the more difficult the atrial access. Newborn infants with very small hearts and abdominal cavities may preclude placement of two leads although dual chamber pacing in infants as young as three days old has been performed at GLH. For infants requiring pacing at the time of birth, placement of a ventricular lead with a smaller single chamber unit may be the best option.

1.6.2 Unipolar or bipolar leads

Epicardial unipolar leads have the advantage of a small electrode surface to attach to the heart and a smaller lead body to fit within the abdominal cavity. Bipolar leads on the other hand require a larger area of healthy epicardium for attachment of the two electrodes. It is recommended that each electrode should be separated by a minimum of 1cm (Medtronic, 4968 capsure® epi technical manual, 2003). The relatively bulky lead region from the electrodes to the bifurcation must be placed within the pericardial cavity, which may be of limited space. Unipolar lead implantation is a simpler procedure due to only attaching one electrode.

Bipolar leads have several perceived advantages including a stronger lead body which may reduce the risk of lead fracture, although this is not proven. In bipolar leads, current flow and sensing is between the two electrodes located 1cm apart, which may reduced the chance of oversensing and twitching compared to unipolar pacing. If a fault develops in one of the lead conductors, there is a potential to use the other conductor by reprogramming the pacemaker to unipolar pacing.

1.6.3 Active versus passive leads

Medtronic state that passive leads are contraindicated in patients who have a heavily infarcted or fibrotic myocardium or patients who have an epicardium suffused with fat (Medtronic 4965 technical manual, 1998). The difficulty is that many paediatric patients require epicardial pacing post surgery with the myocardium suffering from scarring, adhesions or fibrosis. Active fixation leads are able to provide deeper myocardial penetration thus bypassing the damaged epicardial surface. The disadvantage of active fixation leads is that they are not steroid-eluting. Innovative approaches have been tried to overcome the difficulty of achieving adequate pacing with a passive lead when the epicardial state is poor plus wanting to avoid using a NSE lead. Karpawich, *et al*. reported a case where several attempts using epicardial leads had failed to achieve adequate pacing thresholds and therefore a transvenous SE pacing lead was buried into the myocardium with a successful outcome (Karpawich, *et al*. 1998). Placement of a transvenous lead by trans-atrial puncture and transvenous ventricular pacing via the coronary sinus has also been described as alternative options (Goldstein, *et al*. 1999).

1.6.4 Epicardial versus transvenous leads

Transvenous pacing leads in adults have provided reliable pacing function with a low rate of complications over long term follow-up (Helguera, *et al*. 1994; Kazama, *et al*. 1993; Arnsbo and Moller. 2000). Nevertheless there are situations where transvenous lead placement is not possible or contraindicated as summarized in **Table 4**.

Table 4 Epicardial versus transvenous pacing lead indications

Indications for transvenous pacing	Indications for epicardial pacing
• Reduced complication rate	• Small patient size
	• Young age
• History of lower pacing thresholds resulting in increased generator longevity and ultimately reduced rate of re-operation.	• Surgical palliations such as the Fontan operation and Glenn Shunt
	• Congenital defects with right to left shunting including tricuspid atresia
• Less invasive implant procedure	• Tricuspid valve replacement with prosthetic valve
	• Concurrent cardiac surgery
• Can be performed without GA in adults	• Previous venous occlusion
	• Congenital abnormalities of the systemic veins

1.7 Epicardial lead advantages

1.7.1 Patient size

A few centres place transvenous leads in neonates and small children. The leads are large compared to the veins through which the leads are placed. Fibrous tissue growth around the lead may result in attachment of the lead to the vascular wall or intra-cardiac structures. The fixed point of attachment remains unchanged as the patient grows resulting in tension on the lead and any attached structures. Fibrous tissue growth and the bulk of the lead body may reduce blood flow past the lead with the potential for venous thrombosis or total venous occlusion.

The significance of venous thrombosis or stenosis for the patient can vary significantly. Patients may be completely asymptomatic due to formation of collateral vessels, they may develop swelling and pain in the face and arm and there is the potential of sudden death due to pulmonary emboli. Symptomatic venous thrombosis due to transvenous pacing is a relatively rare complication with a reported incidence of between 0.35% to 2.4% (Kar, *et al*. 2000; van Rooden, *et al*. 2004; Crook, *et al*. 1977) although the incidence of asymptomatic thrombosis is much higher. Stoney, *et al*. (1976) found 32% of 34 cases had severe obstruction, Goto, *et al*. (1998) reported a 23% incidence of asymptomatic venous thrombosis in 100 patients and Da Costa, *et al*. (2002) found 64% of 229 patients had abnormal venograms. Treatment ranges from intravenous heparin and, or thrombolytic therapy to surgery to remove the thrombus or lead extraction (described in 1.7.1.1).

Because of the potential complications with transvenous pacing and the repeated interventions to allow for growth, the policy at the majority of hospitals is to implant epicardial leads in small children. The weight and age for the transition from epicardial to transvenous lead placement varies. The policy at some hospitals is to epicardially pace patients weighing less than 10 kg (Warner, *et al*. 1999) while others use 40 kg as the transition point (Thomson, *et al*. 2004). In larger children transvenous lead placement is typical practice although there is no standard weight or age where this is applied. Villain, *et al*. carried out an evaluation of their policy to implant epicardial leads in children weighing less than 10 kg and they reported a satisfactory outcome for 34 patients who received 56 leads in this study with only one lead fracture at 8 years

post implant (Villain, *et al*. 2000). Aside from these few studies, there is not much data to support this practice and the long term outcome for this group is not clear.

The venous system in adult patients can typically accommodate both atrial and ventricular leads. If a transvenous lead fails and needs to be replaced, there may be adequate venous space for a third or fourth lead in an adult. In contrast for small children with transvenous leads, if there is a requirement for further lead implantation due to existing lead failure this may necessitate extraction of the old leads before new leads can be accommodated within the veins. It is important to be aware that these young patients are often looking at a lifetime of pacing with the likelihood of multiple pacemaker related interventions during this time, each of which carries a risk to the patient. Preservation of the venous access is therefore an important consideration in deciding whether to pace epicardially or transvenously.

1.7.1.1 Lead extraction

In cases where multiple transvenous leads have been placed and a new lead is required, lead extraction or epicardial lead placement are the only options. Lead extraction may be achieved using a counter-traction method where a telescopic sheath is advanced over the lead to break any attached fibrotic tissue along the lead shaft, a locking stylet is placed within the lead and lead is pulled while pushing against the endocardium at the lead attachment site using the sheath. Newer techniques involve delivery of electrocautery or laser energy through a sheath in order to release the lead from any attached fibrotic tissue (Kutalek, 2004).

Difficulties or complications which may be encountered with extraction include: an inability to pass the sheath under the clavicle or past an adhesion point resulting in a failed extraction, the lead may come apart during the process resulting in partial extraction and superior vena cava (SVC) tearing or right ventricular rupture may occur necessitating emergency bypass surgery (Love, *et al*. 2000). Bracke, *et al*. (2004) reported 7% of 82 cases had major complications during lead extraction, including 2 deaths. A review of the total lead extraction experience for the United States reported a 1.9% occurrence of major complications from 2561 extractions (Byrd, *et al*. 2002) although the complication rate can be much higher depending on the level of operator

experience (Love, *et al*. 2000). Lead extraction in patients with congenital abnormalities may be further complicated by a tortuous lead route.

1.7.2 Access to the heart

The Fontan procedure, for palliation of a univentricular heart, directs systemic venous blood directly to the pulmonary arteries using either an extra-cardiac shunt or by placement of a baffle within the right atrium. This post-surgical anatomy prevents venous access to the heart for transvenous lead placement. The Glenn shunt or hemi-Fontan, involves the SVC being connected to the right pulmonary artery. Since the usual route of transvenous lead placement is via the SVC this surgery also prevents transvenous lead access to the heart. Achieving permanent pacing in these patients is typically achieved by epicardial pacing (Heinemann, *et al*. 2003; Cohen, *et al*. 2001a). Alternatively transvenous lead placement via atriotomy has been performed in a limited number of cases (Hansky, *et al*. 2005), although systemic embolism remains a concern.

Because the Fontan procedure involves intervention in the region of the sinus node and involves suture lines in the right atrium, these patients may require pacing due to surgically induced sick sinus syndrome, and / or prevention of atrial arrhythmias. The Mid west pacing registry reported a growing trend of pacing for surgical SSS which was also the most prevalent indication for paediatric pacing in their 1999 to 2002 data (Mid West pediatric pacemaker registry, 2002).

Endocardial lead placement within the right ventricle (RV) is not possible in patients with tricuspid atresia or those who have had a previous tricuspid valve replacement to due the inability to access the RV.

1.7.3 Thrombosis risk

The following factors, which relate to pacing in patients with congenital cardiac anomalies, result in an increased risk of thrombus formation or emboli.

- Following Fontan surgery a number of factors, including the low rate of systemic venous blood flow, increase the risk of thrombus and consequently emboli to the systemic or pulmonary circulation.
- Left atrium or left ventricular transvenous lead placement, apart from chamber access difficulties, is usually contraindicated due to the risk of systemic thrombus. Patients with intra-cardiac right to left shunting due to congenital anatomical defects will also have a risk of thrombus reaching the systemic circulation if a transvenous lead is placed within the right ventricle.
- Thrombosis can result in vessel occlusion as discussed previously in section 1.7.1 and emboli in the systemic circulation puts the patient at risk of a stroke or myocardial infarction.

1.7.4 Concurrent cardiac surgery

When pacing is required in the pediatric age group at the same time or close to the time of other cardiac surgery, epicardial lead placement is often performed via the existing sternotomy incision.

1.8 Epicardial lead performance

Previous reports have indicated that epicardial leads have relatively poor performance (DeLeon *et al*. 1990; Villafane *et al*. 1993; Rao *et al*. 1995) compared to transvenous leads. Esperer, *et al*. (1993) found that only 55% of 32 NSE epicardial leads survived to 5 years. Published data in the early 1990's related to NSE epicardial leads only as SE leads became available for use in 1992. Studies since this time are often a mixture of NSE and SE leads.

Table 5 shows a summary of literature reports on NSE leads which reflects the difficulties encountered with the era of epicardial pacing prior to the introduction of SE leads. The predominant finding from early epicardial lead studies was the high rate of lead failure due to exit block or high thresholds.

Table 5 Summary of published data on the performance of non steroid-eluting epicardial leads

Epicardial leads n	Percentage of leads with exit block	Reference
15	40%	Kugler, *et al*. (1988)
285	28%	Rao, *et al*. (1995)
28	47%	Villafane, *et al*. (1993)
97	23%	DeLeon, *et al*. (1990)
26	19%	Esperer, *et al*. (1993)

As shown in **Table 5**, the larger studies reported a 23-28% occurrence of exit block with smaller studies finding the occurrence much higher at 40 to 47%. These NSE lead reports prompted the use of transvenous leads in younger and smaller patients. Early literature reports suggested that endocardial pacing in children is the preferred option over epicardial pacing (Kerstjens-Frederikse, *et al*. 1991; Hayes, *et al*. 1983; Oldershaw, *et al*. 1982).

Since SE epicardial leads were introduced there has been a growing confidence in the use of these leads due to the positive early reports on their performance (Karpawich, *et al*. 1992; Johns, *et al*. 1992). Low stable thresholds and no exit block over 6 years of follow-up has been reported in 26 SE epicardial leads (Cutler, *et al*. 1997) although these leads are not exempt from lead failure due to exit block. Beder *et al*. (1997) reported precipitous exit block occurring in 3 out of 16 steroid-eluting epicardial leads over a two year follow-up period. Since then larger studies (including 82 leads) have reported a much lower risk of EB (2.4%) with SE epicardial leads (Cohen *et al*. 2001b).

1.9 Transvenous lead performance

A number of large studies, which include between 2,600 and 33,000 leads, have been performed, which review transvenous leads implanted in adult patients. Lead survival at 5 years is reported to be 97% to 99% and at 10 years between 94% and 98% (Furman, *et al*. 1990; Arnsbo and Moller, 2000; Helguera, *et al*. 1994).

Studies of transvenous leads in paediatric patients show a different outcome. Esperer, *et al*. (1992) found the survival rate of 33 leads at 10 years to be approximately 50% and Lau, *et al*. (1993) reported a 5 year survival of 76% for 217 leads. Although the studies in paediatric patients are much smaller, the difference in lead survival highlights the complexity of pacing this group of patients.

1.10 The transvenous versus epicardial lead debate

Several studies comparing SE transvenous and SE epicardial pacing leads have reported that the two groups have a similar performance and that epicardial leads are as reliable as transvenous leads (Dodge-Khatami, *et al*. 2000; Ten Cate, *et al*. 2002; Beaufort-Krol, *et al*. 1999). These studies have a relatively low number of leads and less than 3 years follow-up duration. At present there are no large studies comparing the long term performance of transvenous versus epicardial leads in the paediatric age group.

The various factors previously described in sections 1.6 and 1.7 indicate that while there are several options for how to achieve cardiac pacing in paediatric patients the decision is based on multiple factors and often requires a case by case consideration. Agreed guidelines have not been developed and in order to achieve this further studies are required with larger cohorts and longer follow-up to look at the long term outcomes of each option.

1.11 Aim and hypothesis

At this institution (GLH) a high pacemaker lead failure rate is suspected in the group of patients with epicardial leads. This study was performed in order to assess the incidence and timing of lead failure, to identify associated factors and complications and to compare the data collected with that reported by other institutions.

The specific aims of this study are to:

1. Assess pacemaker lead performance over time in relation to the type of epicardial lead implanted
2. Determine the survival rate of epicardial leads
3. Identify factors predicting or associated with lead failure

It is hypothesised that:

- Steroid-eluting epicardial leads have lower pacing thresholds and a reduced failure rate compared to non steroid-eluting epicardial leads.
- Steroid-eluting epicardial pacing leads are not exempt from chronic threshold rises resulting in exit block.
- It may be possible to identify a group of subjects at high risk of lead failure based on analysis of factors such as: implant technique, patient size or age at implant, patient growth and lead type.

2 Methods and Standards of Practice

2.1 Summary of methods

The design, method and collection of data for this study involved completion of the following steps, which are described in this chapter.

- Ethical approval
- Selection of patients and end dates for data collection
- Design of a data collection form
- Design of the main and complication database
- Database development
- Data collection from pacemaker files for Green Lane Hospital (GLH) and Auckland City Hospital (ACH) patients
- Data collection from pacemaker files for non GLH, ACH patients within New Zealand (NZ) and internationally.
- Data collection from echocardiography records
- Data collection from chest X-rays
- Statistical analysis
- Validation of the threshold conversion formula by a preliminary study (Chapter 3)

A retrospective audit was performed on all paediatric and adult patients, aged 1 day to 71.4 years at implant, who had epicardial pacing leads implanted at GLH, Auckland, NZ between 1/1/1977 to 1/12/2002. Green Lane Hospital is the primary centre for implantation of pediatric pacemakers in NZ and also performs a large proportion of NZ adult pacemaker implants.

Prior to December 1993 all epicardial leads implanted were non steroid-eluting (NSE), active fixation leads. After December 1993 steroid-eluting (SE), passive fixation epicardial leads were implanted at GLH as a first choice where possible. NSE active

fixation leads were still implanted when deeper myocardial penetration was required in order to pace through fibrotic tissue.

Information on lead function and patient outcome was collected retrospectively from standard pacemaker follow-up checks that were performed at hospitals throughout NZ. The lead function data was collected at standard intervals (see section 2.8.1) from the time of implantation.

2.2 Ethical approval

An application was submitted to the Northern X Regional Ethics Committee, which is administered by the Ministry of Health. The form submitted was the "application form for projects involving only the retrospective review of patient/client notes or data." The ethics committee confirmed that the project is considered an audit that does not require ethical approval (**Appendix 1a**).

An ethics application (number 05/85) was made to the Auckland University of Technology Ethics Committee (AUTEC) and this application was approved for a period of three years (**Appendix 1b**).

For confidentially reasons, patients were assigned a unique, sequential identifying number. Patient records were kept within the Department of Cardiac Physiology throughout the study. Patients were not contacted during the study and are not identified in the data.

2.3 Patient selection

In order to identify all patients receiving epicardial pacing leads at GLH between 1st January 1977 and 1st December 2002, all pacemaker clinic records within the Department of Cardiac Measurement were reviewed and a total of 96 patients were identified. Both adult and pediatric patients receiving epicardial leads were included. Pediatric patients were classified as those less than 17 years of age at implant.

This end date for patient inclusion was selected to ensure that there was a minimum of two years of follow-up data collected if the lead was still functioning. The study commencement date of 1977 was selected as prior to this date poor records were kept and pacemakers used did not have telemetry capabilities so lead follow-up information was not available.

2.4 Study group

Ninety six patients, 22 adult and 74 paediatric, received a total of 192 epicardial leads. For comparison the leads were grouped as either steroid-eluting leads or non steroid-eluting leads. Twenty nine leads were capped at the time of implant in case they would be required in the future. Twelve of these leads were never connected to a pulse generator and therefore no follow-up data is available. This group of leads are referred to as lead only implants and they were excluded from the follow-up threshold and complication data. A total of 180 leads were implanted and connected to a pulse generator, 72 atrial leads and 108 ventricular leads.

Eight patients moved overseas and although clinical follow-up was available for all but two patients the lead follow-up data is incomplete for these 8 patients.

2.5 Data collection development

Data collected from each patient's pacemaker file was recorded on an individual data collection form designed specifically for this study (**Appendix 2**). This form was designed with one page of patient demographics and cardiac history including surgery received. Subsequent pages collected lead and implant information, follow up measurements and details of any complications, with one page assigned to each lead implanted.

A trial form was developed and tested on 4 complex patients by transferring data from the pacemaker file onto the form. This process identified any changes required to the data collection form. Discussion with senior pacemaker technologists and medical staff and a review of previous literature, identified any further information to be added to the data collection form. Design changes were made and then the final data collection forms were copied and allocated to each patient.

A Microsoft Access ^{TM} database was designed to collate the general patient and lead follow-up data. The following diagram (**Table 6**) shows the database fields and their interrelationships.

Table 6 Data collected for entry in to the access database fields

Patient information			
Patient identification number		Indication for implantation	
Gender		Date of first implant	
Date of birth		Weight at first implant	
Congenital heart disease		Patient status	
Cardiac surgery		Date of death	

↓

Lead data				
	Lead 1	Lead 2	Lead 3	Lead 4…
Lead location • Right atrium • Left atrium • Right ventricle • Left ventricle				
Lead model • 4965 • 4951				
Implant date				
Date of lead failure				
Implant technique • Sternotomy • Thoracotomy • Subxiphoid				
Lead Comment • Functioning • Failure due to Fracture • Other Failure • Lead Only Implant				

↓

Lead follow-up data (Lead 1)						
Follow-up interval	Follow-up date	Voltage threshold @ 0.5ms (volts)	Sensing threshold or P / R wave value (mVolts)	Lead impedance (ohms)	Height (cm)	Complications: • Exit block • High threshold • Fracture • Dislodgement • Twitch • Oversensing • Sensing lost • Insulation problem
Implant						
1 day						
2 weeks						
6 weeks						
4.5 months						
10.5 months						
1.5 years						
2 years						
↓						
28 years						

2.6 Collection of complication data

A separate complication database was also developed to give specific detail of possible associations with each type of complication, which is described in 2.13. This complication database was designed with one form per complication and the fields collected were specific to each complication. Fields common to all forms were: patient identification number, lead model, lead location, implant route, time from implant to complication, patient symptoms and patient outcome. Information collected for each type of complication is described in 2.13.

2.7 Collection of lead function data

2.7.1 Pacing records held at Green Lane Hospital

Each patient who has had a pacemaker implanted at GLH has an individual pacemaker file. These files also include all patients who had a pacemaker implant at GLH and then had their follow-up transferred to another hospital. These pacemaker files were used to obtain the majority of the information required for this study. Pacing files stored within the Department of Cardiac Measurement, GLH (prior to December 2003) and ACH (from December 2003 onwards) were obtained. Patient files that were no longer active (i.e. deceased) were located in and recalled from the basement archives.

The pacemaker file contained 1) technical implant sheets 2) copies of relevant medical history 3) electrocardiograph (ECG) recordings from each pacemaker check and 4) a technical follow-up form. These are discussed in turn below.

1. The technical implant sheet contained details of the implant procedure which are recorded by the technologist involved in the operation. When a pacemaker or lead was replaced for any reason a new technical implant sheet was completed and placed in the pacing file. In most cases the technical implant sheet included:
   - Date of the procedure, patient details, date of birth, weight at implant, indications for implant (ECG abnormalities and symptoms), cardiac congenital diagnosis, surgeon, summary of previous cardiac surgery.

- The manufacturer, model and serial number of the pacemaker and leads implanted and the implant route.
- The results obtained from lead testing: Pacing capture threshold, sensing threshold and lead impedance.
- Comments on any difficulties encountered during the procedure.

2. Copies of the relevant medical history such as previous cardiac surgery operation reports, copies of correspondence between referring doctors and other relevant information from the medical notes.

3. ECG recordings taken at each pacemaker check, which were kept for future reference. The recordings include the presenting ECG, a recording with a magnet over the pacemaker and a recording of the patients underlying (intrinsic) rhythm. Magnet application switches the pacemaker to asynchronous fixed rate pacing which provides information on battery longevity.

4. The technical follow-up form contained the complete history in date order of the results of each follow-up check. At each pacemaker check the following information was generally recorded:
   - Date of follow-up
   - Lead and battery measurements
   - Programmed parameters at completion of the check
   - Comments on the patients symptoms
   - Results of extra testing performed
   - Outcome of annual chest x-rays once reviewed with the physicians
   - Problems found during the check
   - Reasons for programming changes made.

GLH and, due to the recent (2003) merger, ACH, was responsible for the majority (n = 58) of the follow-up pacemaker checks on the 96 patients. Follow-up of the patients living outside of the Auckland region was performed at other NZ hospitals that have a cardiology service. The follow-up hospital was identified in the pacemaker file.

2.7.2 Pacing records from other New Zealand hospitals

Where patients had pacemaker related complications requiring intervention and these were identified at other hospitals throughout NZ, the patients were referred to GLH/ACH for further assessment and surgery. The Department of Cardiac Measurement at GLH/ACH has an advisory role to technical departments at other NZ hospitals where pacemaker follow-up is performed. This is due to the greater experience in paediatric pacing obtained within GLH/ACH. For these reasons, in recent years, a copy of the results from most paediatric patient follow-ups performed at other hospitals should be sent to GLH/ACH and kept in the pacemaker file. These results were not always available in the GLH/ACH files and so requests for follow-up information were sent to the charge technologists of the pacemaker clinics at each hospital throughout NZ (**Table 7**).

A cover letter was sent which explained the purpose of the study, that it was classified as an audit, reference to the attached follow-up form to be completed, time frames for sending the information and my contact details for any questions. Some patients had moved several times during the follow-up period so requests for information were sent to all hospitals that had been involved with the patient.

Table 7 New Zealand hospitals where requests for information were sent

Hospital	Requests sent n
Middlemore	1
Waikato	10
Tauranga	1
Wellington Public	7
Nelson	3
Christchurch	6
Dunedin	2
Invercargill	1
Total	**31**

2.7.3 Pacing records outside of New Zealand

Eight patients had epicardial leads implanted at GLH and then moved or returned overseas. Four patients emigrated to Australia, two returned to Tahiti, one returned to Samoa, and one returned to Indonesia. Four of these patients had no forwarding details. Where a contact name of a cardiologist was available a letter requesting follow-up information was sent. Two patients were permanent residents in Tahiti and were receiving pacemaker follow-up in Tahiti.

Multiple attempts were made to obtain the required information internationally. The follow-up data required could not be obtained from any of the patients that had moved overseas due to no response from the letter of request, lack of available records or poor record keeping.

2.8 Lead follow-up

2.8.1 Lead follow-up intervals

Follow up data was collected at implant, and then at the following intervals post operatively: 1 day, 2 weeks, 6 weeks, 4.5 months and at 6 monthly intervals thereafter. These are the standard follow-up intervals for pacemaker patients in Auckland and for the majority of hospitals throughout NZ. The date at each follow-up check was also recorded. The follow-up checks did not always occur at the exact intervals stated above. In this case, where a follow-up check was performed close to the interval, these follow-up results were used.

Follow-up data collection continued until patient death, lead failure, no further follow-up was performed on the lead (due to the lead being replaced or the patient no longer required pacing), the patient was lost to follow-up or until December 2004.

2.8.2 Lead follow-up testing

The following data was collected on each pacing lead by reviewing pacemaker clinic files:

- Pacing threshold – amplitude (Volts) or pulse width (msecs)
- Sensing threshold or P/R wave value (mVolts)
- Lead impedance (ohms)

These tests were performed using programmers supplied by the pacemaker manufacturers.

2.8.2.1 Programmers

Various pacemaker programmers from each manufacturer as shown in **Table 8** were used to obtain the follow-up measurements and test results. The programmers, supplied by the manufacturers, where replaced as technology changed over the 28 year period.

Table 8 Programmers used since 1977 by each pacemaker manufacturer

Manufacturer	Programmer model
Medtronic	2090, 9790
Guidant	2920 “ZOOM”, 2038, 2901, 2035, 2950
St Jude Medical (Pacesetter)	3510 (APS III), APS II
Intermedics	RX5000, RX2000
Sorin	PMP2000, PMP1000
Telectronics	9602, Optima-MP

2.8.2.2 Pacing threshold

The pacing threshold test is performed by temporarily increasing the pacing rate to approximately 10 to 20 beats above the intrinsic rate, or if the underlying rate is very slow the test is performed at approximately 80 pulses per minute (ppm).

An amplitude threshold test is performed by reducing the amplitude until loss of capture is observed on the surface ECG, at which time the operator immediately stops the test. Loss of capture is seen on the ECG as a pacing spike not followed by a P wave if an atrial threshold is being performed or QRS if a ventricular threshold is being performed. The size of the decrement varies with different pacemakers and may be 0.1 Volts (V) up to 0.5V. The minimum voltage that results in consistent capture is the threshold value. The voltage threshold value is dependant on the pulse width at the time of testing therefore the pulse width must also be noted.

A pulse width threshold test is performed by reducing the pulse width until loss of capture is observed on the surface ECG, at which time the operator immediately stops the test. The size of the decrement varies with different pacemakers and may be 0.03 milliseconds (msecs) or 0.1 msec intervals. The pulse width threshold is dependant on the voltage. In order to gain a more accurate threshold result the pulse width test is often

performed at the programmed voltage and also half and a quarter of the programmed voltage.

Refer to the preliminary study in chapter 3 for an explanation of the method used to standardise threshold measurements.

2.8.2.3 Sensing threshold

Assessment of the capability of the pacemaker to sense the intrinsic electrical activity was performed using different methods depending on the type of pacemaker implanted. Methods include: 1) manual adjustment of the sensitivity parameter until loss of sensing is observed, 2) an automatic sensing threshold test run though the programmer or 3) a measurement obtained by the programmer of the intrinsic P or R wave signal size in millivolts (mV).

Methods 1 and 2 have an upper limit for testing (i.e. 4 mV for a P wave or 12.5 mV for an R wave), which may result in an underestimation of the sensing threshold compared to method three which is more accurate and is often reported to 2 decimal places. The upper limit for testing may be different for different pacemakers, i.e. one pacemaker may measure the atrial sensing as greater than 3.5 mV and from the time of pacemaker replacement the atrial sensing may then be measured as greater than 5 mV. The sensitivity appears to have improved but what has changed is the precision of measurement which is dependant on the method.

Note that a high programmed sensitivity value equals a lower sensitivity and vice versa, i.e. 2.5 mV is more sensitive that 5 mV.

2.8.2.4 Lead impedance

Lead impedance is one of the measurements obtained when the measured data is acquired after the initial interrogation of the device. For the impedance measurement to be obtained the pacemaker must have telemetry capabilities, which is the case in all modern pacemakers but was not the case in all pacemakers followed. Pacing must also be performed in order to measure the impedance and in most pacemakers this requires the intrinsic rate to be below the measurement rate, which is not always the case

particularly in paediatric patients. Most pacemakers report impedance measurements to within 1 ohm (Ω), although generally pacemaker manufacturers quote in their technical manuals that the impedance tolerance limits are ±20% (ranging from 15% to 60%). A normal value for impedance is between 300 to 1200 Ω, although normal values between 250 to 1500 ohms may be quoted depending on the type of lead. A lead fracture would result in an impedance increase of greater than 50% or a value above the measurement range of the pacemaker such as greater than 2500 Ω.

2.8.2.5 Confidence limits

The normal variability between measurements repeated on the same patient would be expected to be as follows:
Pacing capture threshold: ± 0.5 V
Atrial sensing threshold: ± 0.5 mV
Ventricular sensing threshold: ± 1-2 mV
Lead impedance: ± 20 %

2.8.3 National standards of follow-up testing

The method of performing follow-up pacing and sensing tests during a pacemaker check is uniform throughout NZ and the programmers used are the same at all hospitals. Once a test is selected, the programmer will go through a standard sequence of operation. This sequence is constant for each type of pacemaker, although it does vary with different manufacturers.

The technologist performing the test must have sufficient knowledge of pacing and ECG's to be able to set the appropriate mode, rate and interval to perform the test and to interpret loss of capture or loss of sensing. As paediatric pacing is a complex field the pacemaker checks on these patients are typically performed by senior cardiac technologists. Follow-up test results obtained from throughout NZ are therefore able to be compared.

2.9 Lead implantation

2.9.1 Lead implantation testing

At the time of implantation, lead measurements were obtained using a pacing system analyzer (PSA): Telectronics Pacing Systems, Dual Chamber PSA, Model 2410 or Biotronic PSA, Model ERA300B. The following measurements were performed on each lead where possible.

- Pacing capture threshold – an amplitude threshold test was performed at a pulse width of 0.5 msecs.
- Sensing threshold
- Lead impedance – was measured through PSA at time lead is placed. A repeat impedance measurement was obtained in most cases via the programmer once the lead was connected to the pacemaker.

The recommended acceptable measurements at implant, as stated in the Medtronic 4965 lead technical manual are shown in **Table 9**.

Table 9 Recommended minimum acceptable lead implant measurements

Lead measurement	Atrial lead	Ventricular lead
Pacing Threshold*	<1.5V	<1.5V
Sensing Amplitude	>2mV	>4mV

*Measured at a pulse width of 0.5msecs

In paediatric patients the above criteria is aimed for but is often not possible, particularly in cases where epicardial leads are placed at the time of cardiac surgery where the heart may be in a poor state following bypass surgery.

2.9.2 Surgical techniques used at lead implantation

The following surgical incisions were used to access the heart for epicardial lead attachment: Sternotomy, thoracotomy or subxiphoid approach. Where leads were implanted concurrently with cardiac surgery the sternotomy approach was used. The following surgical techniques were described by the implanting surgeons in the operation reports.

2.9.2.1 Sternotomy

A median sternotomy is performed and epicardial leads are sutured on to the heart with 6.0 prolene suture material. The leads are tunnelled through the diaphragm underneath the left costal margin. A transverse incision is placed in the left upper quadrant and a subcutaneous pocket formed for the pacemaker unit. The leads are connected to the pacemaker and some of the excess lead is left coiled in the pocket with the rest of the lead left coiled in the pleural cavity.

This lead route is often used when epicardial leads are placed at or soon after bypass surgery. The leads are attached after coming off bypass.

2.9.2.2 Thoracotomy

Left or right anterolateral thoracotomy is performed through the fifth intercostal space. The pericardium is opened taking care to avoid the phrenic nerve. The epicardial leads are attached using 6.0 prolene sutures. A transverse incision was made in the left or right upper abdominal quadrant and a subcutaneous pocket is created. The leads are brought under the costal margin, through the periphery of the diaphragm and connected to the pacemaker. Any redundant lead is left behind the unit and in the chest cavity.

2.9.2.3 Subxiphoid

A subxiphoid incision is made dividing the xiphoid process and part of the linear alba. The pericardium is opened transversely at its anterior attachment to the diaphragm. The epicardial leads are sutured onto the surface of the heart with 6.0 prolene and then tunneled from the pericardial space through the anterior aspect of the diaphragm and out

through the anterior rectus sheath. Some lead is left coiled in the pericardial cavity and another coil is left in a pocket made between the skin and the rectus sheath. The pacemaker is attached to the leads and inserted into the pocket.

2.10 Medical records

Medical notes were reviewed for all patients to identify the patient's cardiac history including cardiac congenital abnormalities. The pacemaker files hold limited information on the patient history and at times the required information was not present on the technical implant sheet.

Access to the patient's confidential medical records was obtained by completion of an "Access to Patient Information" form, which identified that the study was an audit. This application was approved by the clinical director of the cardiology service at GLH/ACH. Patients who have had recent cardiology follow-up had their medical records scanned onto the clinical record information system (CRIS) and these were available for viewing online. Older paper records were gathered by the medical records department and were viewed within this department.

Operation reports from pacemaker implantation were reviewed to determine the location of the leads, whether there were any complications or difficulties at the time the leads were implanted, implant route and whether the leads were implanted at the time of cardiac surgery. The surgeon's description of the techniques used to implant the leads was also noted. Where cardiac surgery had been performed, the surgical procedures were noted along with the date of surgery. Date and cause of death was obtained from coroners or post mortem reports when these were available.

In order to determine whether a patient's growth could predict the risk of lead fracture, the following data was collected from medical notes:

- Stature at implant (cm) or crown-heal length for infants (cm)
- Height at the time a lead fracture was found
- Height at the time of last lead follow-up
- Any other height measurements during the follow-up period

2.11 Echocardiography

To determine whether the excessive threshold values were related to the state of the myocardium or the functionality of the lead, the myocardial state was collected from echocardiography reports where possible. Echocardiogram (echo) reports performed since 1997 were available for viewing in the echo database. Echo reports prior to 1997 were available in the basement archives. Not all patients who had a high threshold or exit block received an echocardiogram at or close to the time the complication occurred.

The echo reports were reviewed for comment on the ventricular function. The comments on ventricular function were at times referred to as normal ventricular function or mild, moderate or severe ventricular dysfunction but in other cases was referred to as "reasonable" or "satisfactory" which is difficult to interpret.

The echocardiography report often recorded the patient's height and this data was collected for the purpose of assessing patient growth.

2.12 Chest x-ray

Post implant and yearly chest x-rays are performed on the majority of patients to assess lead position and adequacy of lead length with patient growth. The chest x-rays were reviewed on all patients who had lead fractures to determine the location of the lead fracture.

2.13 Lead complications

Complications were identified from pacing files and information related to the complication was collected from the pacing and medical notes.

2.13.1 Lead fracture

A lead fracture was identified by a significant rise in impedance compared to previous impedance measurements. Typically the impedance would suddenly rise to greater than the measurement range of the pacemaker (i.e. greater than 2500 Ω). In some cases a sudden doubling of the lead impedance, associated with loss of capture was considered a positive diagnosis of lead fracture. In some patients a break was visible on the chest x-ray but in many this was not the case. The pacing and sensing threshold values and the impedance measurement at the time the fracture was found were not entered into the main database as these results would skew the other lead follow-up data.

The information shown in **Table 10** relating to the lead fracture complication was also collected and entered into a database.

Table 10 Data collected for the lead fracture complication database

Lead fracture complication database			
Patient ID		Prior measurement changes?	
Lead type		Symptoms 1	
Lead location		Symptoms 2	
Implant route		Underlying rhythm	
Date of birth		Outcome	
Date of lead implant		Fracture location	
Date of fracture		Height at implant	
Measurement changes 1		Height at fracture	
Measurement changes 2		Outcome 2	
Measurement changes 3		X-ray measurements	
Impedance at fracture		Comments	

2.13.2 Exit block and high threshold

Where a significant pacing threshold rise occurred, this was classified as a complication when the threshold value met the exit block or high threshold criteria described by the following definitions.

Exit block (EB) is defined as "failure of the pacemaker output to capture the heart because the stimulation threshold exceeds the output capacity of the pacemaker."
High threshold (HT) was defined as "an elevated pacing threshold resulting in intervention due to the inability to programme adequate safety margin for capture."

If a lead developed a high threshold which later went on to be classified as exit block, this was entered as one complication. The pacing threshold values at the time of the high threshold or exit block were entered into the main database. The information shown in **Table 11** relating to EB and HT complications was also collected and entered into a database.

Table 11 Data collected for the exit block and high threshold complication database

Exit block (EB) and high threshold (HT) complication database			
Patient identification number		Myocardial state	
Lead type		Implant at cardiac surgery	
Steroid or non steroid lead		Implant < 1month since surgery	
Lead location		Cardiac surgery	
Exit block or high threshold		Other measurements worsen	
Threshold value (volts)(V)		Sudden or gradual	
Pulse width (milliseconds)		Typical threshold pre EB, HT (V)	
Time to complication (years)		Outcome 1	
High threshold at implant		Outcome 2	
Complications at implant		Underlying rhythm	
Comments / echocardiography		Symptoms	

Echocardiography reports were reviewed at the time exit block or a high threshold occurred to determine whether the myocardial state is related to the occurrence of these complications. The methods used are previously described in 2.11.

2.13.3 Sensing problems

Sensing problems were classified as:

- Loss of sensing
- Oversensing
- Late sensing

Loss of sensing was classified as a complication where the intrinsic signal was less than two times the maximum programmable sensitivity value. Where loss of sensing occurred due to lead fracture or insulation break, this was not counted as sensing complication.

The information shown in **Table 12** relating to the sensing complications was also collected and entered into a database.

Table 12 Data collected for the sensing complication database

Sensing complication database			
Patient ID		Complications at implant?	
Lead type		Symptoms	
Lead location		Result of sensing problem	
Implant route		Underlying rhythm	
Date of lead implant		Outcome 1	
Date of sensing problem		Outcome 2	
Type of sensing problem		Comments	
Other measurement changes			
Measurement changes seen			

2.13.4 Twitching

Diaphragmatic stimulation (DS) or abdominal muscle stimulation (AMS), due to the abdominal pacemaker site, was identified by patients reporting symptoms such as "pulsing" in the region of the pacemaker. DS and AMS are collectively referred to as twitching. The diagnosis was confirmed by increasing the output on each lead separately and, or by changing the mode and observing the abdominal region for muscle twitching. The voltage at which the twitch occurred was recorded. Twitching was classified as a complication regardless of whether reprogramming of the amplitude, pacing rate or mode solved the problem.

2.13.5 Insulation problem

An insulation fault was classified as a reduction in the impedance to an abnormally low value (less than 250 Ω) when it had been normal in previous pacing checks. If an abnormal insulation appearance was seen by the surgeon at the time of surgery, resulting in lead replacement, this was also classified as an insulation fault.

2.13.6 Infection

Where an infection resulted in lead and unit removal this was classified as a complication.

2.14 Exclusions

Two biventricular leads were not included because of the inability to obtain separate measurements on each lead due to the pacemaker design. The ventricular leads were joined by a Y connector with a common input to the pacemaker.

Two leads used for dual site atrial pacing were also excluded for this reason.

2.15 Statistical analysis

Descriptive statistics for continuous variables were summarised by their mean and either standard deviation or 95% confidence interval, and for categorical variables, by their frequency and percentage. Groups have been compared using the two-sample Student t-test for normally distributed continuous variables, and the Mann Whitney U test for those with a non-normal distribution. Categorical variables have been compared using the chi square test or the Fisher exact test when more than half of the expected counts were less then five. Odds ratios have been obtained using logistic regression, and these have been presented with their 95% confidence intervals. For analyses over time, Kaplan Meier survival curves have been developed to estimate risk and compare the probability of survival of each group. Univariate Cox hazard regression has been applied to identify risk factors related to different lead complications. For those risk factors with a p-value less than 0.25, multivariate Cox hazard regression was performed to identify the dominant factor(s). Unless otherwise noted, the 5% level of significance was used for all statistical tests. Analyses were performed using statistical analysis software SAS 8.1.

3 Preliminary Study – Validation of a Technique to Standardise Pacing Thresholds

Due to the range of pacemaker models and lead measurement methods used during the study period, some of the pacing thresholds were measured at different pulse widths. Since one of the main aims of this study is to review trends in pacing thresholds over time, it is necessary to standardise the threshold measurements. This section evaluates a formula which is proposed for use in converting pacing thresholds, measured at a range of pulse widths, to a pacing threshold at a standard pulse width. This formula is referred to as the threshold conversion formula. The aim of this study is to determine whether the proposed threshold conversion formula is suitable to be applied to the pacing threshold data in the main study.

It is hypothesised that pacing thresholds measured at pulse widths other than 0.5 msecs may be accurately converted to a voltage threshold at 0.5msecs using the following threshold conversion formula, which is adapted from a formula described by Stokes and Bornzin (1985): $V_2 = V_1 \times (t_2/t_1)^{-0.6}$ (cited by Ellenbogen, *et al.* 1995).

3.1 Introduction

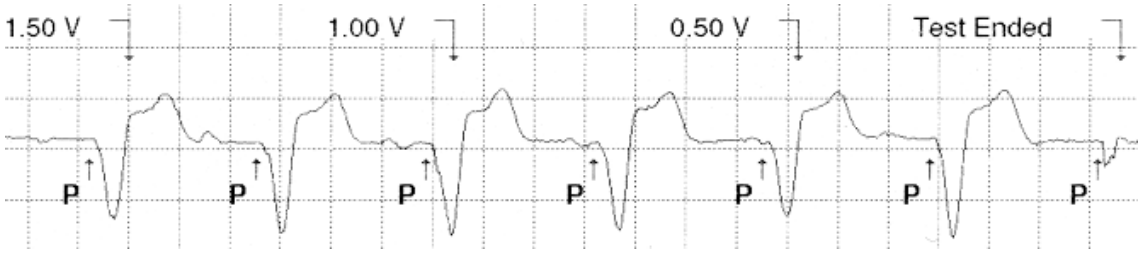
The pacing threshold is defined as "the minimum stimulus amplitude (volts) at any given pulse width (milliseconds) required to consistently achieve myocardial depolarization outside the heart's refractory period." (Furman, *et al*. 1975).

Because the pacing threshold value varies in relation to the pulse width it may be measured in two common ways.

3.1.1 Voltage threshold

A voltage pacing threshold is performed by reducing the amplitude at a fixed pulse width until loss of capture is seen (**Figure 11**).

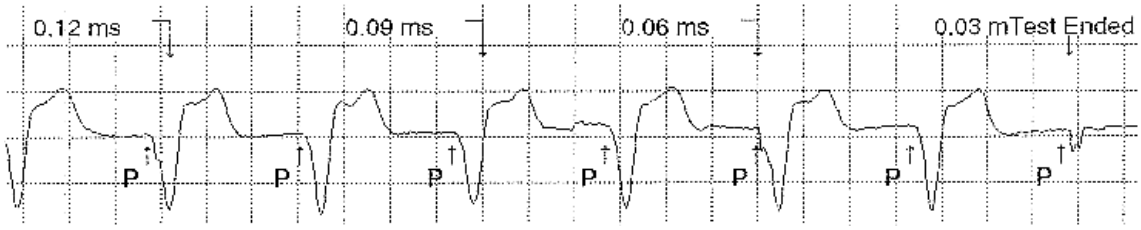
Figure 11 Electrocardiograph recording during a voltage threshold



3.1.2 Pulse width threshold

A pulse width pacing threshold is performed by reducing the pulse width at a fixed amplitude until loss of capture is seen (**Figure 12**). Pulse width thresholds are often performed at several amplitude settings for a more specific threshold result.

Figure 12 Electrocardiograph recording during a pulse width threshold

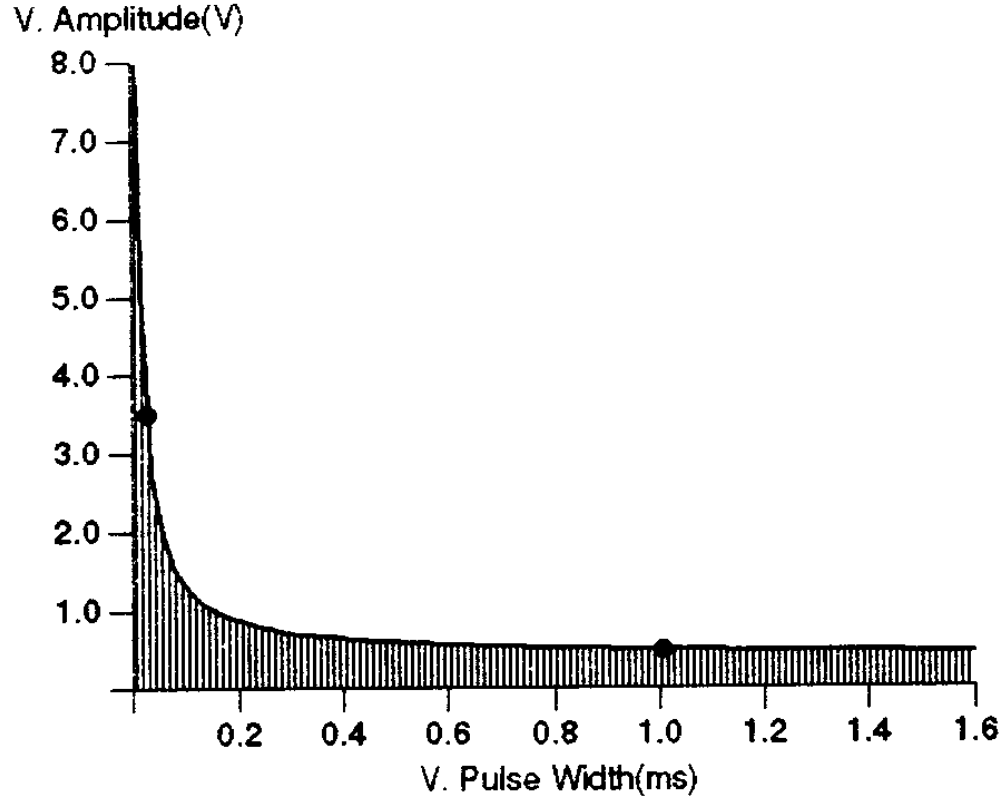


3.1.3 Significance of the pacing threshold

The purpose of measuring a pacing threshold is to ensure that the pacemaker output is programmed to a value that ensures adequate safety margin for capture without excessive battery drain. Safety margin for capture refers to the minimum programmed amplitude and pulse width that should be programmed to ensure reliable capture. If a voltage threshold is performed, the pacemaker output is programmed to twice the threshold value, with minimum amplitude of 2 volts. The programmed safety margin for capture when a pulse width threshold is performed is three times the threshold value.

The relationship between the pacing threshold (volts), pulse amplitude (voltage) and pulse duration (msecs) can be represented by the strength-duration curve shown in **Figure 13**. The 2 black dots are the measured pacing thresholds and the shaded area represents the output where there is no capture.

Figure 13 Strength duration pacing threshold curve



A voltage pacing threshold is dependant on the pulse width at which it is performed. The pulse width may be any value within the programmable range of the pacemaker. Therefore two voltage thresholds performed at different pulse widths cannot be compared unless they are standardized in some way. For retrospective studies such as this one there are several reasons why pacing thresholds may be performed using different methods or at different pulse widths. Firstly most retrospective pacing studies report that a range of pacemaker models have been implanted because of the time period over which the study has taken place (Ten Cate, *et al*. 2002; Sachweh, *et al*. 2000). Different pacemaker models will perform pacing thresholds using different methods i.e. voltage or pulse width thresholds. Secondly in order to optimize battery longevity the programmed pulse amplitude and pulse width may be adjusted from the nominal value at pacemaker follow-up.

A review of 16 published papers (**Table 13**) on paediatric pacing revealed 38% of the studies measured and reported a voltage pacing threshold, 31% measured and reported a pulse width pacing threshold and 31% calculated and reported an energy pacing threshold (ET) which is described in section 3.1.4.

Table 13 Published studies where voltage, pulse width or energy pacing thresholds have been reported

Voltage (volts)	**Pulse width (msecs)**	**Energy (µJ)**
Dodge-Khatami, *et al*. 2000	Beder, *et al*. 1997	Beaufort-Krol, *et al*. 1999
Sachweh, *et al*. 2000	Henglein, *et al*. 1984	Cohen, *et al*. 2001
Ten Cate, *et al*. 2002	Johns, *et al*. 1992	Hamilton, *et al*. 1997
Valsangiacomo, *et al*. 2000	Kugler, *et al*. 1988	Karpawich, *et al*. 1992
Villain, *et al*. 2000	Villafane, *et al*. 1993	Ramesh, *et al*. 1999
Warner, *et al*. 1999		

3.1.4 Energy threshold

An energy threshold is calculated using the following formula where voltage and pulse width are the threshold values and resistance is the measured lead impedance at the time of the pacing threshold test.

$$ET\ (uJ) = \frac{\text{Voltage (V)}^2 \text{ x Pulse Width (msecs) x } 10^6}{\text{Resistance } (\Omega) \text{ x 1000 msecs/sec)}}$$

This formula is derived from an amalgamation of several standard electronic formulae:

$$\text{Voltage}_{(\text{Volts})} = \text{Current}_{(\text{amperes})} \text{ x Resistance}_{(\text{ohms})}$$

$$\text{Power}_{(\text{Watts})} = \text{Energy}_{(\text{Joules})} / \text{Time}_{(\text{seconds})}$$

$$\text{Power}_{(\text{Watts})} = \text{Current}^2_{(\text{amperes})} \text{ x Resistance}_{(\text{ohms})}$$

Expressing the pacing threshold as an energy threshold (microjoules) has the advantage of enabling all threshold measurements to be compared, regardless of whether voltage or pulse width thresholds are performed. An impedance measurement at the time of the pacing threshold is required for the calculation. The disadvantage of using energy to express the threshold value is that energy is not typically used in clinical practice as an expression of threshold. This results in difficulty interpreting the results due to the unfamiliar units.

3.1.5 Conversion to voltage thresholds

To overcome this interpretation difficulty it is proposed that pacing thresholds measured at pulse widths other than 0.5msecs may be converted to a voltage threshold at 0.5msecs using the threshold conversion formula. The text Clinical Cardiac Pacing by Ellenbogen, Kay and Wilkoff (1995) states that "the constant voltage strength duration curve for a modern, very low polarising electrode approaches a straight line within pulse widths of clinical significance (≤ 1.0 msec). The linear portion of these curves has about the same slope, which when measured on canines was found to be about -0.6 $\pm$ 0.07 V/msec. In most cases the slope of the curve does not change significantly with time. Polarisation, which is a buildup of charge opposing flow of current, is relatively small at or below 0.5 msecs pulse duration. Assuming polarization is low the following equation can be used to indicate the threshold: $V = At^m$.

Where V = Voltage threshold

A = constant that determines the location of the curve on the Y axis

(A increased as threshold increases)

t = pulse width (msecs)

m = slope of the line (-0.6 V/msec)"

To convert a voltage pacing threshold (V_1) measured at pulse width (t_1) to a standard pulse width (t_2) the following equations are combined:

$V_1 = A\ t_1^m$ $\qquad$ $V_2 = A\ t_2^m$

V_1 = Measured voltage threshold (volts) at pulse width t_1
V_2 = Calculated voltage threshold (volts) at pulse width t_2
t_1 = Pulse width for the measured voltage threshold (msecs)
t_2 = Standard pulse width (msecs)

The equation $V_2 = V_1 \times (t_2/t_1)^{-0.6}$ is a result of this combination and is referred to as the "threshold conversion formula." In the main study the standard pulse width that all threshold results are converted to is 0.5 msecs, therefore in the main study the equation used is: $V_2 = V_1 \times (0.5/t_1)^{-0.6}$

3.1.6 Validation study

In the main study the pacing thresholds were measured using varying methods. Some pacing thresholds were voltage thresholds (VT) measured at a range of pulse widths. Some were pulse width thresholds (PWT) performed at a range of voltages. In both of these cases the pacing threshold needs to be standardised to enable comparison of threshold values. To cover both scenarios this validation study used two methods which are described in 3.2 and 3.3.

3.2 Method 1 – Voltage pacing threshold

During follow-up testing, more than one voltage threshold test is often performed when the pacing threshold has risen to greater than 1 volt at 0.4 or 0.5 msecs. In this situation a second threshold test would be performed at a wider pulse width of 0.7 or 1 msec, usually giving a lower voltage threshold value. This allows optimization of the permanent voltage and pulse width programming to values that allow adequate safety margin for capture while minimising the lead current drain. That is, the current drain is lower when the pacemaker is programmed to 2V @ 1msec than if programmed to 3.5V @ 0.5ms.

Approximately 400 pacemaker files were randomly selected out of the 3341 patient files at the Auckland City Hospital pacemaker clinic. Each record is filed alphabetically according to the patient's surname. The random selection was performed by choosing the first 20 files (approximately) at each letter of the alphabet. From each file the follow-up data was reviewed to identify the occasions where the voltage threshold test had been performed at more than one pulse width at the same follow-up visit. Multiple voltage threshold tests were identified in 59 patient follow-ups. From each follow-up, the two pacing threshold results were tabulated and the threshold conversion formula was applied to the data as demonstrated in the following example.

3.2.1 Example of voltage threshold results from one patient follow-up

In this example the threshold was initially measured as 2 volts at 0.4 msecs. A repeat threshold test was performed at a longer pulse width of 0.7 msecs and the voltage threshold was measured to be 1.5 volts (**Table 14**).

Table 14 Data obtained from two consecutive voltage pacing thresholds performed on one patient

	Voltage Threshold A (VT_A)	**@ Pulse Width A** (PW_A)
Threshold Measurement A	2 V	0.4 ms
	Voltage Threshold B (meas VT_B)	**@ Pulse Width B** (PW_B)
Threshold Measurement B	1.5 V	0.7 ms

meas: measured, ms: milliseconds, PW: pulse width, V: volts, VT: voltage threshold

3.2.2 Calculation demonstration

During the validation study method 1 the variables in the threshold conversion formula ($V_2 = V_1 \times (t_2/t_1)^{-0.6}$) are indicated by the following symbols which relate to the example in **Table 14**:

V_1 = Measured voltage threshold B (meas VT_B)

V_2 = Calculated voltage threshold B (calc VT_B)

t_1 = Pulse width for measured voltage threshold B (PW_B)

t_2 = Standard pulse width, which in this case is the pulse width during threshold A (PW_A)

From threshold measurement B, the voltage threshold (VT_B) at 0.7 msecs, was entered into the threshold conversion formula to convert it to a voltage threshold at 0.4 msecs (PW_A).

$$\text{Calc } VT_B = \text{meas } VT_B \times (PW_A/PW_B)^{-0.6}$$

If the hypothesis is correct the calculated VT_B should equal the measured voltage threshold A (VT_A). The difference between the measured (VT_A) and calculated (calc VT_B) voltage threshold indicates the error in the threshold measurement technique plus the error in the formula.

Using the above example: Calc $VT_B = 1.5 \times (0.4/0.7)^{-0.6}$

Calc $VT_B = 2.1$ volts

The measured voltage threshold @ 0.4 msecs is 2.0 volts so the difference between the measured and calculated thresholds is 0.1 volts.

3.2.3 Accuracy of the measured voltage threshold

Pacemaker programmers alter the voltage in increments of between 0.1 and 0.5 volts during the pacing threshold test and therefore the error arising from the pacing threshold measurement technique is up to $\pm$ 0.5 volts.

3.3 Method 2 – Pulse width pacing thresholds

Several pacemaker models only have the capacity to perform pulse width pacing threshold tests. Pulse width threshold tests are usually performed at the programmed voltage and then at half the programmed voltage and may also be performed at a third or quarter of the programmed voltage for a more specific threshold result and to ensure adequate safety margin for capture is programmed.

The Paceart 2000^{TM} database was utilised to identify the patients who have pacemakers which perform pulse width threshold tests. The pacemakers searched for were: Sorin: Minior 100, Orion 60, Orion 60B, Orion 65, Orion 65B and Medtronic Minuet 7108. From the 226 patients identified as having one of these types of pacemakers, approximately 2 pulse width threshold results were selected from each patient file until a total of 80 pulse width threshold results were obtained. The pulse width threshold at each voltage was tabulated and the threshold conversion formula was applied to the data as demonstrated in the following example.

3.3.1 Example of pulse width threshold results from one patient follow-up

In this case the threshold was performed at two different voltages and was measured as 0.12 msecs at 2.5 volts and 0.36 msecs at 1.2 volts (**Table 15**).

Table 15 Data obtained from two consecutive pulse width pacing thresholds performed on one patient

	Pulse Width Threshold A (PWT_A)	@ Voltage A (V_A)
Threshold Measurement A	0.36 ms	1.2 V
	Pulse Width Threshold B (PWT_B)	@ Voltage B (meas V_B)
Threshold Measurement B	0.12 ms	2.5 V

meas: measured, ms: milliseconds, PWT: pulse width threshold, V: volts

3.3.2 Calculation demonstration

During the validation study method 2 the variables in the threshold conversion formula ($V_2 = V_1 \times (t_2/t_1)^{-0.6}$) are indicated by the following symbols which relate to the example in **Table 15**:

V_1 = Measured voltage B (meas V_B)

V_2 = Calculated voltage B (calc V_B)

t_1 = Pulse width for measured voltage B (PWT_B)

t_2 = Standard pulse width, which in this case is the pulse width threshold A (PWT_A)

From threshold measurement B, the voltage (V_B) at which the pulse width threshold was performed is entered into the threshold conversion formula to convert it to a voltage at PWT_A.

$$\text{Calc } V_B = \text{meas } V_B \times (PWT_A/PWT_B)^{-0.6}$$

$$\text{Calc } V_B = 2.5 \times (0.36/0.12)^{-0.6}$$

$$\text{Calc } V_B = 1.29 \text{ volts}$$

Threshold measurement A is considered to be the most precise since it is performed at the lowest voltage and therefore it is used as the standard that the calculated voltage is compared too. The measured pulse width threshold at 0.36 msecs is 1.2 volts and the calculated threshold at 0.36 msecs is 1.29 volts so the difference between the measured and calculated thresholds is 0.09 volts.

3.3.3 Accuracy of the measured pulse width threshold

During a pulse with threshold test the pacemaker programmer will alter the pulse width in increments of between 0.03 and 0.25 msecs, although 0.06 is the most common incremental change used (Medtronic Minuet technical manual, 1991)

The example calculation was repeated with a pulse width $\pm$ this measurement error to indicate the effect on the final calculation.

PWT_B + 0.06 ms, calculated V_B = 1.65V, voltage is over estimated by 0.36V (1.65V – 1.29V = 0.36V).

PWT_B - 0.06 ms, calculated V_B = 0.85V, voltage is under estimated by 0.44V (1.29V – 0.85V = 0.44V).

The pulse width measurement error of approximately 0.4V is similar to the voltage threshold measurement error of 0.5V.

3.4 Results

3.4.1 Method 1 results

Table 16 gives an example of ten sets of data obtained from this method of validating the threshold conversion formula (see **Appendix 3** for the full data).

Table 16 Measured voltage thresholds performed at two different pulse widths compared to voltage thresholds calculated using the threshold conversion formula

Threshold A (Measured)		**Threshold B (Measured)**		**Threshold B (Calculated)**	**Measured A vs Calculated Difference**
Voltage Thr (VT_A)	**at PW_A (ms)**	**Voltage Thr (VT_B)**	**at PW_B (ms)**	**Calc VT_B (volts)**	**VT_A minus Calc VT_B**
1.5	0.4	1	0.8	1.52	0.02
1.8	0.5	1.5	0.8	1.99	0.19
1.2	0.5	0.9	0.7	1.10	-0.10
1.3	0.5	1	1	1.52	0.22
5	0.5	3.2	1	4.85	-0.15
1.25	0.4	1	0.6	1.28	0.03
1.5	0.4	1	0.6	1.28	-0.22
1.3	0.4	1	0.6	1.28	-0.02
1.4	0.6	1.3	1	1.77	0.37
1.4	0.8	1.3	1	1.49	0.09

Calc: calculated, ms: milliseconds, PW: pulse width, Thr: threshold, vs: versus, VT: voltage threshold

3.4.2 Method 2 results

Table 17 gives an example of ten sets of data from this method of validating the threshold conversion formula (see **Appendix 3** for the full data).

Table 17 Measured pulse width thresholds performed at two different voltages compared to the voltage calculated using the threshold conversion formula

Threshold A (Measured)		**Threshold B (Measured)**		**Threshold B (Calculated)**	**Measured A vs Calculated Difference**
Voltage (V_A)	**PWT_A (ms)**	**Voltage (meas V_B)**	**PWT_B (ms)**	**Calc V_B (volts)**	**V_A minus calc V_B**
0.5	0.4	1	0.06	0.32	0.18
0.8	0.48	1.6	0.18	0.89	-0.09
0.5	0.4	2.5	0.03	0.53	-0.03
1	0.4	1.6	0.06	0.51	0.49
0.5	0.4	1.5	0.06	0.48	0.02
0.5	0.4	1.5	0.06	0.48	0.02
1.25	0.5	5	0.06	1.40	-0.15
1.25	0.5	2.5	0.25	1.65	-0.40
1.25	0.5	2.5	0.12	1.06	0.19
1.25	0.25	2.5	0.06	1.06	0.19

Calc: calculated, meas: measured, ms: milliseconds, PWT: pulse width threshold, V: voltage

3.5 Analysis of values outside the acceptable margin of error

The data collected from method 1 and 2 were combined and reviewed to identify the values outside the acceptable margin of error, which was classified as $\pm$ 0.5 volts. Where the difference between the measured and calculated threshold value was greater than 0.5 volts these values were examined to determine the limitations of the threshold conversion formula. The following **Table 18** gives an example of ten sets of data which fall into this category.

On review of the data, a measured minus calculated difference greater than 0.5 volts was found to have occurred in 14% (n = 19/138) of the results. This occurred equally in voltage (8/59) and pulse width thresholds (11/80). The largest error was 1.84 volts.

Table 18 Data sets where the difference between the measured and calculated thresholds was greater than 0.5V

Threshold A (Measured)		Threshold B (Measured)		Threshold B (Calculated)	Measured Voltage A minus Calculated Voltage B
Voltage (A)	PW (A) ms	Voltage (B)	PW (A) ms	Calc Voltage (B)	
1.25	1	0.5	1.5	0.64	0.61
1.25	0.75	2.5	0.5	1.96	-0.71
3.5	0.6	3	1	4.08	-0.58
2.3	0.5	1.9	1	2.88	-0.58
1.25	0.75	2.5	0.5	1.96	-0.71
0.8	0.12	2.5	0.06	1.65	-0.85
0.8	0.12	4	0.06	2.64	-1.84
2.5	0.5	5	0.06	1.40	1.10
2.5	0.5	5	0.06	1.40	1.10
1.25	0.5	2.5	0.06	0.70	0.55

Calc: calculated, ms: milliseconds, PW: pulse width

3.5.1 Explanation of results outside the acceptable margin of error

The following reasons were identified as causes of a greater than 0.5 volt difference between the measured and calculated pacing threshold results.

3.5.1.1 Inaccurate pulse width thresholds

Where a pulse width threshold was performed at several voltage values, the measured minus calculated difference reduces with increasing precision of the threshold measurement, that is the lower the voltage the greater the precision. This is shown by converting thresholds a, b and c in **Table 19** to a voltage threshold at a pulse width of 0.48 using the threshold conversion formula. The calculated threshold was then compared to the measured threshold "d)" which is 0.8 V.

Table 19 Effect of the voltage, that a pulse width threshold is performed at, on the precision of measurement

Measured Threshold	Calculated Threshold (volts)	Difference (volts)
a) 4.2V = 0.06 ms	1.15	0.35
b) 2.5V = 0.12 ms	1.09	0.29
c) 1.6V = 0.18 ms	0.89	0.09
d) 0.8V = 0.48 ms		

Ms: milliseconds, V: volts

Pulse width thresholds performed at 2.5V or greater which have a PW threshold at or close to the minimum PW value, as seen in measured threshold "a" above, are more likely to fall outside of the acceptable margin of error.

The pulse width thresholds from method 2 (n = 80) were separated into two groups for comparison:

Group A: threshold measured as ≤ 0.1msecs at ≥ 2.5 volts (n = 22)

Group B: all pulse width thresholds not in group A (n = 58).

Group A: A measured minus calculated difference greater than 0.5 volts occurred in 36% (n = 8/22) of the measurements, with a maximum difference of 1.84 volts.

Group B: A measured minus calculated difference greater than 0.5 volts occurred in 3% (n = 2/58) of the measurements, with a maximum difference of 0.59 volts.

The difference between group A and B was statistically significant with a p value of 0.004 (two sided Student t test). Of the 18 results from method 1 and 2 where the measured minus calculated difference was greater than 0.5 volts, 44% of these can be explained by an inaccurate pulse width threshold measurement.

Accuracy improves when the pulse width threshold used for the conversion is the lowest possible voltage, which is the threshold with the pulse width closest to 0.5 msecs.

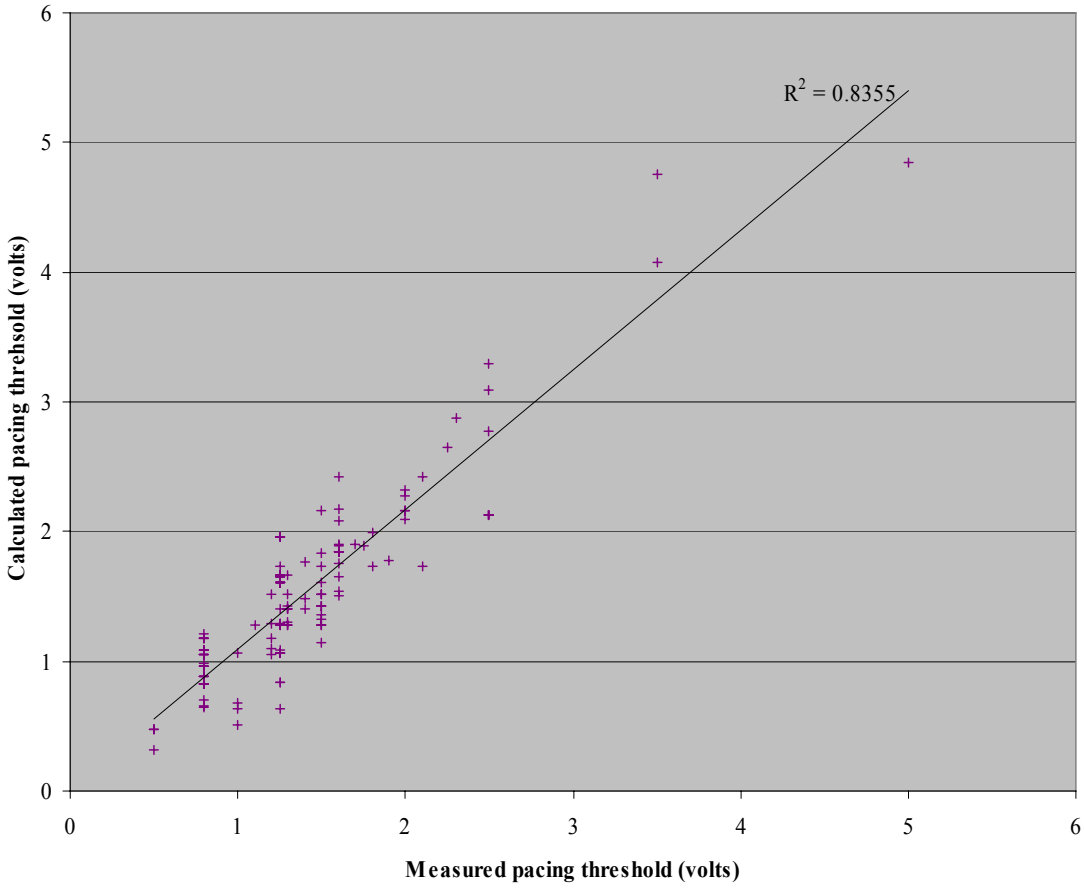
3.5.1.2 Accuracy is greatest at low thresholds

At higher voltage thresholds there was a trend towards a greater difference between the measured and the calculated values. The calculated threshold was used as a measure of the voltage threshold as this standardised result was able to be compared for all sets of data. Where the measured minus calculated difference was greater than 0.5V, the calculated voltage was on average 2.7V. Where the measured minus calculated difference was less than 0.5V, the calculated voltage was on average 1.5V.

3.6 Final results

Reanalysis of the initial data set from method 1 and 2 was performed excluding the identified inaccurate pulse width threshold data. **Figure 14** shows a strong positive linear correlation between the measured and calculated pacing thresholds as shown by the Spearman's correlation coefficient (r) of 0.91 ($p < 0.0001$). The spread around the line of agreement is quite narrow. Linear regression analysis gives: Calculated threshold = 1.07 measured threshold + 0.02 (volts).

Figure 14 The calculated threshold value versus the measured threshold value



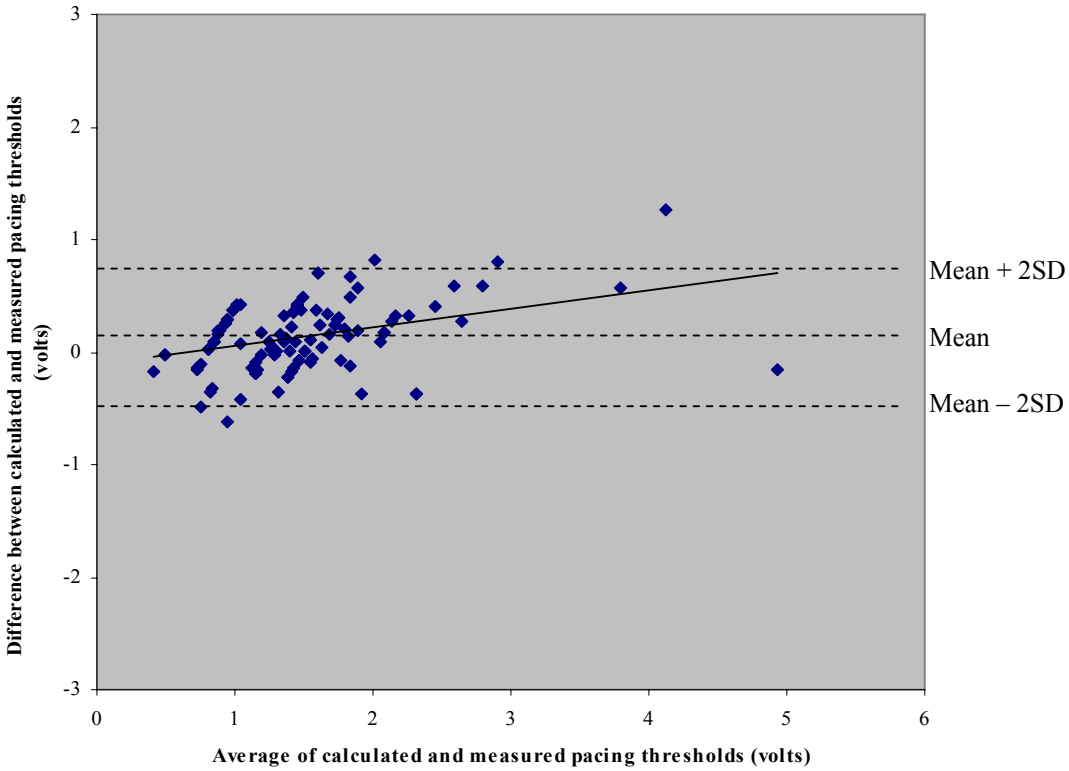
Statistical analysis of the calculated compared to the measured threshold data gives a mean square error of 0.11, a mean absolute difference of 0.26 volts, and a repeatability coefficient of 0.65.

When the data is displayed on a Bland and Altman plot (**Figure 15**) this suggests that the agreement between the calculated and measured pacing threshold becomes less reliable at higher voltages with higher calculated values at higher voltages. It is important to note that even at higher voltages the majority of values are still within 2 standard deviations of the mean which is not clinically significant. The mean difference and limits of agreement between the calculated and measured values are as follows:

Mean + 2SD = +0.14 + (2 x 0.3) = 0.74 volts

Mean – 2SD = +0.14 – (2 x 0.3) = -0.46 volts

Figure 15 The difference between the calculated and measured pacing thresholds versus the average of the calculated and measured pacing thresholds



3.7 Discussion and conclusion

3.7.1 Discussion

It is common practice in literature to convert pacing thresholds to an energy threshold in order to standardize threshold measurement results (Hamilton *et al*. 1997; Beaufort-Krol *et al*. 1999; Thomson *et al*. 2004). However converting threshold measurements to a voltage threshold at a standard pulse width of 0.5 msecs using the threshold conversion formula has not been published previously. This study set out to prove that the threshold conversion formula was an accurate method of standardizing pacing thresholds. The low mean square error, low mean absolute difference and low repeatability coefficient, which are consistent with the high correlation coefficient, indicate that there is good agreement between the calculated and measured pacing thresholds. Therefore the proposed threshold conversion formula is an acceptable method to use and can be applied to the measured pacing threshold data obtained in the main study. This will enable the thresholds to be reported as voltage thresholds at a standard pulse width of 0.5 msec. Pulse width pacing thresholds that are measured to be less than 0.1 msecs at greater than 2.5 volts will not have the threshold conversion formula applied to them in the main study as the threshold conversion formula becomes inaccurate at these values.

3.7.2 Limitations

A limitation of this preliminary study is that most of the measurement results were at low thresholds although the few high thresholds that were compared did have a relatively close correlation. All threshold results above 8 volts have a similar significance for the patient, that is, intervention to replace the lead is typically required.

3.7.3 Future research

A relatively small number of cases were evaluated in this preliminary study. It is recommended that a larger cohort be assessed for further conformation of these findings.

3.7.4 Conclusion

The threshold conversion formula is a reasonably accurate method of standardizing pacing thresholds, which are measured at a range of pulse widths, to pacing thresholds at a standard pulse width. The application of this formula to the pacing thresholds in the main study will allow meaningful comparisons to be made between the measured pacing threshold data.

4 Results

The findings of this audit of epicardial pacing leads that were implanted in New Zealand between 1977 and 2002 are described under the following sections; patients (having epicardial leads implanted), lead characteristics, pacemaker models, lead follow-up, complications and outcome of lead only implants.

4.1 Patients

4.1.1 Characteristics of patients at first lead implant

The characteristics of the 96 patients who received epicardial lead implants at Green Lane Hospital between 1977 and 2002 are shown in **Table 20**. The majority (77%) of patients were paediatric, with the youngest being 3 days old. Patients were classified as paediatric where their age was less than 17 years at the time the first lead was implanted. Of the 22 patients in the adult age group, 14 patients, aged 17 to 41 years, had congenital heart disease (ACHD).

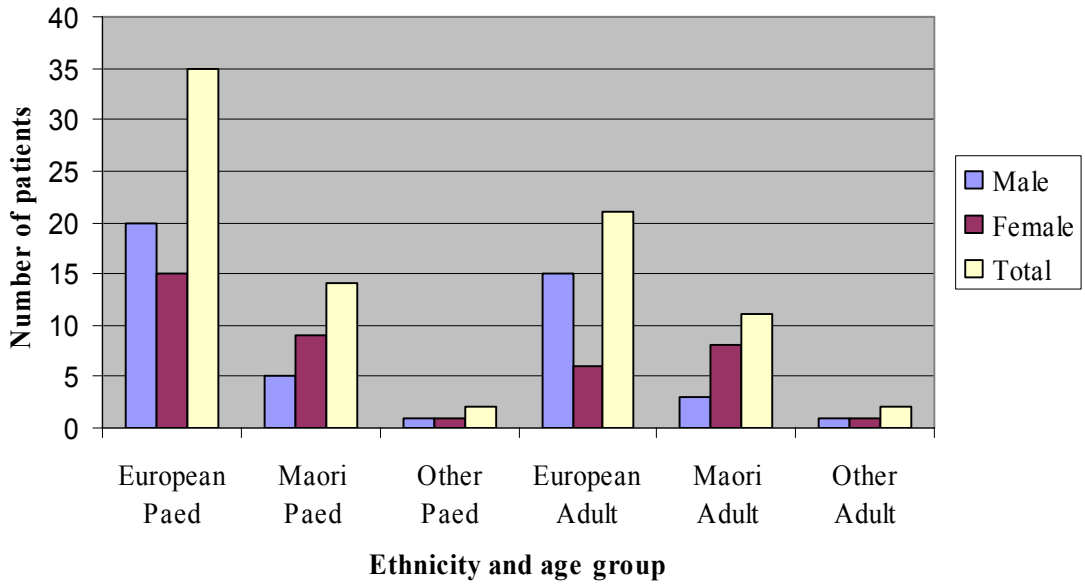
Table 20 Characteristics of patients who received epicardial lead implants at Green Lane Hospital between 1977 and 2002

	Number n	Gender M / F	Mean age (years)	Median age (years)	Age range (years)
All patients	96	52 / 44	11	1.7	0.0 - 71.5
Paediatric	74	45 / 29	3	1.2	0.0 – 14.5
Adult	22	7 / 15	38	29	17 – 71.5

F: female, M: male

The distribution of patients grouped according to age, ethnicity and gender is shown in **Figure 16**. The majority of patients (paediatric and adult) were European. Maori and Maori/European children represented 16% of all paediatric implants. Other ethnicities include: African (2), Indonesian (2), Maori / European (2), Tahitian (2), Chinese (1), Indian (1), Filipino (1), Samoan (1) and Tongan (1).

Figure 16 Distribution of ethnicity in relation to gender and age group (paediatric is classified as less than 17 years of age) for all patients who received epicardial pacing leads



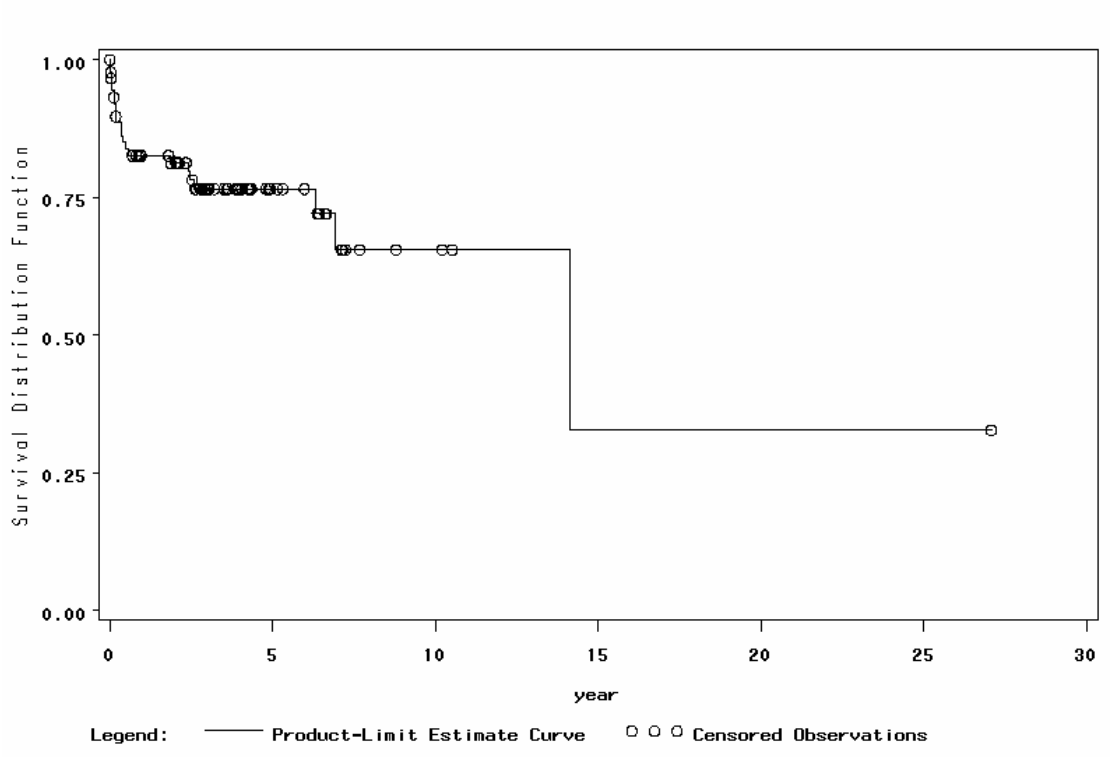
4.1.2 Patients weight at first implant

The average weight of all paediatric patients was 11.4 kg (median = 8 Kg), with weight ranging from 1.8 to 52.7 kg. Fifty seven percent (n = 42) of the 74 paediatric patients weighed less than 10 kg at implant. The average weight of this low weight group was 5.2 kg, and the average age was 0.45 years. The smallest patient in this study weighed 1.8 kg and was 3 days old at the time of pacemaker implantation. This infant received the smallest pacemaker available at the time (Microny, St Jude Medical) with one ventricular lead as the patient was considered too small to receive two leads and a larger dual chamber pacemaker.

4.1.3 Patient mortality

Twenty four (25%) of the 96 patients died during the 28 years from the date of the first implant to the date the last follow-up was performed. Sixteen of the deceased were paediatric patients and 8 were adults. The average age at death for the paediatric age group was 11 months (2 weeks to 5.5 years). For the patients who received follow-up the 2, 5 and 10 year survival probability (and standard deviation) were: 81% (4%), 77% (5%) and 66% (8%) respectively (**Figure 17**). There was no significant difference in patient survival in relation to the indication for implantation (see **Appendix 5a**).

Figure 17 Kaplan Meier survival curve for patients who received epicardial lead follow-up



From the information available there did not appear to be any deaths that could be attributed to pacemaker failure or lead related complications. One possible exception is an adult congenital patient with a slow underlying rate (approximately 30bpm) and a NSE lead, who died suddenly. However, the lead function measurements had been stable for 14 years and the patient was known to have moderate RV dysfunction, severe RV dilatation, dilated LV and mildly impaired LV function, therefore ventricular tachyarrhythmia seems more likely.

Causes of death in the adult group included: heart failure (n = 4), multi-organ failure ± septicaemia (n = 2), pneumonia (n = 1) and murder (n = 1). Causes of death in the paediatric group were: complex congenital heart disease (n = 6), heart failure ± septicaemia (n = 5), heart failure due to cardiomyopathy (n = 3), multi-organ failure with septicaemia (n = 1) and endocarditis with cardiomegaly (n = 1).

4.1.4 Congenital and acquired cardiac abnormalities

Congenital heart defects were present in 79 of the 96 patients (82%). Acquired cardiac abnormalities, which included endocarditis, coronary artery disease and rheumatic valve disease, occurred in 6 adult patients. The majority (88%) of patients in the paediatric age group had complex congenital heart defects requiring surgical intervention. The cardiac anatomy of each patient was classified according to the diagnoses listed in **Table 21**. The most common cardiac congenital defects are complex single ventricle with levotransposition or dextrotransposition of the great arteries, ventricular septal defect and Tetralogy of Fallot.

Table 21 Cardiac diagnoses of patients who received epicardial lead implants at Green Lane Hospital between 1977 and 2002

Diagnosis	All patients	Paediatric
	n	n
Normal heart	11	9
Complex single ventricle – LTGA	9	8
Complex single ventricle – DTGA	9	8
Ventricular septal defect (VSD)	9	7
Tetralogy of Fallot (ToF)	8	7
Tricuspid atresia – all forms	8	4
Pulmonary atresia / stenosis, LTGA, VSD	5	5
DTGA	4	3
Secundum atrial septal defect	4	4
Ebsteins	4	1
Endocarditis	4	0
Patent ductus arteriosus (PDA)	3	3
Complete AV canal	3	3
ToF, pulmonary atresia	3	2
Interrupted aortic arch, VSD	3	3
Partial AV canal	2	2
Cardiomyopathy	2	2
Pulmonary stenosis	1	1
DTGA, double outlet right ventricle	1	1
LTGA, PDA	1	1
Coronary artery disease	1	0
Rheumatic valve disease	1	0
Total	**96**	**74**

AV: atrio-ventricular, DTGA: dextrotransposition of the great arteries, LTGA: levotransposition of the great arteries

4.1.5 Cardiovascular surgery

Cardiovascular surgery was performed on 89% of the patients with congenital heart disease. In the paediatric age group, 84% of the patients received cardiac surgery. These numbers exclude 4 patients who had ligation of a patent ductus arteriosus as the only surgery performed. Of the patients who had cardiac surgery, 33% had more than one surgical correction performed with two patients having 5 surgical procedures each. The most common surgical procedures performed were; Fontan, ventricular septal defect closure and bidirectional Glen.

4.1.6 Indications for implant

The electrocardiographic indications for initial pacemaker implant were classified into seven groups as follows.

1. Surgical atrio-ventricular block (AVB) (n = 47) includes all patients who developed intermittent or complete AVB following cardiac surgery.

2. Congenital atrio-ventricular block (n = 25) includes all patients born with type 2 or 3 AVB requiring pacing.

3. Prevention of atrial arrhythmias (n = 10) includes patients paced to prevent atrial fibrillation, atrial flutter or other atrial arrhythmias. Four patients in this group had a pacemaker implanted after Fontan surgery $\pm$ cryoablation and $\pm$ right atrial reduction.

4. Sick sinus syndrome (n = 5) includes all patients (1 adult) who developed sinus bradycardia, sinus pauses and junctional rhythm.

5. Atrio-ventricular node disease (n = 6) includes patients with acquired intermittent AVB (2 ACHD, 1 paediatric) or permanent AVB (3 adult) not due to cardiac surgery.

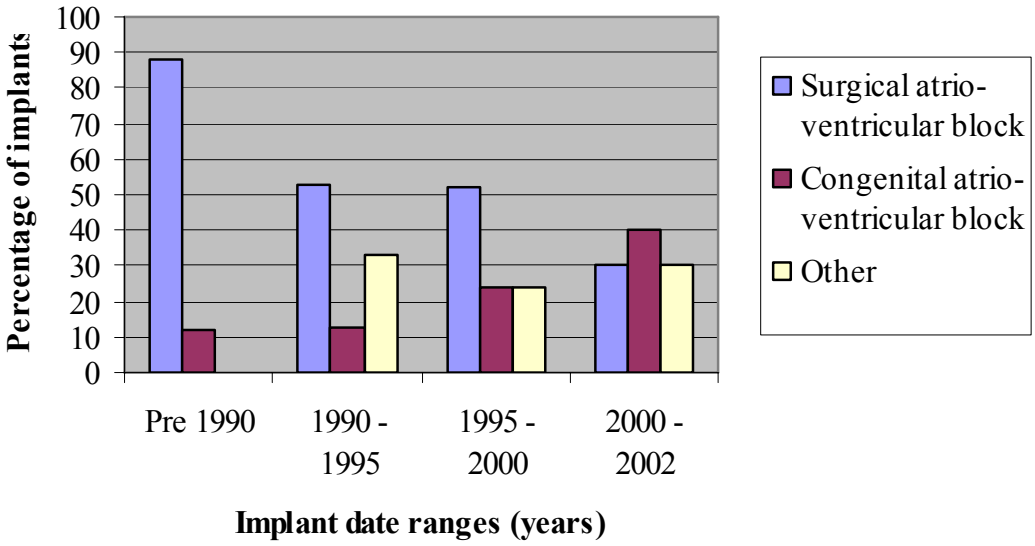
6. Long QT syndrome (n = 2): both patients in this group were paced for congenital long QT syndrome and had associated 2:1 AVB.

7. Other (n = 1) includes a paediatric patient who had periods of asystole during reflex anoxic seizures.

A total of 12 implants were due to surgical SSS or prevention of atrial arrhythmias with post surgical sinus bradycardia.

Figure 18 shows that since 1990 the percentage of implants for surgical AVB has reduced from 88% to 30% with a simultaneous trend of an increasing number of implants for congenital AVB. Prevention of atrial arrhythmias as an indication for pacing, which is included in the other group, has remained relatively stable at 11% of all implants since 1990.

Figure 18 Pacemaker implant indications for patients receiving epicardial leads between 1977 and 2002



Other includes: Prevention of atrial arrhythmias, Sick sinus syndrome, Atrio-ventricular node disease, Long QT syndrome and asystole during reflex anoxic seizures

The most common cardiac surgical procedures that resulted in AVB were; ventricular septal defect closure or enlargement (± other cardiac surgery) (n = 20), tricuspid valve replacement or repair (n = 8), Tetralogy of Fallot repair (n = 5) and mitral valve replacement (n = 3).

4.2 Lead characteristics

This section describes the characteristics of the 192 epicardial leads that were implanted between January 1977 and December 2002.

4.2.1 Number of leads

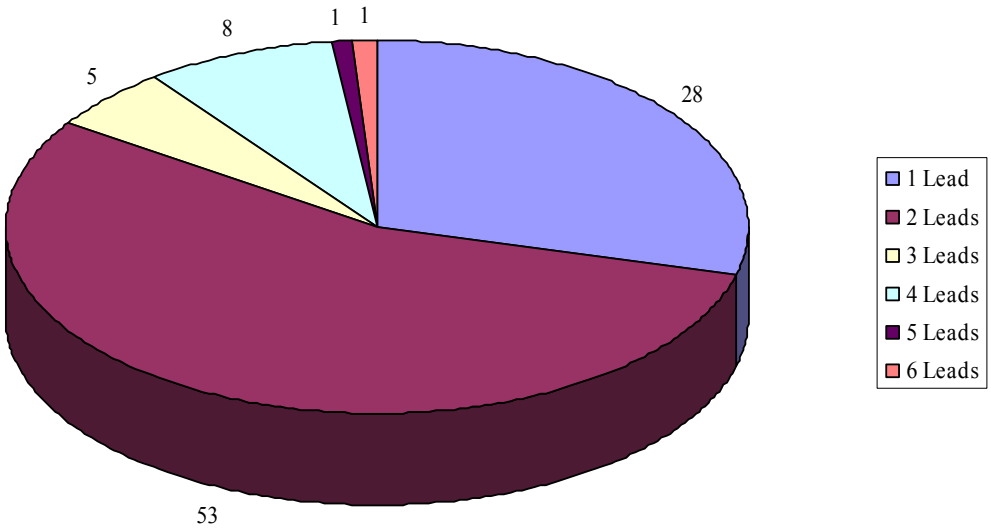
Of the 192 leads implanted during the study period, 143 (74%) were implanted in paediatric patients and 49 (26%) were implanted in adults (**Table 22**). Twelve of these leads (7 paediatric and 5 adult) were never connected to a pacemaker for reasons described in section 4.7. These leads with no follow-up are referred to as lead only implants and are excluded from the lead follow-up and complication data. The 180 leads that did have follow-up testing performed, were predominantly steroid-eluting (83%).

Table 22 The number of leads implanted and the number that received follow-up testing

	Leads implanted	**Leads followed**
	n	**n**
All leads	192	180
Leads in paediatric patients	143	136
Leads in adult patients	49	44
Steroid-eluting leads	155	150
Non steroid-eluting leads	37	30
Ventricular leads	118	108
Atrial leads	74	72

Multiple leads were implanted in patients due to dual chamber pacing (requiring atrial and ventricular leads), replacement of failed leads or elective replacement to avoid lead fracture with patient growth. The majority of patients had two leads implanted during the study period with one patient receiving 6 leads (**Figure 19**).

Figure 19 Number of epicardial pacing leads implanted in each patient



4.2.2 Lead models

The majority of the 192 leads implanted during the study period were Medtronic 4965 steroid-eluting (SE) leads (**Table 23**). The majority of non steroid-eluting (NSE) leads implanted were Medtronic 4951 leads, with small numbers of other NSE lead models also implanted. SE leads were implanted between 1/12/1993 to 11/10/2002. A range of NSE lead models were implanted between 31/5/1977 and 14/2/1999.

Table 23 Epicardial lead models implanted at Green Lane Hospital between 1977 and 2002

Steroid-eluting leads	Number	Non steroid-eluting leads	Number
Medtronic 4965	151	Medtronic 4951	23
Medtronic 4968 (includes 10366)	4	Telectronic 033-571	5
		Medtronic 5815	3
		Medtronic 637-702	2
		Telectronics 030171	2
		Telectronics 033-572	1
		Possis 1111	1
Total	**155**		**37**

4.2.3 Polarity

Of the leads models implanted during the study period the majority (98%, n = 188) were unipolar leads. All of the lead only implants were unipolar. Only the Medtronic 4968 leads were bipolar (2.3%, n = 4).

4.2.4 Fixation

All SE epicardial leads use a passive fixation method, where the lead is sewn on to the epicardial surface. All NSE epicardial leads implanted are active fixation and used either a barbed hook or screw to attach the lead to the myocardium (see 1.4.2.3).

4.2.5 Lead location

Of the 192 leads implanted; 74 were atrial and 118 were ventricular. Of the 180 leads that were connected to a pacemaker, the majority were SE ventricular leads (**Table 24**).

Table 24 Location of steroid-eluting and non steroid-eluting epicardial leads that received follow-up

	SE leads	NSE leads	Total
	n	n	n
Atrial	71	1	72
Ventricular	79	29	108
Total	150	30	180

NSE: non steroid-eluting, SE: steroid-eluting

4.2.6 Follow-up duration

The study period included a total of 600 follow-up years with a maximum follow-up duration of 27.1 years for one lead. As seen in **Table 25**, the average follow-up duration of non steroid-eluting leads was 1.4 years longer than steroid eluting leads. The 12 lead only implants are not included in the average follow-up durations.

Table 25 Follow-up duration of epicardial leads

	Mean (years)	Median (years)	Maximum (years)
All leads followed (n = 180)	3.3	2.8	27.1
Leads in paediatric patients (n = 136)	3.2	2.8	27.1
Leads in adult patients (n = 44)	3.6	3.6	14.1
Steroid-eluting (n = 150)	3.1	2.8	8.8
Non steroid-eluting (n = 30)	4.5	2.7	27.1

Excluding lead only implants, 27 leads had follow-up less than 2 months for the following reasons; patient deceased (n = 13), lead failure (n = 9) and patient lost to follow-up due to moving overseas (n = 5).

4.2.7 Lead outcomes

At 5 years only a quarter of the leads implanted were being followed and another quarter of the leads had failed for reasons explained in section 4.6 (**Table 26**).

Table 26 Outcome of epicardial leads at 5 years post implant

Lead outcome	n	Percent
Leads still working and being followed	48	(25%)
Follow-up less than 5 years due to recent implant	36	(19%)
Patient deceased	30	(15.5%)
Failed for reasons other than fracture	26	(13.5%)
Fractured	20	(10%)
Lead only implant with no follow-up	12	(6%)
Lost to follow-up	8	(4%)
Lead electively replaced	6	(3%)
Pacing no longer required so no follow-up	3	(2%)
Lead removed due to infection	3	(2%)
Total	**192**	**(100%)**

By 7 years post implant only 10% of leads were still working and being followed. This is predominantly due to; lead failure of all causes (28%), leads being implanted recently (27%) and patients deceased (17%).

4.2.8 Implant techniques

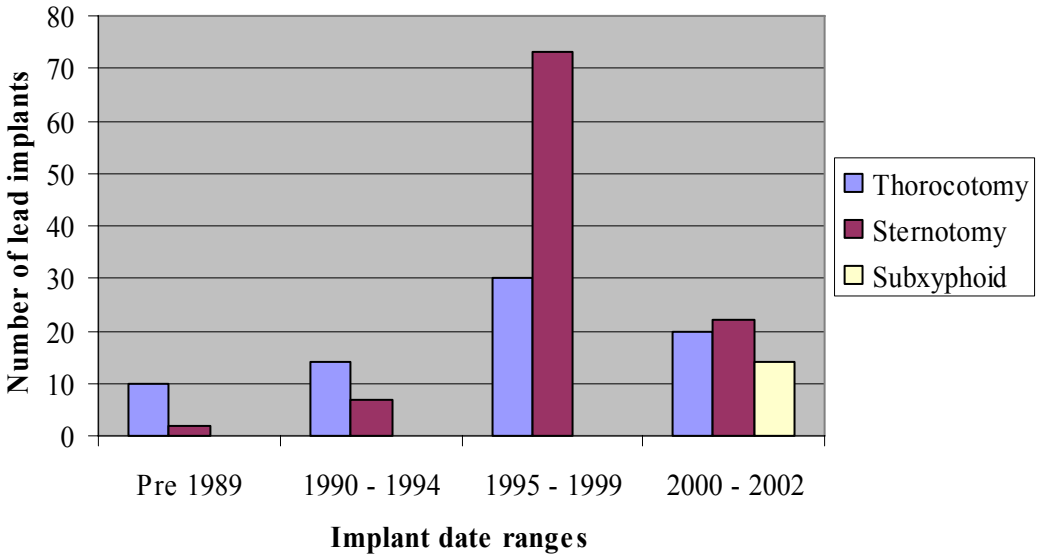
Lead implantation was most often performed via the sternotomy route (**Table 27**) which was predominantly used when the leads were placed at or close to the time of cardiac surgery. The subxiphoid route has a much shorter average follow-up compared to the thoracotomy and sternotomy techniques because of its more recent introduction at GLH.

Table 27 Implantation techniques and follow-up duration of epicardial leads

	Leads implanted n (%)	**Leads followed n (%)**	**Mean / Median follow-up (years)**	**Maximum follow-up (years)**
Sternotomy	104 (54%)	97 (54%)	3.3 / 2.7	27.1
Thoracotomy	74 (39%)	69 (38%)	3.6 / 3.9	14.1
Subxiphoid	14 (7%)	14 (8%)	2 / 2	3.1
Total	**192**	**180**		

Prior to 1995 the majority of implants were performed using the thoracotomy technique although since 1995 there has been an increase in the use of the sternotomy route (**Figure 20**). The most recent implant performed using the thoracotomy route was carried out in 2001. The first implant performed using the subxiphoid route took place in 2002 and this has become the route of choice when lead implantation is not performed at or close to the time of other cardiac corrective surgery.

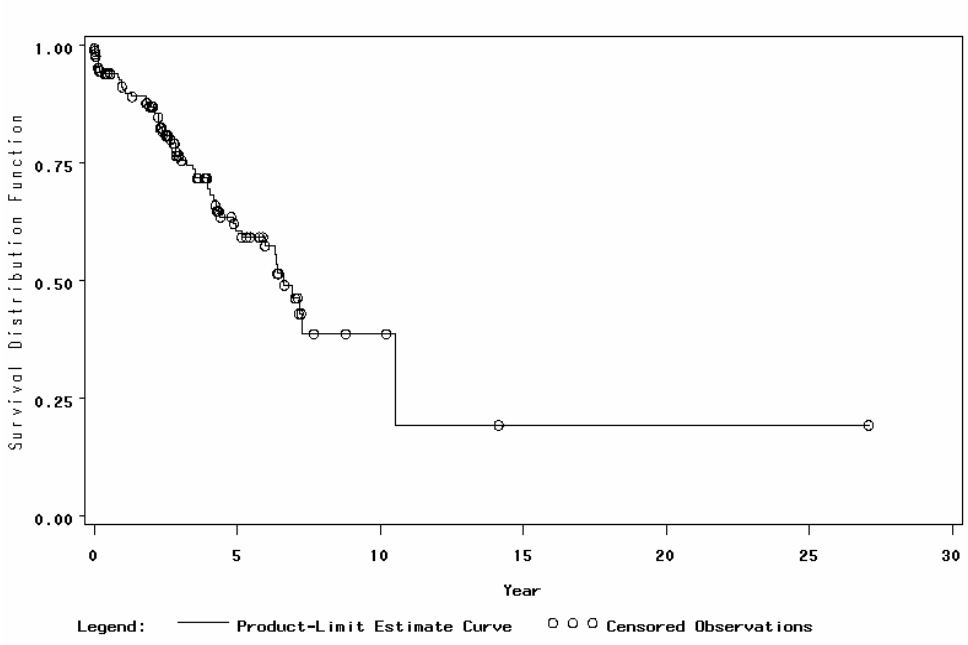
Figure 20 Implant routes used for placement of epicardial leads



4.2.9 Lead survival

The median survival time for all epicardial leads followed (n = 180) was 6.6 years (**Figure 21**). The 1, 2, 5, 10, and 15 year freedom from lead failure (and standard deviation) for all leads is: 91% (2%), 86% (3%), 61% (5%), 39% (7%), and 19% (10%). The values at 10 and 15 years represent NSE leads only.

Figure 21 Kaplan Meier survival curve for all epicardial leads receiving follow-up



The following factors were examined to determine whether any predictors of lead failure could be found; patients age at implant, gender, weight at implant, patient having had previous cardiac surgery, lead polarity, lead type, indication for pacing and implant route. There was a significant difference in lead failure rate depending on lead type (SE or NSE lead). NSE leads were 6 times more likely to fail than SE leads (**Table 28**). SE lead freedom from lead failure (and standard deviation) at 2, 5 and 7 years was 91% (3%), 66% (5%) and 51% (7%) respectively where as for NSE leads at 2, 5, 10 and 15 years freedom from lead failure was 68% (9%), 41% (10%), 29% (10%) and 15% (9%) respectively (see **Appendix 5b**).

Table 28 Odds ratio for lead failure of steroid-eluting versus non steroid-eluting epicardial leads

	Point estimate	95% Wald confidence limits		p value
SE versus NSE leads	5.895	2.536	13.703	<0.0001

NSE: non steroid-eluting, SE: steroid-eluting

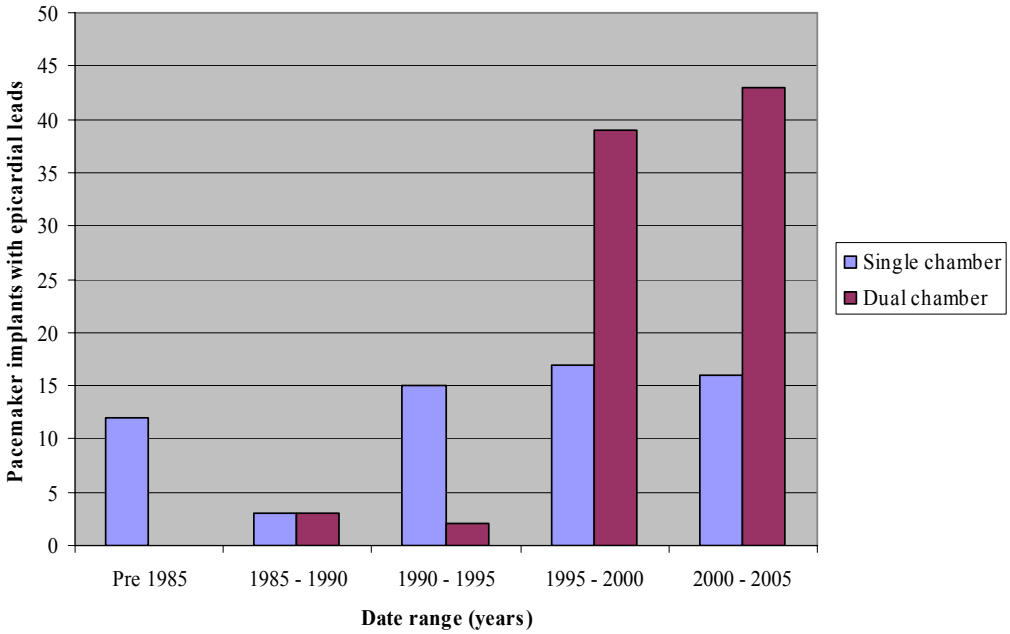
A hazard ratio estimate of 0.492 (p = 0.014) was determined which indicates that the relative risk of NSE lead failure was approximately twice that of SE lead failure.

There was no significant difference in lead failure in any of the other groups examined or between adult and paediatric patients.

4.3 Pacemaker models

Throughout the 28 year period a variety of pacemaker models were used with epicardial leads. Manufacturers included: Guidant (Cardiac Pacemakers Incorporated (CPI)), Intermedics, Medtronic, Sorin, St Jude Medical (Pacesetter) and Telectronics. The number and percentage of dual chamber pacemakers implanted has dramatically increased since 1995 while the number of single chamber pacemaker implants has remained relatively constant since 1990 (**Figure 22**).

Figure 22 Number of single and dual chamber pacemakers implanted with epicardial leads



4.4 Lead follow-up

From the 180 leads that were connected to a pacemaker, 1498 follow-up checks provided lead measurement results over the 28 year study period. Of these follow-up checks 85% were performed on SE and 15% on NSE leads. Due to a low number of NSE atrial leads being implanted, there were relatively few follow-up checks (n = 18) performed in this group. The lead function tests performed were; pacing threshold, sensing threshold and the lead impedance. Not all of these tests could be performed at each follow-up check for reasons explain under limitations of the study (section 5.3.2).

4.4.1 Pacing threshold

Measured pacing thresholds were converted to a voltage threshold at 0.5 milliseconds using the threshold conversion formula described in chapter 3. A total of 1387 pacing thresholds were measured and 84% of those were from SE leads. Pacing thresholds measured from SE and NSE leads were compared in the following lead groups: all leads, atrial leads only and ventricular leads only.

4.4.1.1 Pacing thresholds all leads

A comparison of the SE and NSE average pacing thresholds and standard deviations for all leads over a 6 years follow-up period are shown in **Table 29**. NSE leads had significantly higher pacing thresholds than SE leads at 6 weeks, 10.5 months, 3 and 5 years post implant and had non-significantly higher thresholds at 2, 4 and 6 years post implant. The average SE lead pacing threshold over 6 years was 1.3 volts (SD = 1.0) and the average pacing threshold for NSE leads was 2.7 volts (SD = 2.1).

Table 29 Average pacing thresholds over 6 years of follow-up for steroid-eluting and non steroid-eluting epicardial leads

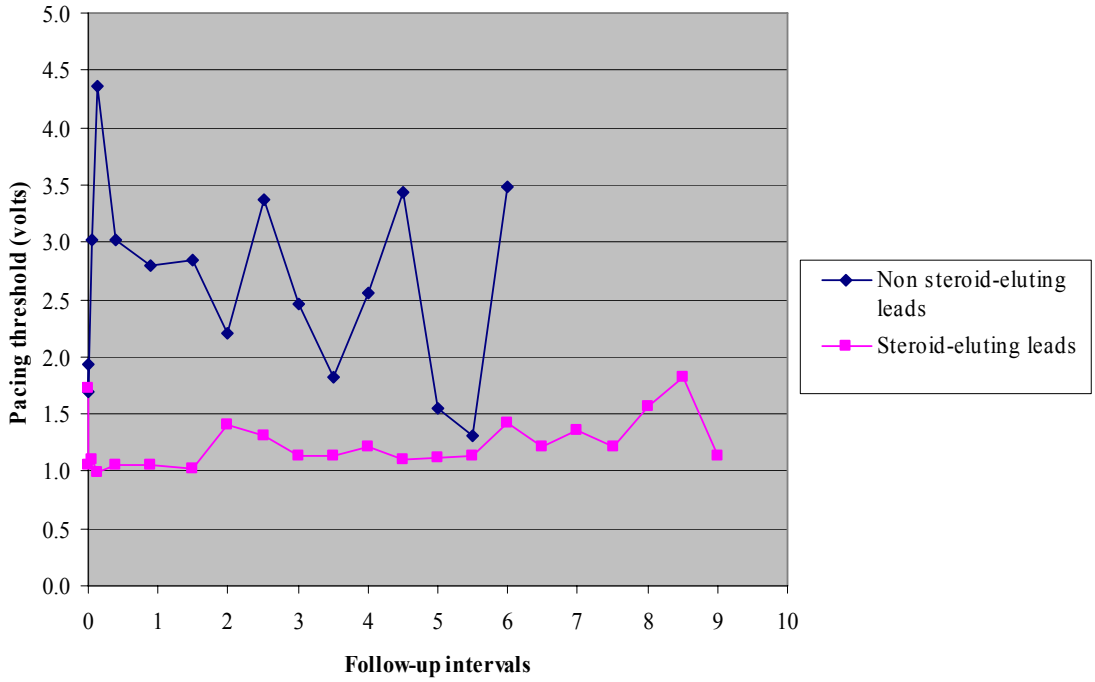
Follow-up interval	SE lead pacing thr. (volts) (SD)	SE leads n	NSE lead pacing thr. (volts) (SD)	NSE leads n	1 tailed t test p
Implant	1.7 (1.3)	153	1.9 (2.6)	34	0.330
6 weeks	1.0 (0.4)	88	4.4 (3.1)	12	0.002
10.5 months	1.1 (0.7)	95	2.8 (1.6)	11	0.003
2 years	1.4 (2.0)	86	2.2 (1.0)	7	0.052
3 years	1.2 (1.0)	48	2.5 (1.5)	7	0.030
4 years	1.2 (0.5)	46	2.6 (2.3)	7	0.090
5 years	1.1 (0.6)	30	1.5 (0.6)	5	0.010
6 years	1.4 (1.6)	25	3.5 (4.0)	6	0.140

NSE: non steroid-eluting, SE: steroid-eluting, thr: threshold

SE leads had average pacing thresholds of less than 1.8 volts at each follow-up interval over a 9 year period following implantation (**Figure 23**). NSE leads had higher pacing thresholds than SE leads at each follow-up interval over a 6 year period. Beyond 6 years, pacing thresholds for NSE leads were not included due to the low number of leads being followed.

At implant, SE leads were observed to have a higher pacing threshold (1.7 volts) compared to follow-up values but by 1 day post implant the pacing threshold had reduced to the chronic threshold levels.

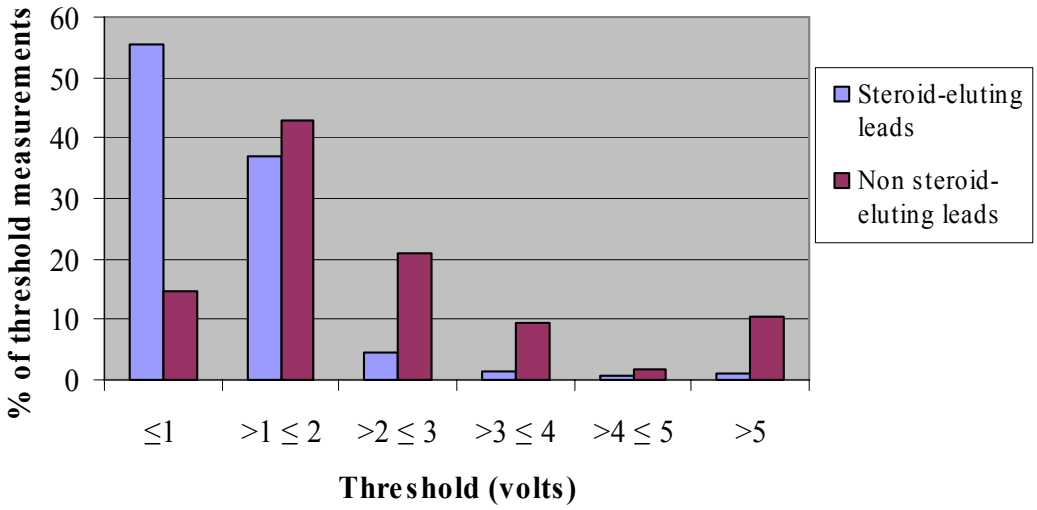
Figure 23 Average pacing thresholds for all steroid-eluting and non steroid-eluting epicardial leads



The average number of SE lead pacing threshold measurements at each follow-up interval was 53 over the 9 year period. The average number for NSE leads was 10 over 6 years. The apparent variation in the NSE threshold values between 2 and 6 years is likely to be due to the low number of leads being followed.

Figure 24 shows that the majority of SE leads had thresholds less than 2 volts. Two percent of the SE pacing threshold measurements (n = 21) were greater than 4 volts whereas 12% of the NSE lead measurements (n = 27) were greater than 4 volts. For SE leads 48% (n = 10) of the greater than 4 volt thresholds occurred at implant or 1 day post implant, where as only 11% (n = 3) of the high thresholds occurred at implant or 1 day checks in the NSE group.

Figure 24 Comparison of the pacing thresholds of steroid-eluting and non steroid-eluting epicardial leads

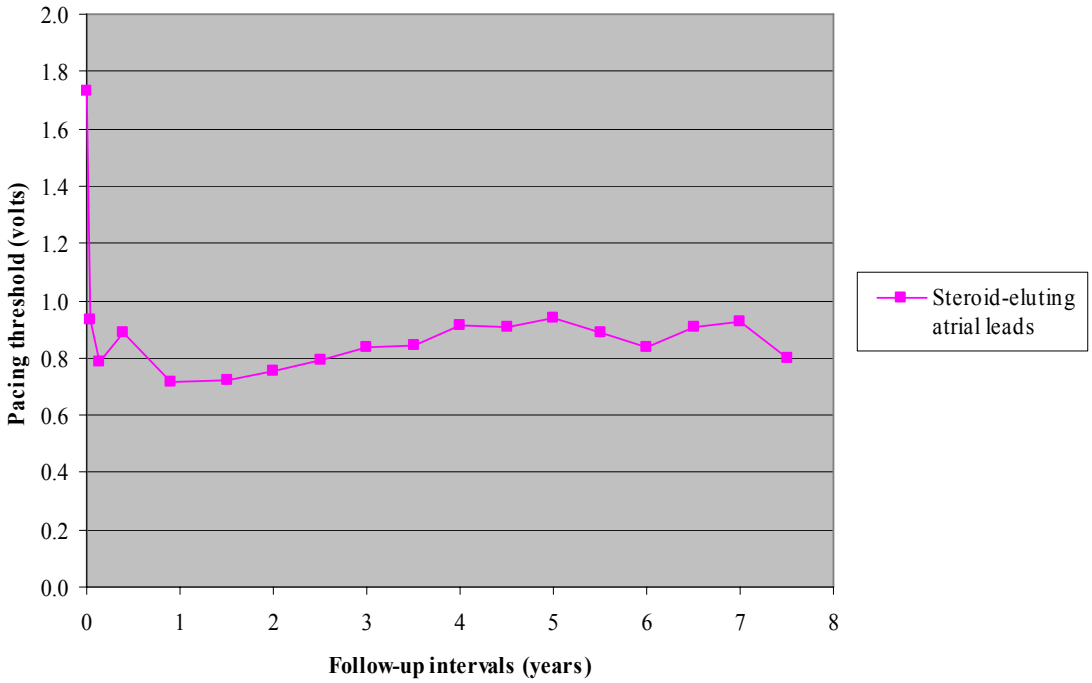


4.4.1.2 Atrial pacing thresholds

Seventy four atrial leads had pacing threshold testing performed. The average atrial pacing thresholds for SE leads remained low and stable over a 7.5 year follow-up period (**Figure 25**). The average atrial SE lead pacing threshold was 0.9 volts with a standard deviation of 0.4. On average 27 atrial threshold measurements were performed at each follow-up interval. At implant the average pacing threshold was 1.8 volts but by the following day this had fallen to the average chronic threshold value. Post implant, the maximum single SE lead threshold value was 2.6 volts, which occurred at 5 years post implant.

There were a low number of atrial, NSE leads implanted and therefore the threshold measurements for these leads are not graphically displayed. The average threshold for the one atrial NSE lead which did have pacing threshold measurements performed was 3.5 volts over a 6 year follow-up period.

Figure 25 Average pacing thresholds over a 7.5 year follow-up period for atrial steroid-eluting epicardial leads

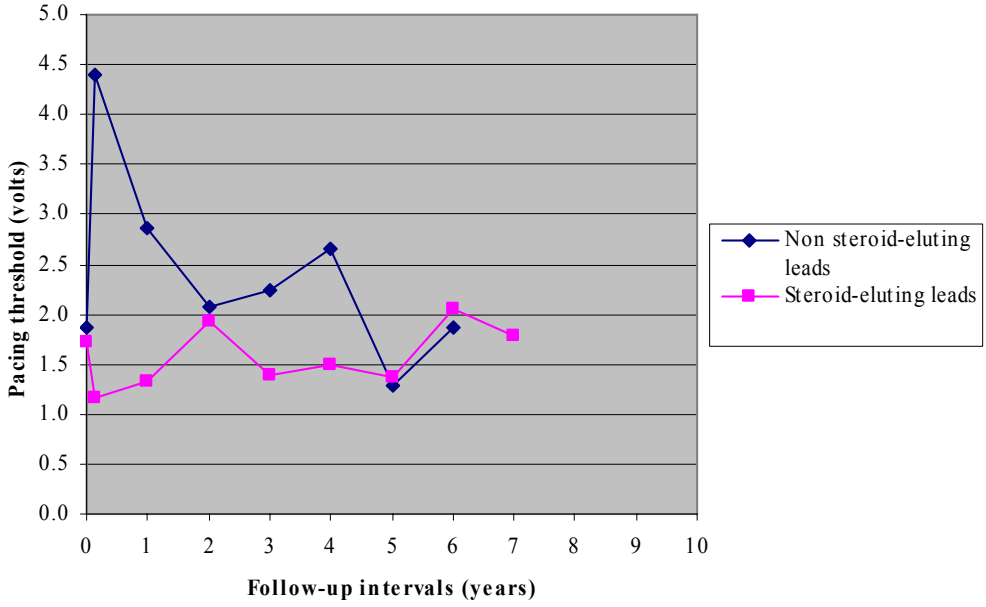


4.4.1.3 Ventricular pacing thresholds

Pacing threshold tests were performed on 118 ventricular leads. The average ventricular pacing thresholds for SE leads were relatively low and stable over a 7 year follow-up period (**Figure 26**). The average ventricular SE lead pacing threshold was 1.6 volts with a standard deviation of 1. On average 35 ventricular pacing thresholds were performed at each follow-up interval.

The average pacing threshold for NSE leads peaked at 4.4 volts 6 weeks post implantation and then remained higher than SE lead pacing thresholds over the next 4 years. The average NSE ventricular lead pacing threshold was 2.4 volts (SD =1.7) over the 6 year period. For NSE ventricular leads there were on average 10 measurements at each interval although after 4 years there were less than 6 NSE leads being followed.

Figure 26 Average pacing thresholds over a 7.5 year follow-up period for ventricular epicardial leads

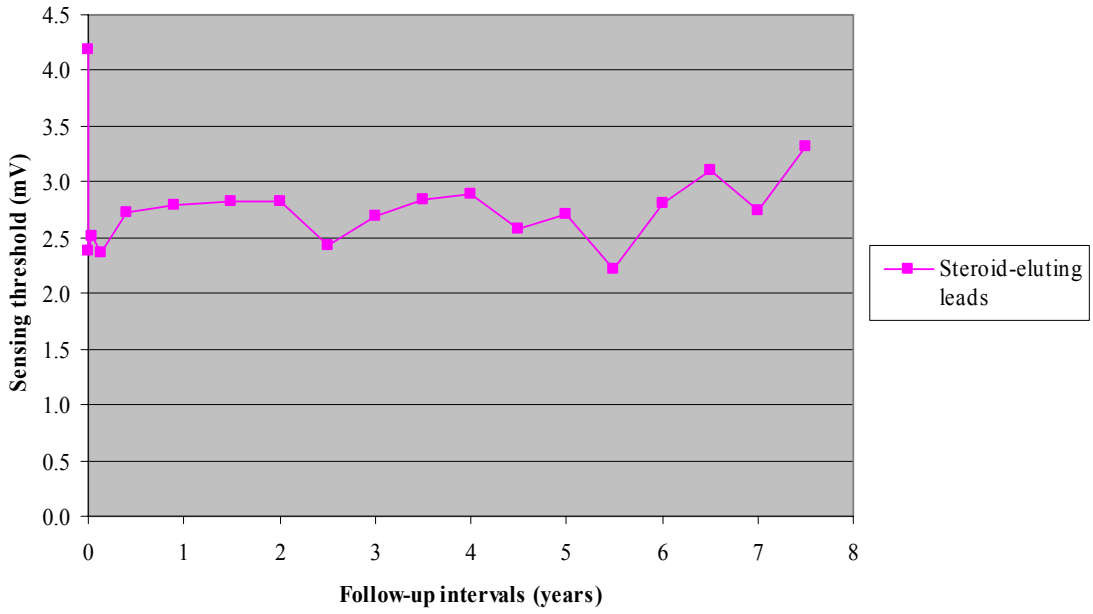


4.4.2 Sensing thresholds

4.4.2.1 Atrial sensing

The sensing function of 71 SE atrial leads was observed over a 7.5 year period **(Figure 27)**. Throughout this time 506 atrial sensing thresholds were measured with an average threshold of 2.8 mV. During the follow-up period sensing remained relatively stable with a standard deviation of 1.5. Beyond 8 years the number of SE leads followed was too small for meaningful analysis. Only 1 NSE atrial lead was implanted and sensing thresholds were not measured on this lead.

Figure 27 Average sensing thresholds over an 8 year follow-up period for atrial steroid-eluting epicardial leads

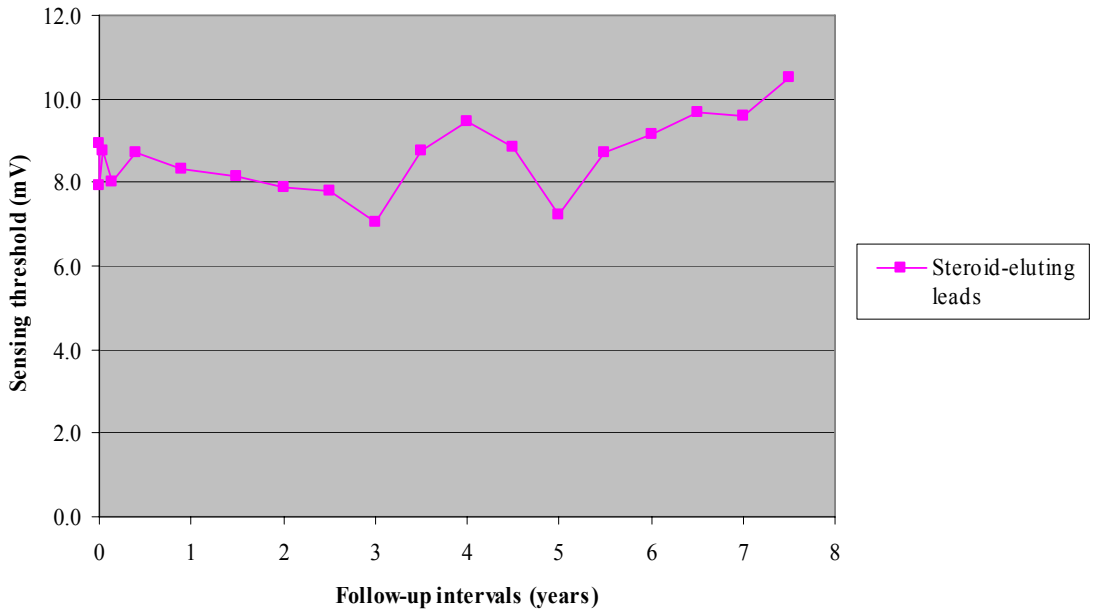


4.4.2.2 Ventricular sensing

The sensing function of 61 SE ventricular leads was observed over a 7.5 year period (**Figure 28**). During this time a total of 457 SE lead, ventricular sensing threshold measurements were performed with an average of 24 measurements at each interval. The average ventricular sensing threshold for SE leads during this time was 8.6 mV. SE lead sensing thresholds remained relatively stable with a standard deviation of 4.4. Follow-ups longer than 8 years for SE leads were not included due to the low number of lead measurements at each interval.

A total of 18 ventricular NSE leads had sensing thresholds performed although on average there were only 2.7 sensing measurements at each follow-up interval. The low number of measurements during follow-up is due to the smaller number of leads in the initial group, early lead failures and the leads being connected to pacemakers without lead testing capabilities. The NSE leads that had ventricular sensing tested had an average threshold of 7.1 mV over a 6 year follow-up period. Due to the low number of sensing thresholds per follow-up interval the NSE sensing threshold measurements are not graphically displayed.

Figure 28 Average sensing thresholds over an 8 year follow-up period for ventricular steroid-eluting epicardial leads



4.4.3 Lead impedance

Over an 8 year period 1198 lead impedance measurements were performed on SE leads and over a 6 year period 93 impedance measurements were performed on NSE leads. Beyond 6 years there were only 1 or 2 impedance measurements at each follow-up interval for NSE leads. The average impedance for NSE leads was higher than SE leads over the time periods described (**Table 30**). Impedance measurements performed at implantation were excluded from the average as these were not measured through the pacemaker.

Table 30 Average lead impedance measurements for all steroid-eluting and non steroid-eluting epicardial leads

	Average impedance (ohms) (SD)	**Impedance range (ohms)**
Steroid-eluting leads	372 (73)	218 – 1007*
Non steroid-eluting leads	443 (128)	277 – 723

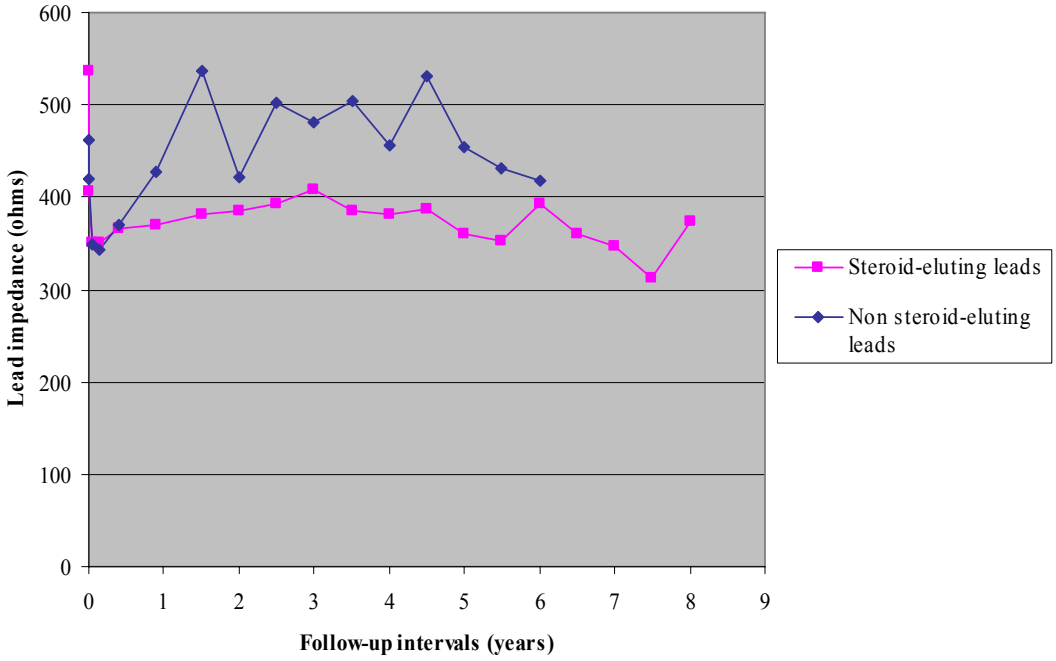
* Impedance measurement at 1 day post lead implantation

Steroid-eluting epicardial leads are observed to have stable impedance measurements from 2 weeks post implant over an 8 year follow-up period (**Figure 29**).

The higher impedance values seen at implant were measured through the pacing systems analyzer, which accounts for a sudden reduction in the impedance at 1 day post implant at which time the impedance was measured through the pacemaker.

The apparent variability of the NSE lead impedance seen in **Figure 29** is likely to be a result of the low number of measurements performed in this group for similar reasons as those described for NSE ventricular sensing threshold measurements (section 4.4.2.2).

Figure 29 Average impedances of steroid-eluting and non steroid-eluting epicardial leads



4.5 Lead measurements at implant

The lead measurements performed at the time of lead implantation were; pacing capture threshold, atrial and ventricular sensing threshold and lead impedance. There was no significant difference between the implant measurements obtained from SE leads compared to NSE leads (**Table 31**). Average pacing thresholds for both SE and NSE leads exceeded the recommended minimum value of 1.5volts at 0.5 milliseconds (recommendations are described in 2.9.1). Where atrial and ventricular sensing thresholds could be measured the average threshold values were approximately twice the recommended minimum values for both SE and NSE leads. Due to a low number of non steroid-eluting atrial lead implants the sensing threshold and standard deviation could not be determined for these leads. Average lead impedance values obtained at implant were within the normal range of 300 to 1200 ohms.

Table 31 Average lead implant measurements for steroid-eluting and non steroid-eluting epicardial leads

	Steroid-eluting leads	**Non steroid-eluting leads**	**2 tailed t test p value**
Pacing threshold, volts* (SD)	**1.7 (1.3)**	**1.9 (2.6)**	0.668
n	*153*	*34*	
Atrial sensing threshold, mV (SD)	**4.2 (2.4)**	-	-
n	*68*		
Ventricular sensing threshold, mV (SD)	**8.9 (4.1)**	**8.5 (4.7)**	0.748
n	*61*	*18*	
Impedance, ohms (SD)	**537 (258)**	**462 (182)**	0.060
n	*148*	*31*	

* Measured at a pulse duration of 0.5 milliseconds

4.5.1 Implant difficulties

Difficulties were encountered during 45 of the lead implants with the majority of these being related to trying to obtain an adequately low pacing threshold. The four most common difficulties encountered are described below with some lead implants having more than one of the following problems:

1. Multiple attempts (>2) were made to obtain a lead position that had an adequate pacing and/or sensing threshold (n =26)
2. The epicardium was covered in fat, scars or adhesions (n = 14)
3. The myocardium was in a poor state post bypass surgery (n = 3)
4. The ventricle was very irritable during lead placement resulting in episodes of ventricular fibrillation (n = 3)

4.5.1.1 Outcome of implant difficulties

For the leads which had implant difficulties, the outcomes that were achieved at implant and the complications which developed during follow-up are described below. Some leads developed more than one complication. In other leads the occurrence of complications is unknown due to the leads having less than 6 weeks or no follow-up due to patient death or lead only implantation respectively. Complications considered to be relevant included those related to pacing or sensing thresholds such as exit block, high threshold or loss of sensing.

- Satisfactory pacing thresholds (<1.5 volts at 0.5msecs) were ultimately obtained for 10 leads. Two (20%) of these leads developed complications during follow-up including: high threshold (1) and loss of sensing (1). Occurrence of complications was unknown in 1 lead.

- Sub-optimal lead measurements (pacing thresholds > 1.5 volts at 0.5 msecs) were accepted for 31 of the lead implants, with an average pacing threshold for these leads of 3.7 volts. Seven (22%) of these leads had follow-up complications including: exit block or high threshold (5) and loss of sensing (2). Complication occurrence is unknown in 6 leads.

- The epicardial surface was cleared by scraping with a scalpel or diathermy to remove fat or until the muscle fibres were visible. This allowed lead placement on or in the epi-myocardium (n = 8). In two cases, the surgeon cut down until the muscle was exposed and the lead tip was buried into the myocardium. This lowered the pacing threshold from 2.8 volts to 0.7 volts in one case and from greater than 10 volts to 1.5 volts in the second case. Neither of these leads developed complications during follow-up.

- In two cases attempts to use a passive lead were abandoned due to excessively high thresholds and an active (NSE) lead was placed, which gave improved pacing thresholds at the time of implant. Both of these active (NSE) leads failed during follow-up, one due to exit block and the other due to a high threshold.

4.6 Complications

The type and number of complications which occurred with epicardial leads between January 1977 and December 2004 are shown in **Table 32**. Lead fracture was the most prevalent complication followed by exit block or high threshold. Lead failure was not the ultimate outcome of all lead complications as in some cases pacemaker reprogramming was able to resolve the problem. The specific findings relating to each complication are discussed in the following sections.

Table 32 Prevalence of complications occurring with epicardial leads and the number of patients in which each complication occurred

Complication	Patients (n = 96) n	All leads (n = 180) n	SE leads (n = 150) n	NSE leads (n = 30) n
Lead fracture	23	27	23	4
Exit block or high threshold	19	24	7	17
Sensing problems	16	18	16	2
Twitch	10	13	9	4
Insulation fault	3	4	4	0
Lead dislodgement	1	1	1	-
Infection	5	-	-	-
Total	**76**	**86**	**60**	**27**

NSE: non steroid-eluting, SE: steroid-eluting

4.6.1 Lead fracture

Lead fracture occurred in 27 of the 180 leads that were followed with 3 fractures occurring in adult patients. Fractures occurred equally in atrial and ventricular leads (**Table 33**). A hypothesis based on observation was that leads fractured more often when implanted using the thoracotomy approach but the Chi square test showed only marginal significance (p = 0.0998) for this premise. The 2, 5 and 10 year freedom from lead fracture (and standard deviation) was: 96% (2%), 79% (4%) and 56% (9%).

Table 33 Prevalence of lead fractures according to lead location and implant route for epicardial leads

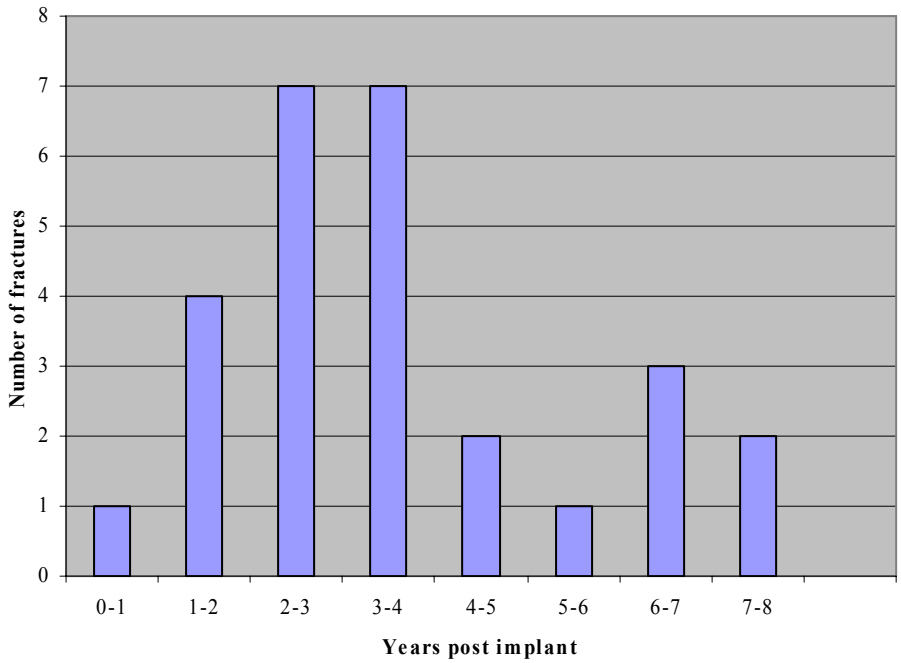
	Fractures n (%)
All leads (n = 180)	27 (15%)
Atrial leads (n = 72)	12 (17%)
Ventricular leads (n = 108)	15 (14%)
Leads implanted by thoracotomy (n = 69)	15 (22%)
Leads implanted by sternotomy (n = 97)	12 (12%)
Leads implanted by subxiphoid (n = 14)	0* (0%)

*No fractures occurred in the leads implanted by the subxiphoid route although there were a low number of leads in this group (n = 14) and their mean follow-up duration was only 2 years.

4.6.1.1 Time to lead fracture

As seen in **Figure 30** the highest rate of lead fracture was seen in the 2nd and 3rd year post implant with a median time from implant to fracture of 2.5 years.

Figure 30 Number of epicardial lead fractures each year post implant



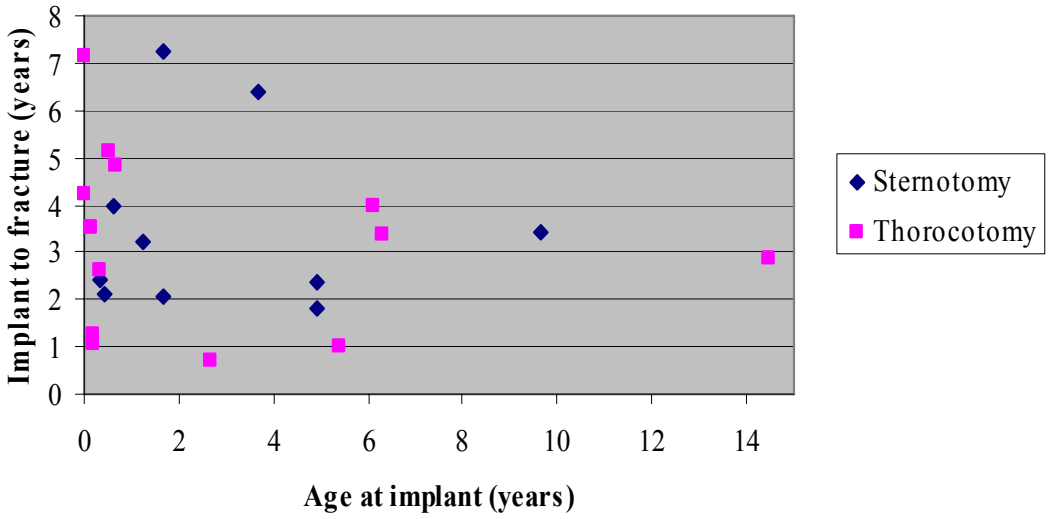
4.6.1.2 Potential risk factors for lead fracture

Factors examined to determine associations with rate of lead fracture were: lead polarity, lead site, lead type, patient age, gender and lead implant route. There was no significant difference in the occurrence of lead fracture in any of these groups (see **Appendix 5c**). All fractures occurred in unipolar leads although due to the low number of bipolar leads implanted (n = 4) a comparison could not be made between these groups.

4.6.1.3 Age at implant

The patient's age at implant was compared to the time from implant to fracture for the paediatric age group. A wide variation in time to fracture is seen regardless of whether the patients were infants when the lead was first implanted or whether the lead was implanted when they were older children (**Figure 31**). The implant route did not affect how early a lead fractured. The time it took leads to fracture ranged from 0.7 to 7.2 years for the whole group with a median of 3.2 years.

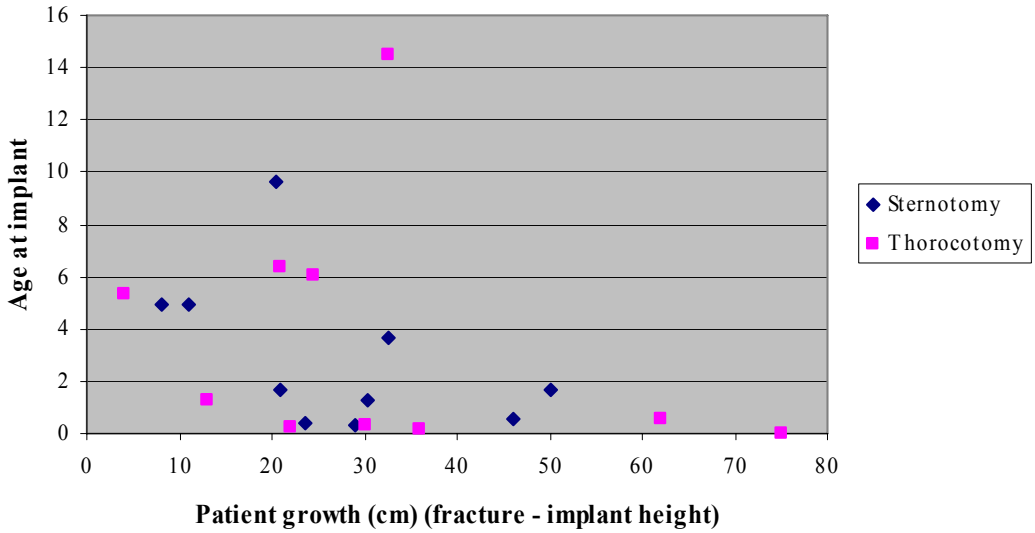
Figure 31 Time from implant to fracture in relation to the patients age at lead implant and implant route



4.6.1.4 Patient growth

Twenty paediatric patients who developed lead fractures had height measurements performed at implant and at the time of lead fracture. On average the patients grew 30 cm from the time the lead was implanted to the time the fracture occurred. For the 15 lead fractures where the patients were under 2 years of age at implant the average implant to fracture height difference was 38cm, varying from 13cm to 75cm (**Figure 32**). There was no relationship between the lead implant route and patient growth resulting in fracture.

Figure 32 Age implant compared to patient growth for all fractured epicardial leads that were implanted in paediatric patients



4.6.1.5 Lead measurement changes at fracture

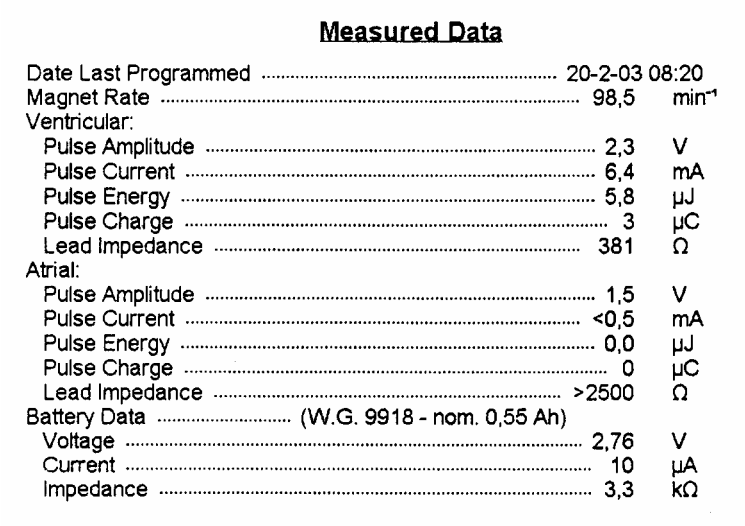
For 24 of the fractured leads, measurement testing was performed at or close to the time the fracture was discovered. For 3 leads the fracture was discovered on chest x-ray and these leads did not undergo testing. The most common lead measurement changes seen at the time of lead fracture were an impedance rise and loss of capture (**Table 34**). Sensing function was the least likely lead test to show a change when a fracture had occurred. Impedance measurements were above the measurement range of the pacemaker in 17 cases (i.e. > 2000 ohms). Five leads had a large rise in impedance but the value was still within the normal impedance range of 300 – 1200 ohms. The smallest rise in impedance at lead fracture was 242 ohms. Sixteen (67%) of the leads tested showed changes in all 3 lead measurement tests.

Table 34 Measurement changes observed in fractured epicardial leads that had lead function tests performed (n = 24)

Lead test	Number of leads showing a change	Percentage (of fractured leads that were tested)	Function change
Pacing capture	20	83%	loss of capture
	3	13%	threshold increase
Sensing function	12	50%	loss of sensing
	3	13%	decreased sensing
	1	4%	oversensing
Lead impedance	24	100%	impedance rise

The telemetered data shown in **Figure 33** was recorded from a patient with an atrial lead fracture and the atrial pulse amplitude programmed to 1.5 V. The lead impedance was measured as >2500 Ω and because of the high impedance the energy delivered to the myocardium was 0 μJ therefore loss of capture was observed on the surface ECG.

Figure 33 Pacemaker telemetered measured data recorded from a fractured atrial pacing lead and a normally functioning ventricular lead



Measured Data

Date Last Programmed	20-2-03 08:20	
Magnet Rate	98,5	min^{-1}
Ventricular:		
Pulse Amplitude	2,3	V
Pulse Current	6,4	mA
Pulse Energy	5,8	μJ
Pulse Charge	3	μC
Lead Impedance	381	Ω
Atrial:		
Pulse Amplitude	1,5	V
Pulse Current	<0,5	mA
Pulse Energy	0,0	μJ
Pulse Charge	0	μC
Lead Impedance	>2500	Ω
Battery Data	(W.G. 9918 - nom. 0,55 Ah)	
Voltage	2,76	V
Current	10	μA
Impedance	3,3	kΩ

4.6.1.6 Measurement changes prior to fracture

Seven of the fractured leads (26%) showed lead measurement changes at prior follow-up pacemaker checks as follows; two showed an impedance increase of 100 and 500ohms, 2 had oversensing, 1 had loss of sensing and 2 had a pacing threshold rise. Of the 7 leads showing changes prior to fracture, 4 were atrial and 3 of the ventricular leads were implanted in patients who had underlying sinus rhythm with an adequate ventricular rate.

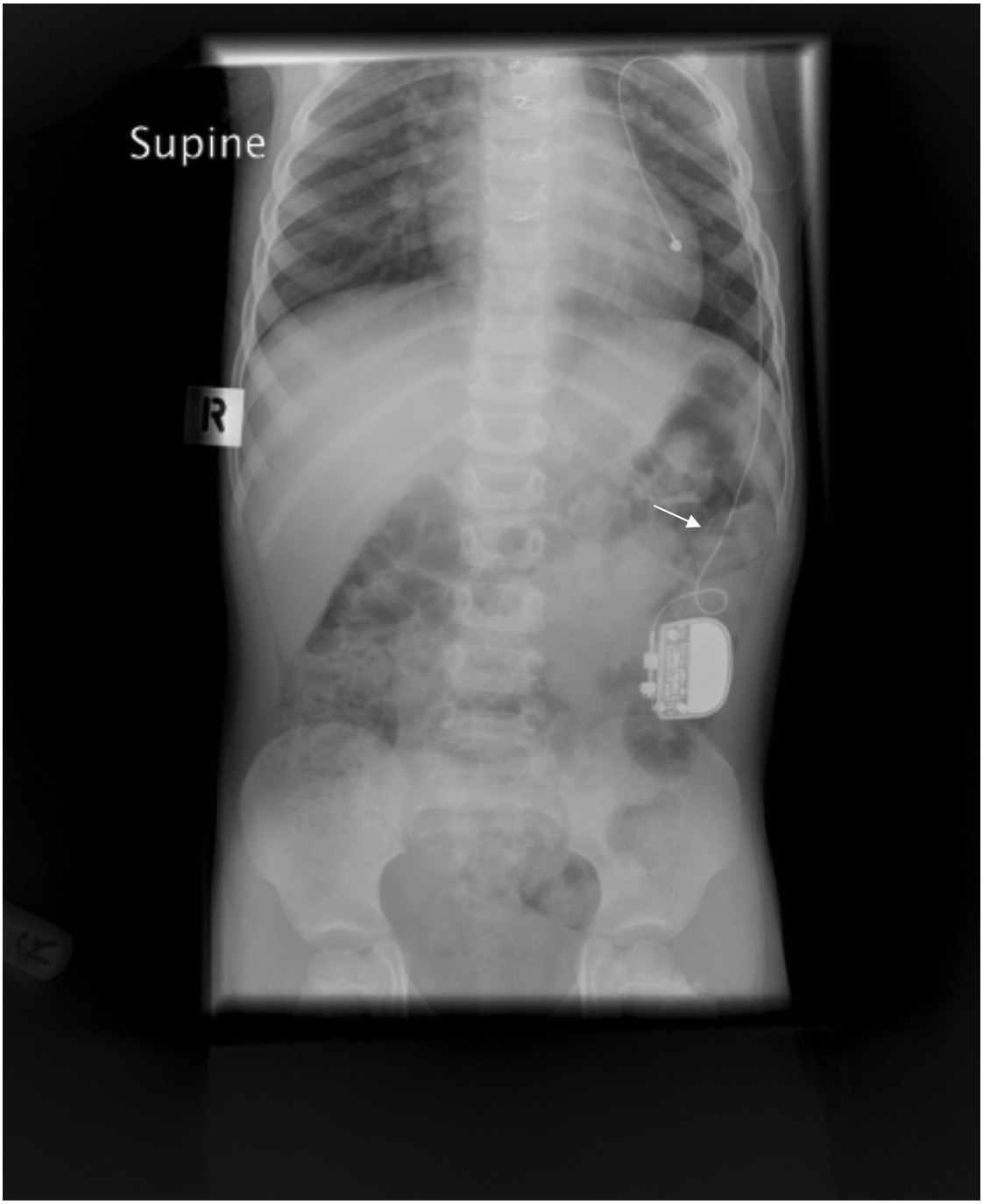
4.6.1.7 Daily measurements with fracture

One patient who had an atrial lead fracture had a Guidant Discovery 1273 pacemaker with the capability of daily lead impedance and intrinsic amplitude measurements. The daily measurement readings (**Appendix 4**) show that atrial lead impedance remains relatively stable until the time of lead fracture when the impedance suddenly doubles. In this case, once the lead had fractured the lead impedance was variable but generally abnormally high compared to pre-fracture impedance values, although some normal values are still recorded. The daily measurements also recorded an increased intrinsic atrial amplitude measurement (1mV to greater than 3.5mV) over the time that the lead fracture was occurring. This is likely to be due to oversensing.

4.6.1.8 Fracture location on chest x-ray

Chest x-rays were reviewed for the majority of lead fractures. The location of the fracture was typically close to the pacemaker site and was often seen at the point that the lead passed through the diaphragm or in the portion of the lead between the diaphragm and the pacemaker as seen in **Figure 34**.

Figure 34 Chest x-ray of a patient with a ventricular epicardial lead fracture



4.6.1.9 Patient presentation at lead fracture

From the information available there did not appear to be any deaths due to lead fracture although three patients presented with acute hospital admission. For 14 of the 27 lead fractures the patients presented at routine follow-up checks with no symptoms. This included 9 atrial lead fractures and 5 ventricular lead fractures where there was a good underlying ventricular rate. The patients who did present with symptoms had: syncope, presyncope, lack of energy, tiredness, shortness of breath and a chesty cough.

4.6.1.10 Lead outcome following fracture

The majority of fractured leads were replaced as shown in **Table 35**. For 3 atrial leads fractures the mode of pacing was changed from dual chamber to ventricular pacing only. One lead was repaired but went on to fracture again 10 months later.

Table 35 Outcome of fractured epicardial leads

	Total leads n = 27	**Atrial leads n = 12**	**Ventricular leads n = 15**
Leads replaced	20	7	13
Mode changed	3	3	0
Pacing no longer required	3	2	1
Lead repaired	1	0	1

4.6.2 Exit block and high threshold

Exit block (EB) was defined as "failure of the pacemaker output to capture the heart because the stimulation threshold exceeds the output capacity of the pacemaker." Exit block was observed in 12 of the 180 leads followed.

High threshold (HT) was defined as "an elevated pacing threshold resulting in intervention due to the inability to programme an adequate safety margin for capture." A high threshold was observed in a further 12 of the 180 leads followed.

The occurrence of exit block or a high threshold with SE and NSE leads is summarised in **Table 36**.

Table 36 Prevalence of exit block and high thresholds with steroid-eluting and non-steroid eluting epicardial leads

	Exit block	**High threshold**	**Total**
	n	**n**	**n (%)**
All leads followed (n =180)	12	12	24 (13%)
Steroid-eluting leads (n = 150)	4	3	7 (5%)
Non steroid-eluting leads (n = 30)	8	9	17 (57%)

Lead models developing EB or HT were 4951 (n = 10), 4965* (n = 6), 033-571 (n = 2), 030-171 (n = 2), 5815 (n = 2), 637-702 (n = 1) and 4968* (n = 1) *SE leads.

4.6.2.1 Risk factors for EB or HT

Multivariate analysis revealed that NSE leads were more likely to develop EB or HT (**Table 37**). There was a trend to suggest ventricular leads, and male patients were also at a higher risk (see **Appendix 5d** and **5e**).

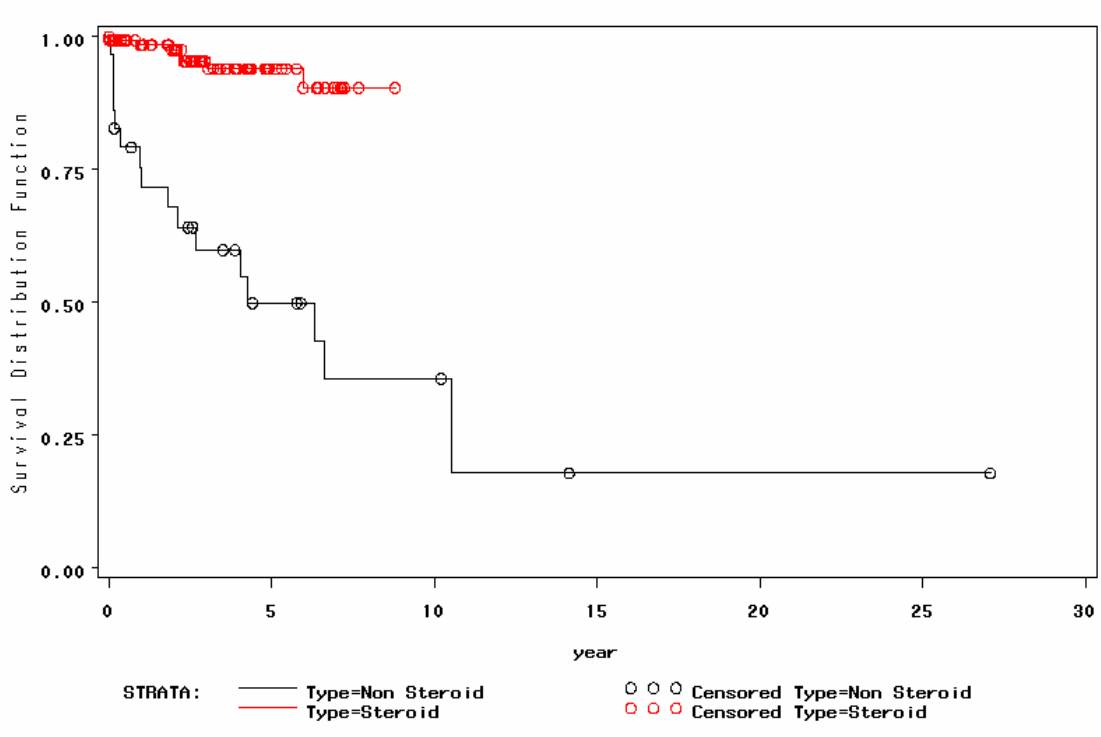
Table 37 Results of multivariate analysis of risk factors for exit block or high threshold

Variable	P value*	Hazard ratio
Steroid-eluting or non steroid-eluting lead	0.0001	0.161
Atrial or ventricular lead	0.1062	5.584
Gender	0.1527	0.523

* Cox hazard regression

As seen in (**Figure 35**) the freedom from EB or HT for NSE leads at 2, 5 and 10 years is 68% (9%), 50% (10%) and 36% (11%). Freedom from EB or HT for SE leads at 2 and 5 years is 98% (1%) and 94% (2%).

Figure 35 Kaplan Meier survival from exit block or high threshold for steroid-eluting and non steroid-eluting epicardial leads



A greater number of ventricular SE leads developed EB or HT compared to atrial SE leads (**Table 38**).

Table 38 Prevalence of exit block or high threshold with lead type and lead location

	Steroid-eluting leads **n / n (%)**	**Non steroid-eluting leads** **n / n (%)**
Atrial	0 / 71 (0%)	1/1 (100%)
Ventricular	7 / 79 (9%)	16 / 29 (55%)

4.6.2.2 Sudden or gradual EB or HT

Exit block and high thresholds were classified as "sudden" when the follow-up check preceding the complication showed a stable and low threshold.

Two SE leads developed sudden EB or HT at 1.9 and 2 years post implant. In one case the patient presented with syncope and the other case presentation was with reduced exercise tolerance. Three SE leads showed gradual threshold rises and in a further 2 cases the time course was unknown because previous follow-up checks had not been performed. One of the SE leads which gradually developed a high threshold at 7 months post implant was found to have an infection at the lead tip when it was removed.

Four NSE leads developed sudden EB or HT at 5 weeks to 6.5 years post implant. One of these patients presented with syncope. Six NSE leads showed gradual threshold changes and 7 were unknown because previous follow-up checks had not been performed.

4.6.2.3 Other lead measurement changes

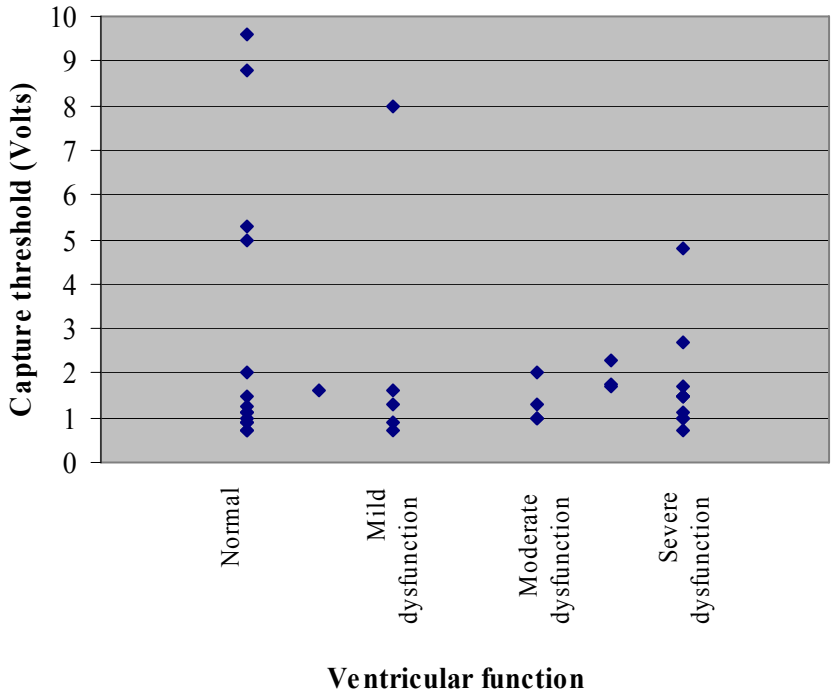
Three ventricular leads (1 SE lead and 2 NSE) which developed exit block also had oversensing (n = 1) or loss of sensing (n = 2) at the time exit block occurred.

4.6.2.4 Pacing threshold in relation to ventricular function

Where available the echocardiography (echo) reports were reviewed for patients who developed exit block or a high threshold during their follow-up. Echo reports at or close to the time of EB or HT were not available for 67% of cases and therefore the findings are inconclusive. Of the 7 cases where echo's were done at or close to EB or HT, 4 had normal ventricular function, 2 had moderate ventricular dysfunction and 1 had severe ventricular dysfunction.

All of the patients followed were then reviewed and where echo's were performed at the same time as pacemaker follow-up, these findings were then considered to see if there was a relationship between ventricular function reported by echo and the ventricular pacing threshold. Thirty seven echo results from 28 patients were reviewed and as seen in **Figure 36** there is no apparent relationship between ventricular function and pacing threshold. Low thresholds (less than 1.5 volts) were seen with normal ventricular function through to severe dysfunction.

Figure 36 Relationship between pacing capture threshold and ventricular function reported by echocardiography



4.6.2.5 Outcome of patients with EB or HT

Twenty one patients had leads implanted which developed EB or HT. The outcome of the 6 patients with SE leads that developed EB or HT was as follows: 4 patients who had underlying complete heart block had the leads replaced. In one of these patients a backup lead had been implanted due to the patient having a history of developing exit block and high thresholds. This back-up SE lead had acceptable measurements on testing and was therefore used. Two patients had underlying sinus rhythm and following Holter monitoring or electrophysiological testing were determined to no longer require pacing so these leads were not replaced.

The outcome of the 15 patients with NSE leads that developed EB or HT was: 7 patients had 8 lead replacements; two of these patients were initially given oral or an intra-venous infusion of steroids to try to reduce the pacing threshold, which was unsuccessful. Two patients had the pacemaker generator replaced with a higher output unit (this occurred in 1980 and 1983). Three patients had the pacing mode changed, resulting in single chamber pacing, 2 patients no longer required pacing and in 1 patient a back up lead was used.

4.6.3 Sensing problems

This section reports sensing problems which did not occur at the same time as complications such as exit block or lead fracture. A variety of sensing problems occurred throughout the study period as shown in **Table 40**.

Table 39 Prevalence of sensing problems in epicardial leads in relation to lead location and lead type

	Total number of leads **n**	**Atrial / Ventricular** **n / n**	**Steroid-eluting / Non Steroid-eluting** **n / n**
Loss of sensing	6	2 / 4	5 / 1
Oversensing	8	6 / 2	7 / 1
Late sensing	3	1 / 2	3 / 0

4.6.3.1 Loss of sensing

Loss of sensing (sensing threshold less than 1 mV) occurred in 3% of all leads including 3% of atrial leads and 4% of ventricular leads. The average time from implant to loss of sensing was 3.1 years, ranging from 11 days to 10.5 years. In 4 cases there were difficulties finding good electrode positions at implant although acceptable sensing measurements were eventually obtained in all but one case.

Outcomes included 1 lead replacement and in 5 cases no action was taken for the following reasons: the patient had a slow underlying rate, patient deceased (unrelated to the complication) or the patient was asymptomatic and therefore loss of sensing did not justify further surgery.

4.6.3.2 Oversensing

Oversensing, discovered on Holter monitor recordings or by muscle inhibition testing at routine pacemaker clinic checks, occurred in 4% of all leads followed including 8% of atrial leads and 2% of ventricular leads. In all cases of oversensing the leads were unipolar. The average time from implant to oversensing was 5 years, ranging from 1 month to 7.1 years.

The one NSE lead which had oversensing also had a low sensing threshold (0.6mV on an atrial lead) which prevented reprogramming to resolve the oversensing. This patient was asymptomatic so the inability to programme around the complication was not an issue. In one patient there was noise on the lead at implant and the lead was replaced 1 month later due to oversensing noise. The outcome of the other leads with oversensing was; in 2 cases no action was required due to underlying sinus rhythm with an adequate ventricular rate and in 5 cases the sensitivity was reduced which resolved the oversensing.

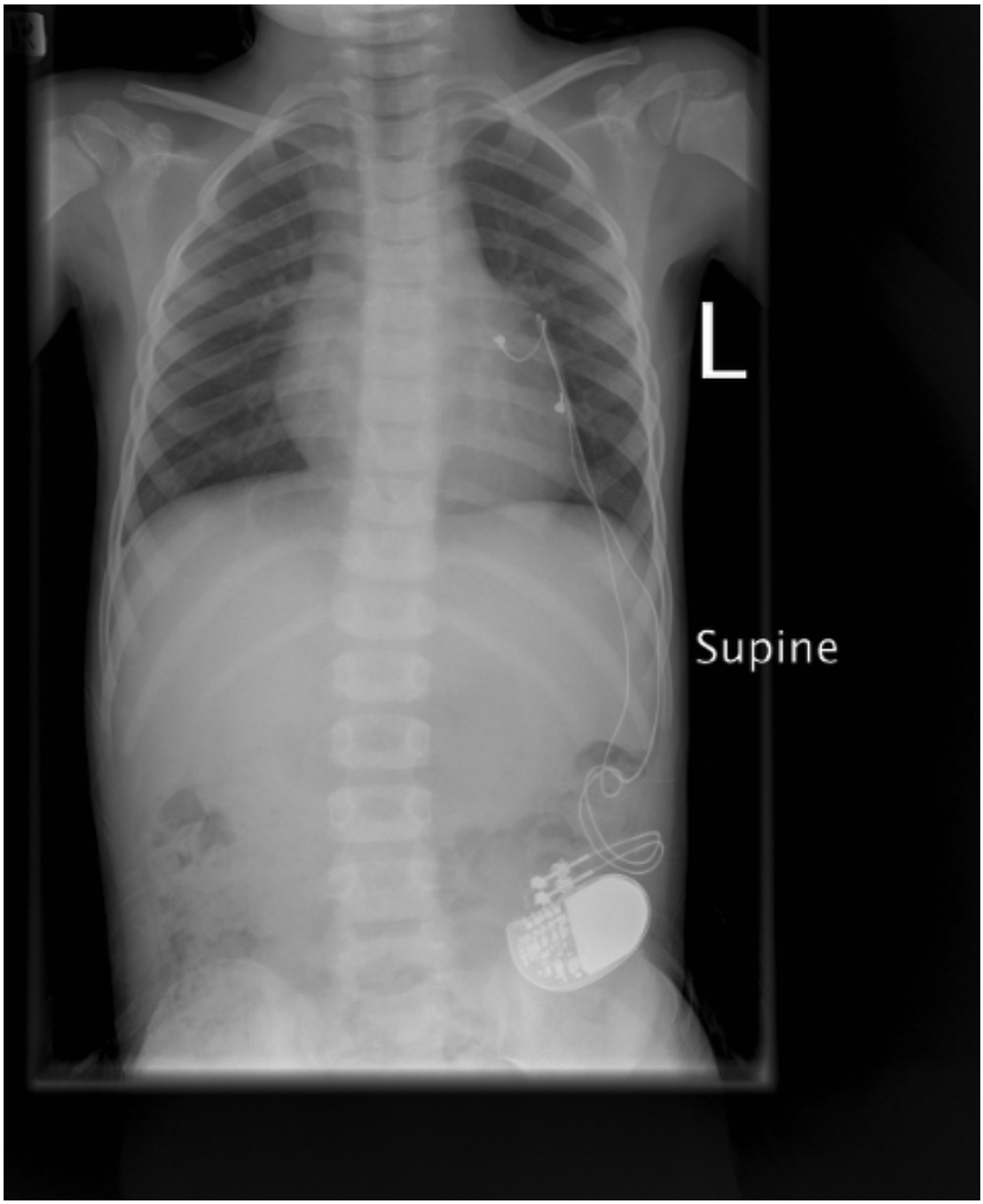
4.6.3.3 Late sensing

Late sensing was identified during routine pacemaker clinic checks and occurred in 3 (1.6%) of the leads followed. The effect of the late sensing was an abnormally long PV interval in 2 patients and inappropriate ventricular pacing in one patient. Pacemaker reprogramming of the AV delay parameters to extremely short or long values was performed in all cases. This minimized but did not fully resolve the effect of the late sensing. None of the patients with late sensing were symptomatic. Two of the cases with late sensing are described:

Case 1

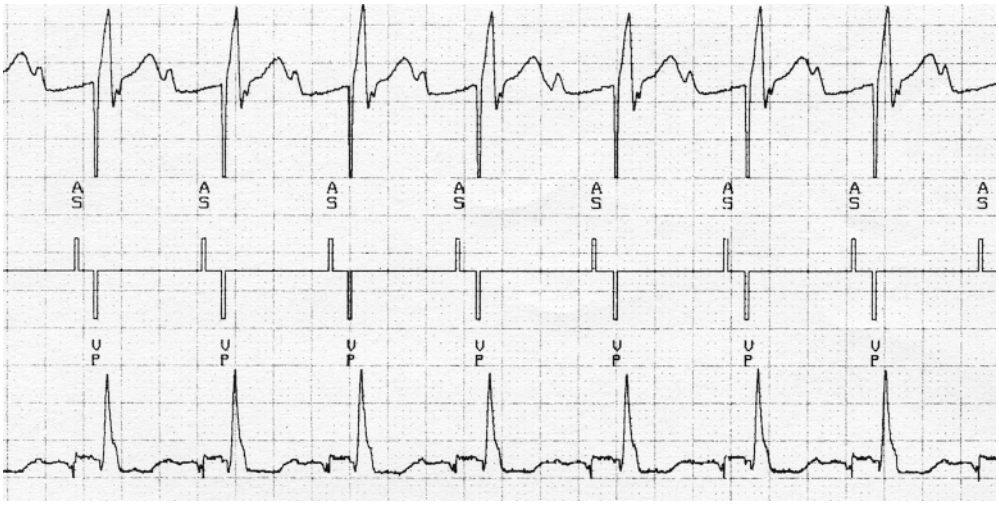
A patient with late atrial sensing had a chest x ray performed (**Figure 37**) which showed that the atrial lead was positioned very laterally on the left atrium. In this case the atrial sensitivity was programmed to 0.5 mVolts.

Figure 37 Chest X-ray of a patient with late atrial sensing showing epicardial lead locations on the heart



In **Figure 38** the sensed atrio-ventricular delay (SAVD) is programmed to 120msecs, but atrial sensing as seen by the position of the atrial sense marker (AS) approximately 200msecs after the peak of the P wave, has resulted in first degree AV block with an effective P wave to ventricular pace (PV) interval of 300msecs. This is because the timing of the ventricular pacing output is dependant on the previous atrial event.

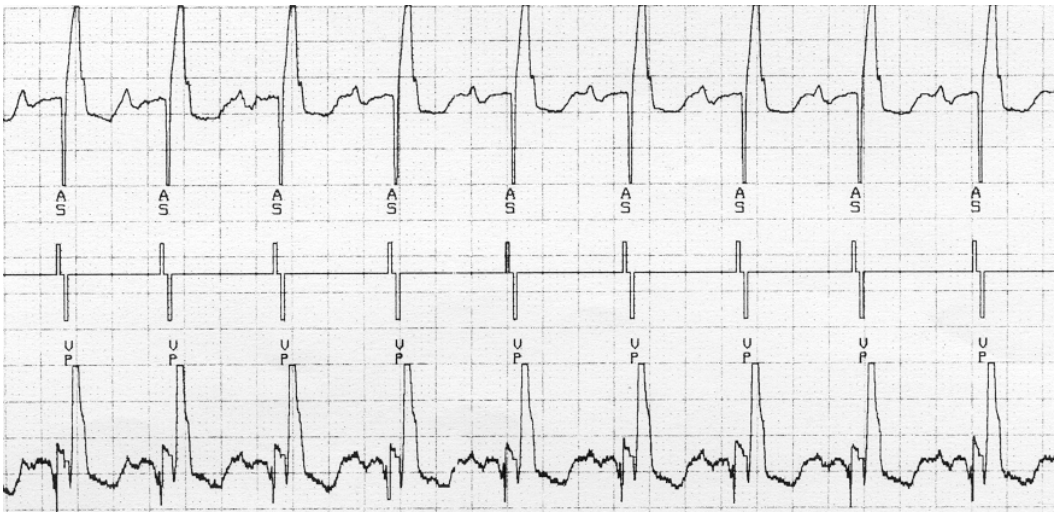
Figure 38 ECG, programmer marker channel and intra-cardiac ECG recording showing late atrial sensing with a SAVD of 120 msecs



ECG: electrocardiograph, SAVD: sensed atrio-ventricular delay

In **Figure 39** the SAVD is programmed to the minimum value of 30 msecs, which results in a PV interval of 200 msecs, which is close to a normal value.

Figure 39 ECG, programmer marker channel and intra-cardiac ECG recording showing late atrial sensing with a SAVD of 30 msecs



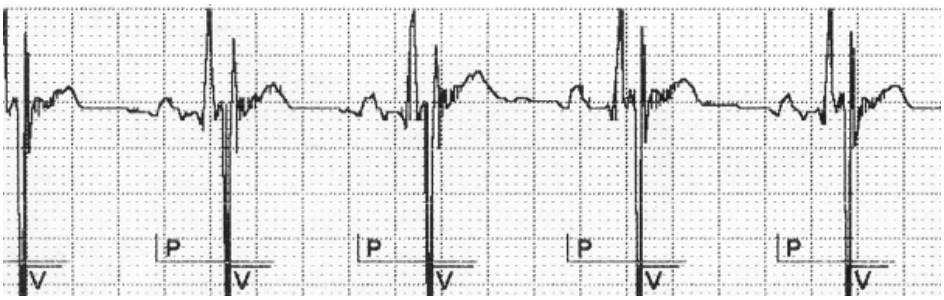
ECG: electrocardiograph, SAVD: sensed atrio-ventricular delay

Case 2

Late ventricular sensing was seen in a patient with Ebsteins anomaly who was aged 11.4 years at the time the lead was implanted on the right ventricle. The patient was paced because of intermittent complete AV block but was in normal sinus rhythm the majority of the time. They also had a known history of atrial flutter for which antiarrhythmic medication was prescribed.

Because of the late V sensing, the AV delay timed out and the ventricular pacing output was delivered before the intrinsic R wave was sensed, resulting in a ventricular pacing output occurring after the intrinsic QRS (**Figure 40**). The consequences of the late V sensing were, far field R wave sensing resulting in inappropriate mode switching, false over detection of atrial arrhythmias reported in the diagnostic counters and unnecessary ventricular pacing resulting in premature battery depletion.

Figure 40 Electrocardiograph and pacemaker programmer marker channel recordings showing late ventricular sensing



The AV delay was programmed to the maximum value of 300 msecs, but this did not resolve the late sensing. At the time of unit replacement this patient received a Medtronic Enpulse pacemaker which has the capacity to programme the AV delay to 350msecs. At this interval ventricular sensing was intermittently achieved. Ideally the patient would receive a mode conversion device in the future although these were not approved for clinical use in NZ at the time the pacemaker was replaced.

4.6.4 Twitch

Abdominal muscle stimulation (AMS) or diaphragmatic stimulation (DS) occurred in 13 of the 180 leads followed. AMS occurred in 7 leads and DS in 6 leads with both AMS and DS occurring equally regardless of implant route and lead location and therefore these are collectively referred to as twitching.

Twitching was observed more often in NSE than SE leads and equally in atrial and ventricular leads (**Table 39**). All twitching occurred in unipolar leads although due to the low number of bipolar leads (n = 4) in the study a comparison between the incidence of twitching and lead polarity could not be made.

Table 40 Prevalence of twitching in epicardial leads in relation to lead location and lead type

	Twitching n (%)
All leads (n = 180)	13 (7%)
Steroid-eluting leads (n = 150)	9 (6%)
Non steroid-eluting leads (n = 30)	4 (13%)
Ventricular leads (n = 108)	7 (6%)
Atrial leads (n = 72)	6 (8%)

4.6.4.1 Presentation of twitching

The majority of twitching (n = 11) occurred within one year of lead implantation, with one lead developing a twitch at 5.3 years post implant. The average time from implant to presentation of the twitch was 0.8 years. The average voltage where twitching occurred was 4.5 volts, ranging from 1.5 to 8 volts.

4.6.4.2 Outcome of patients and leads with twitching

For 89% of the SE leads that developed a twitch the output was able to be reduced to resolve the problem. In one case the lead was later replaced because of an inability to program an adequate safety margin for capture (pacing threshold of 2.3 volts and twitching occurred at 2.4 volts). In one patient the twitch resolved spontaneously.

Of the 4 NSE leads: 2 leads were replaced, 1 had the output initially reduced then the mode was changed and 1 had the pacing rate reduced then later was found to no longer require pacing. In the majority of cases a high threshold prevented the output being reduced therefore resulting in lead replacement or a mode change. In one patient the twitch only occurred because the output was programmed to 8V due to a high threshold.

4.6.5 Other complications

Other pacing related complications observed during this study were insulation faults, lead dislodgement and infection. These complications are described in turn.

4.6.5.1 Insulation problems

A fault in the lead insulation occurred in 4 of the Medtronic 4965 leads (2%). In one case opacity was seen in the insulation but a change in the lead function had not occurred. One patient had an abnormal atrial lead impedance of less than 80 Ω at 1 day post implant, possibly due to the lead being inadvertently cut at the time of implantation.

The leads which developed an insulation fault had impedance measurements of between 80 – 223 ohms (average 174 ohms) at the time the fault was discovered. The impedance had reduced from a previously stable value by 159 ohms on average, ranging from 106 to 201 ohms. Lead function changes at the time included: decreased sensing, loss of sensing, over sensing and a rise in the pacing threshold. In two cases decreased and over sensing occurred at the same time. No prior warning was seen with any of the leads that developed an insulation fault. The time from implant to insulation fault ranged from 1

day to 4.4 years, with an average of 2.5 years. The outcome in all 4 cases was lead replacement.

4.6.5.2 Lead dislodgement

Of 180 leads followed over a period of up to 27 years, lead dislodgement occurred in one patient. Lead dislodgement occurred at 3 days post lead implant and coincided with removal of temporary pacing wires which had been placed during recent cardiac surgery. At the time of surgery to reattach the permanent epicardial lead, the electrode was seen to be partially torn out off the epicardium. Lead measurement changes observed with the dislodgement were a threshold rise and reduced sensing.

4.6.5.3 Infection

Pacing system infection occurred in 5 of the 96 patients (5%). Infections presented between 2 and 11.5 months post implant or pacemaker generator change (average 5.7 months post operation).

In four cases the entire pacing system was explanted, antibiotics were started and a period of no pacing transpired, which lasted between 4 days and 1.5 years before a new pacing system was implanted. The duration of no pacing was dependant on the ventricular rate of the underlying rhythm. In all four cases there was no further infection once the new system was implanted.

One patient with underlying congenital complete heart block at 35 bpm developed an infection 3 months post unit change. This was initially treated with antibiotics, which was unsuccessful leading to pacemaker erosion. The pacemaker generator was explanted and a new system implanted in a different site with existing leads. One month later the infection remained so the pacemaker and leads were explanted and the patient was paced through a temporary pacing wire for 15 days. A new pacemaker and endocardial lead were then implanted and 43 days later further infection was seen. The whole system was then explanted with a period of no pacing for 12 days after which time new epicardial leads and a dual chamber pacemaker were implanted. The patient has now remained infection free for greater than 1 year.

4.7 Lead only implants

Twenty nine leads implanted in 24 patients, were capped at the time of implant in case they would be required in the future. The main reasons for lead only implants were:

1. Back-up NSE leads (n = 10). Due to the previous high failure rate of these leads a second NSE lead was also attached in case the first lead failed. These implants all occurred prior to 1993 so SE leads were not being used. Four of the 10 leads were successfully used when the first lead failed (**Table 41**).

2. Patient size (n = 3). Three patients were too small for a dual chamber pacemaker at the initial implant. An atrial lead was implanted so that when the patient had reached an adequate size, upgrading to DDD pacing would be minimally invasive. As shown in **Table 41**, two of the 3 leads were used as intended and the third lead had fractured prior to the upgrade being performed. Although all three atrial leads caused ventricular pacing, at higher outputs, at the time of implant testing (due to the close proximity to the AV groove), this did not occur at the time of upgrade.

3. Implantation of leads during cardiac surgery (n = 11). Pacing leads were attached at the time of cardiac surgery in case the patient required pacing in the future. Seven of the 11 leads were later used.

4. Other reasons for lead only implants included one patient with a history of lead related complications and two patients where there was considered to be a risk of AV block developing. When SE leads were first used their performance was unknown and therefore in two cases backup SE leads were placed in case the first lead failed. The outcome of these leads is described in **Table 41**.

Table 41 Pacing indications and outcomes of epicardial lead only implants

Lead type	Lead location	Year of implant	Adult or paediatric	Indication for pacing	Reason for lead only implant	Lead used	Time from implant to lead used	Why lead was used or not used	Lead tested post implant?
NSE	V	1978	Paediatric	CCAVB	Back up NSE lead	Yes	6 weeks	EB on 1st lead	Yes
NSE	V	1990	Paediatric	Surgical AVB	Back up NSE lead	Yes	10.5 months	EB on 1st lead	Yes
NSE	V	1981	Adult	Surgical AVB	Back up NSE lead	No		EB on both leads	Yes
NSE	V	1984	Paediatric	Surgical AVB	Back up NSE lead	Yes	10.5 months	HT on 1st lead	Yes
NSE	A	1991	Paediatric	Surgical SSS	Back up NSE lead	No		EB on 1st lead. Both leads replaced with a SE lead	No
NSE	V	1990	Adult	Surgical AVB	Back up NSE lead	Yes	2.5 years	1st lead fractured	Yes
NSE	V	1988	Paediatric	Surgical AVB	Back up NSE lead	No		1st lead never failed in 14yrs follow-up	No
NSE	V	1992	Adult	AVN disease	Back up NSE lead	No		Deceased 9 months post implant	No
NSE	V & V	1991	Paediatric	Surgical AVB	Back up NSE lead	No x 2		Deceased 1 week post implant	No
NSE	V	1991	Paediatric	AVN disease	Temporary AVB post cardiac catheterisation	No		Pacing not required	No
NSE	V	1997	Paediatric	SSS	AAIR paced, backup V lead in case AV conduction deteriorated	No		Lead replaced with SE lead (2002) when V pacing was required	No
SE	A	2000	Paediatric	Surgical AVB	Patient size: 4kg. Lead V pacing at 5V	Yes	1.5 years	Upgraded to DDD	Yes

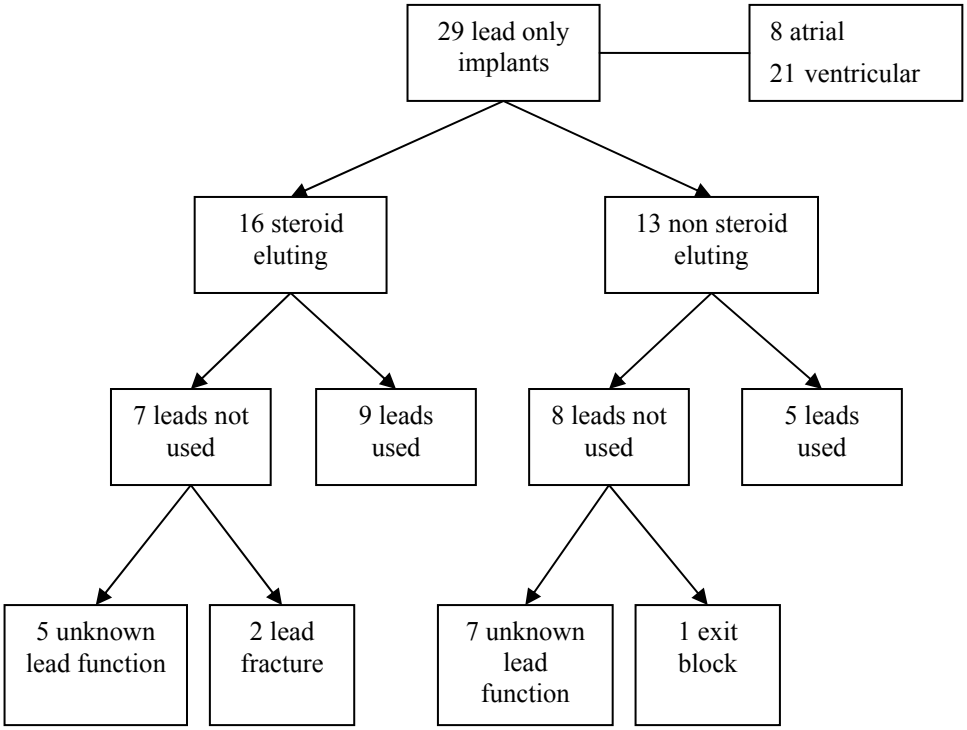
Lead type	Lead location	Year of implant	Adult or paediatric	Indication for pacing	Reason for lead only implant	Lead used	Time from implant to lead used	Why lead was used or not used	Lead tested post implant?
SE	A	2000	Paediatric	CCAVB	Patient size: 3.4kg. Lead V pacing at 3V	No		Lead fractured	Yes (Xray)
SE	A	2000	Paediatric	CCAVB	Patient size: 4kg. Lead V pacing at 5V	Yes	10.5 months	Upgraded to DDD	Yes
SE	A & V	1998	Paediatric	Surgical SSS	Implant at Fontan repair	Yes x 2	4 years	Holter showed 5.5 sec pauses	Yes
SE	A & V	1999	Paediatric	Surgical AVB	Implant at ToF repair	Yes x 2	4.5 months	AVB remained	Yes
SE	A & V	1999	Paediatric	CCAVB	Implant at PDA closure	Yes x 2	4.5 months	Heart failure and rates to 50bpm on Holter	Yes
SE	V	1999	Adult	Surgical AVB	Implant at TVR	No		Pacing not required	No
NSE	V	1977	Paediatric	Surgical AVB	Implant at MVR	Yes	8 days	AVB remained	Yes
SE	V	2002	Adult	Prevention of AA	Implant at MVR + cryoablation	No		Pacing not required	No
SE	A & V	1999	Paediatric	Surgical AVB	Implant 3 days post MVR	No		Patient deceased 21 days after implant	No
SE	V	1999	Adult	AVB	History of high thresholds -> multiple interventions back up SE lead	Yes	4.5 years	Possible insulation failure seen on 1st lead at unit change	Yes
SE	V	2001	Paediatric	CCAVB	Backup SE lead	No		1st lead never failed	No
SE	V	1994	Adult	SSS	Backup SE lead	No		Both leads fractured	Yes

Key: A: atrial, AA: atrial arrhythmias, AAIR: atrial rate responsive pacing, AVB: atrio-ventricular block, AVN: atrio-ventricular node, CCAVB: congenital complete atrio-ventricular block, DDD: dual paced, EB: exit block, GLH: Green Lane Hospital, HT: high threshold, MVR: mitral valve replacement, NSE: non steroid-eluting, PDA: patent ductus arteriosus, SE: steroid-eluting, SSS: sick sinus syndrome, ToF: Tetralogy of Fallot, TVR: tricuspid valve replacement, V: ventricular.

4.7.1 Summary of lead only implant outcomes

SE leads, implanted in case they would be required in the future, went on to be used in 56% of cases (**Figure 41**). NSE leads were implanted predominantly in case the first NSE lead failed and these went on to be used in 38% of cases. Of the 15 leads that were never used, 3 leads had a known lead failure. Twelve of the leads were never tested so it is unknown whether these leads had failed.

Figure 41 Summary of the outcomes of the lead only implants



5 Discussion and Conclusions

5.1 Discussion

This retrospective audit was performed because a high pacemaker lead failure rate was suspected in the group of patients who had epicardial leads implanted at Green Lane Hospital.

The specific aims of this study were to:

- Assess pacemaker lead performance over time in relation to the type of epicardial lead implanted.
- Determine the survival rate of epicardial leads.
- Identify factors predicting or associated with lead failure.

The results of this audit have clearly shown that:

- Steroid-eluting (SE) leads are superior to non steroid-eluting (NSE) leads with regard to pacing thresholds and incidence of lead failure. Average pacing threshold of all NSE leads over 6 years was 2.7 volts and for all SE leads was 1.3 volts (p value 0.001). Survival of SE leads at 5 years was 66% where as survival of NSE leads in the same time period was 41%.
- Five percent of the SE leads followed developed gradual or sudden exit block (EB) or high thresholds (HT) requiring intervention at greater than 6 months post implant.
- Fifteen percent of epicardial leads developed lead fracture.
- The freedom from lead failure for all epicardial leads was 61% at 5 years
- The risk of lead failure due to exit block is 6 times higher in NSE leads compared to SE leads. Other factors were not found to predict an increased rate of lead failure.

5.1.1 Epicardial lead performance overview

The poor performance of NSE leads found in this study is not unexpected and the suspected high rate of lead failure due to EB or HT has resulted in these leads not being implanted since early 1999. The findings of this study confirm these suspicions with 41% of NSE leads surviving at 5 years and 29% surviving at 10 years. The use of NSE leads is therefore not recommended and in situations where passive fixation SE leads are contraindicated due to a poor epicardial surface, alternative techniques such as burying the lead in the myocardium should be attempted as an initial option to achieve pacing. There remains a need for development of SE active fixation leads for situations where SE passive fixation leads are contraindicated.

The overall performance of the currently used SE leads was found to be good in relation to pacing and sensing thresholds and lead impedance measurements but relatively poor in relation to lead failure rate which was found to be 66% at 5 years and 51% at 7 years. When compared to other literature the failure rate observed in this study is much higher. Thomson, *et al*. (2004) found a 75% survival of SE epicardial leads at 5 years and Cohen *et al*. 2001 reported 83% lead survival at 5 years. In comparison to this study, Cohen had older patients (median 4.1 yrs at implant) with a greater average implant weight (17 kg) and twice the number of subxiphoid lead implants, with no failures in this group of leads. A smaller number of SE leads were studied (82 versus 150 in this study) with only half the mean follow-up duration. Thompson followed a smaller number of patients and leads with a much lower number of patients having structural heart disease (44% compared to 82% in this study). A greater number of 4968 leads were used and none of these leads failed. This comparison of studies suggests that placement of bipolar (4968) leads via the subxiphoid route will improve the SE epicardial lead failure rate. Patient characteristics, including younger age, smaller weight at implant and the presence of complex structural heart disease may play a significant part in reducing epicardial lead survival. The GLH experience, which is a relatively large and long study, may provide a more accurate indication of the survival of SE epicardial leads.

This high failure rate raises the possibility of whether implanting transvenous leads in this population would have an improved outcome. A study has not been performed to look at the lead performance and failure rate of transvenous leads in patients implanted at GLH and therefore a comparison cannot be made.

There have been no large studies comparing epicardial and transvenous pacing in the paediatric population. Lau, *et al.* (1992) found a 5 year survival of 76% for transvenous leads implanted in paediatric patients which is comparable to the survival rate of epicardial leads reported by Thomson, *et al*. (2004). This suggests that implantation of transvenous leads would have a similar outcome. When Lau's findings (Lau, *et al.* 1992) are compared with reports of transvenous leads implanted in the adult population a striking difference is seen. Several large studies of transvenous pacing in adults have reported a 98.7% survival at 5 years and 97% survival at 10 years (Helguera, *et al*. 1994; Arnsbo and Moller, 2000). The discrepancy in lead survival between adult and paediatric studies highlights the fact that the cardiac pacing in paediatric patients is complex. The performance of epicardial leads is not the sole reason for the high failure rate and multiple factors such as patient growth, activity level and implantation of leads post bypass surgery onto a myocardium with scar tissue, adhesions, fat or fibrosis are all factors which increase the risk of lead failure.

Transvenous lead placement in children weighing less than 10 kg has been found to be feasible and effective although not without complications (Kammeraad, *et al*. 2004). Patients with inaccessible cardiac chambers have also been successfully paced transvenously using innovative approaches (Karpawich, *et al*. 1998). The reasons for using the transvenous approach over epicardial are driven by the perception that transvenous pacing is superior due to lower pacing thresholds and a reduced complication rate although no large studies comparing these methods have been performed. One significant factor to be considered with the use of transvenous leads is the likelihood of patients having to undergo lead extraction if a lead fails or if venous occlusion occurs. In Kammeraad's study of 39 patients weighing less than 10 kg who were transvenously paced, 23% underwent lead extraction (which is explained in section 1.7.1.1) during the study period (Kammeraad, *et al*. 2004). In this institution (GLH) the experience in lead extraction is relatively limited resulting in an increased risk of major complications occurring during this procedure, therefore discouraging the use of endocardial leads in very small patients.

The high lead failure rate seen in this study is primarily due to the high rate of lead fracture as failure due to other causes was low. In an attempt to reduce the occurrence of lead fractures, the practice has changed to implantation of more robust bipolar leads via a subxiphoid rather than throracotomy approach.

5.1.2 Patient characteristics

The majority of epicardial leads were implanted in paediatric patients who have complex congenital heart disease and have had cardiac surgery. Because of this, suboptimal lead positions may need to be accepted at implant due to difficulties finding viable myocardium when leads are placed post cardiac surgery. Another complicating factor for some patients is their small size which makes access to the heart difficult and limits the selection of hardware. These factors add a significant degree of complexity to this patient group.

5.1.2.1 Weight

The group of patients weighing less than 10 kg had a similar rate of lead failure (31%) compared to the paediatric patients weighing greater than 10 kg at implant (34%). This indicates that smaller patients are not at an increased risk of lead failure.

5.1.2.2 Ethnicity

The majority of patients were European although Maori and Maori/European children represented 16% of all paediatric implants. Census data from 2001 indicates that Maori children made up 25% of the under 15 year old New Zealand (NZ) population (Statistics NZ, 2001). This data shows that the patient group is broadly representative of the NZ population and Maori are not at an increased risk of requiring epicardial pacing.

5.1.2.3 Mortality

The 25% mortality rate of all patients observed in this study is markedly higher than that reported in other studies of paced paediatric patients which range from 1.4% to 14% (Cohen, *et al*. 2001; Sachweh, *et al*. 1999; Rao, *et al*. 1995). The paediatric patients had a mortality of 22% and therefore this high mortality rate is not attributed to

the older patients that are included in the study. This high mortality rate is partially a reflection of the long time period (28 years) which the study covered and the complexity of the patients who received epicardial pacing. This is seen in the wide range of cardiac diagnoses and that 88% of paediatric patients had congenital heart disease and 84% of these patients had corrective or complex palliative surgery performed. The majority of the patients with congenital heart disease had complex single ventricle anatomy with LTGA or DTGA and had received multiple cardiac surgical procedures. There did not appear to be any deaths attributable to pacemaker or lead failure and therefore the high rate of complications found in this study was not linked to the high mortality rate.

5.1.2.4 Indications for implant

The decrease in surgical AVB as an indication for pacemaker implantation in paediatric patients that was seen in this study is similar to that reported by the Mid West pediatric pacemaker registry (MWPR) (Mid West pediatric pacemaker registry, 2002). The improvement in surgical techniques resulting in an improved post surgical patient outcome is the likely cause of this trend. This study reported that 26% of implants were due to congenital AVB which is comparable to the MWPR which reported 22% over the same 7 year period. The main difference between this study and the MWPR was their increase in implantation rate of pacemakers for surgical SSS. By 2002 this was their main indication for pacing whereas this study had very low numbers in this indication group. This discrepancy is likely to be due to one large centre, reporting to the MWPR, which receives referrals for Fontan upgrades from all over the US (Mavroudis, *et al*. 2001). In this centre the Fontan upgrade involves removal of the sinus node when the classical Fontan is changed to a lateral channel Fontan. At GLH the approach is more conservative with fewer such operations.

5.1.3 Lead characteristics

5.1.3.1 Lead models

The range of lead models implanted is a reflection of the lead development that occurred during the 26 implant years that the study was carried out over. The

availability and positive performance reports for the SE epicardial leads (Johns, et al. 1992; Karpawich, *et al*. 1992) resulted in a change in practice from 1993 onwards with the SE leads becoming the predominant lead implanted at GLH. Active fixation NSE epicardial leads were still implanted where deeper myocardial penetration was required to overcome an epicardial surface layer of fat, fibrosis, scaring or adhesions. The use of passive fixation epicardial leads is contraindicated in these cases and therefore there are limited options for achieving pacing in these patients. In recent years reports have been published of alternative methods of overcoming these obstacles including endocardial lead placement by atriotomy and burying the epicardial lead into the myocardium (Hansky, *et al*. 2005; Karpawich, *et al*. 1998). This study found that these alternative techniques have been attempted in this institution (GLH) with increasing success over recent years.

5.1.3.2 Follow-up duration

Although the longest follow-up in one lead was 27 years the median follow-up duration of all leads was only 2.8 years. Although relatively short this is greater than that of Cohen's study which had an average follow-up of 2.4 years (Cohen, *et al.* 2001). The reasons for the short median follow-up duration in this study are outlined in section 4.2.7 and were predominantly unavoidable.

5.1.3.3 Implant techniques

The majority of leads were implanted using the sternotomy route which is a reflection of the fact that approximately one third of the patients had lead implants at or close to the time of cardiac surgery. Early implants were more frequently performed by the thoracotomy route as this was standard practice in the early years of epicardial pacing. The bipolar epicardial lead technical manual suggests that the subxiphoid and sternotomy route have a lower incidence of lead fracture compared to the thoracotomy route (Medtronic 4968 technical manual, 2003). Only 7% of the leads were implanted by the subxiphoid route although in recent years the use of this method has increased and the use of the thoracotomy route has decreased. This will be discussed further under the discussion of lead fracture (section 5.7.1).

5.1.3.4 Lead survival

Lead survival for all leads is relatively low with only 61% of epicardial leads surviving at 5 years. Previous studies which include a similar lead population have reported 74 to 76% survival at 5 years (Cohen, *et al*. 2001: Thomson, *et al*. 2004). The only factor found to increase the risk of lead failure was NSE over SE lead type which is not unexpected. The high rate of lead failure at this institution (GLH) is of concern and is likely to be linked to the high fracture rate (15%) compared to other studies (5 to 8%) (Cohen, *et al*. 2001; Horenstein, *et al*. 2003).

5.1.4 Pacemaker models

Over the 28 year study period there was a growing trend to implant dual chamber pacing systems whereas the number of single chamber systems remained relatively consistent. This is a reflection of the improvements in technology occurring over the study period. Achievement of atrio-ventricular synchrony by dual pacing is significantly advantageous for this group of patients who may have compromised haemodynamic status due to their cardiac anatomy or post operative cardiac function.

5.1.5 Lead follow-up

5.1.5.1 Pacing thresholds SE versus NSE

The majority of pacing thresholds measured from SE leads were low (less than 1.5 volts) and stable with an average threshold value of 1.3 volts (SD = 0.9) over 9 years. Therefore in the majority of patients the pacemaker output can be safely programmed to 2.6 volts at 0.5 msec which allows the standard two times safety margin for capture. SE leads did not show the acute threshold rises seen in NSE leads at 6 weeks post implant and therefore high output programming post implant is not required.

NSE leads had greater average thresholds (2.7 volts) requiring higher output programming (greater than 5 volts) leading to a greater pacemaker battery drain. NSE pacing thresholds were significantly higher than those for SE leads at 6 weeks, 10.5 months, 3 and 5 years and remained consistently higher over 6 years of follow-up. These findings are similar to those reported by Cohen, *et al*. (2001) who found NSE

pacing thresholds to be significantly higher than SE leads at 1 month and 2 years post implant.

Based on data supplied from Guidant NZ, Medtronic Inc. and St Jude Medical, pacemaker longevity* would increase by 50-60% (which translates to an increase of between 3 to 5 years of battery life) if a pacemaker output was programmed from 5 volts to 2.6 volts. If this data is applied to a hypothetical patient who received their first pacemaker at 6 months of age with a life expectancy of 70 years, **Table 42** indicates the approximate number of unit replacements that would be expected during their lifetime. Values provided are approximate and vary (between 9 and 17 replacements) depending on the manufacturer and battery capacity of the pacemaker.

Table 42 The estimated number of pacemaker replacements required over 69.5 years depending on the programmed pacemaker output

Total number of replacements in a patients lifetime	**5 volts (NSE lead)**	**2.6 volts (SE lead)**
Pacemaker manufacturer 1	17	8
Pacemaker manufacturer 2	17	10
Pacemaker manufacturer 3	9	5

*The longevity data is estimated based on a current single chamber pacemaker, programmed to 60 or 70 ppm, with a lead impedance of 500ohms, without rate response or automatic capture adjustment programmed on. This provides a best case scenario but in reality devices implanted are typically dual chamber, are pacing at much faster rates and will have lower lead impedances. These factors will result in shorter battery longevity and a greater number of pacemaker replacements.

This study has shown steroid-eluting epicardial leads to have low and stable thresholds, which allows low output programming and therefore patients will have a reduced number of pacemaker replacement operations throughout their lifetime. The few NSE leads that survived past 7 years had stable thresholds, with one NSE lead lasting up to 27 years. Regardless these leads may still fail in the later years as seen in one lead which developed EB at 11 years post implant.

5.1.5.2 Atrial versus ventricular pacing thresholds

Previous studies have had differing reports with regard to atrial versus ventricular pacing thresholds. Cutler, *et al*. (1997) reported significantly higher ventricular pacing thresholds compared to atrial thresholds over four years of SE epicardial lead follow-up. Cohen's relatively large study of 83 SE epicardial leads showed ventricular leads had an insignificantly higher pacing threshold compared to atrial leads (Cohen, *et al*. 2001).

In this study a comparison of atrial versus ventricular pacing thresholds for SE leads showed that ventricular leads had significantly higher average pacing thresholds (1.6 volts) compared to atrial leads (0.9 volts) over 7 years ($p < 0.0001$). This is likely to be a reflection of the state of the ventricular myocardium since a large number of the patients were paced post cardiac surgery. With the growing trend towards surgery involving the atria such as the Fontan procedure, a rise in atrial pacing thresholds may be seen in future studies.

For the 76% of patients in this study where AVB was the indication for pacing, maintaining an adequate ventricular safety margin for capture, is more essential than for the atrial lead. The pacing technologist should expect higher ventricular thresholds necessitating higher ventricular output programming compared to atrial outputs in the majority of cases.

5.1.5.3 Atrial sensing thresholds

Given that a high sensitivity value represents a low sensitivity (4 mV is less sensitive than 1mV) and permanent programming of the sensitivity typically requires a safety margin of twice the sensing threshold, a sensing threshold greater than 1 mV enables a pacemaker to be programmed to a sensitivity value of 0.5mV (which is the maximum sensitivity in some pacemakers). This study found an average atrial sensing threshold of 2.7 mV (SD = 1.5) which remained stable over an 8 year period. This is well above the 1mV sensitivity value required to program a maximum sensitivity. These results indicate SE lead performance with regard to the sensing function is good. Due to low numbers of atrial non steroid lead implanted and receiving follow-up measurements the sensing function of these leads could not be determined.

5.1.5.4 Ventricular sensing thresholds

The nominal programmed sensitivity value for a ventricular lead is 2.5 mV therefore a sensing threshold value of greater than 5 mV is ideally required in order to programme an adequate safety margin for sensing. With unipolar leads, when a high sensitivity (lower value) is programmed there is an increased possibility of myopotential inhibition (oversensing) resulting in no pacing output being delivered. This may result in patient symptoms of dizziness. To avoid or correct this problem the sensitivity would be programmed to a higher value, i.e. 3 mV or above, in the ventricle. If oversensing is present a higher sensing threshold (for example greater than 6mV) is more likely to enable programming of an adequate safety margin for sensing. This study has demonstrated that the average ventricular sensing threshold for SE leads was > 6mV throughout the 8 year follow-up period. These findings indicate that steroid-eluting leads achieve adequate sensing thresholds to enable optimal programming for avoiding oversensing while maintaining adequate safety margins for sensing.

Non steroid-eluting leads achieved an average sensing threshold of 7.1 mV. A greater variability was seen in the average sensing thresholds, with several measurements less than 6mV being measured throughout the 6 year follow-up period. In general NSE leads had a lower average sensing thresholds compared to SE leads and therefore the likelihood of not being able to programme around an oversensing complication was greater.

5.1.5.5 Lead impedance

The average impedance measurements for both steroid-eluting and non steroid-eluting epicardial leads were within the normal range of 300 – 1200 ohms. The average steroid-eluting lead impedance was 370 ohms over a 9 year follow-up period. Previous literature comparing epicardial and transvenous leads in children have had mixed reports on impedance although all previous studies have relatively small numbers. Dodge-Khatami, *et al*. (2000) found epicardial leads to have significantly lower impedances than transvenous leads where as Ten Cate, *et al*. (2002) found no difference. Generally previous studies shows that transvenous lead impedances are greater than 500 ohms whereas epicardial leads have impedances less than 500 ohms, which was also seen in this study.

Pacemaker battery drain is increased with lower lead impedance (see section 1.4.1) and therefore the low impedance of epicardial leads results in greater battery depletion and reduced longevity than if the pacemaker was connected to a transvenous lead. The long term effect of this is a greater number of pacemaker replacements in a patient's lifetime.

New transvenous lead technology has resulted in production of high impedance leads for the purpose of increasing battery longevity. This technology has not been applied to epicardial leads but would be beneficial.

This study showed that the majority of steroid-eluting leads had very stable impedances (SD = 73 ohms) at each follow-up check. Early stages of lead fracture may produce intermittently abnormal impedance measurements as seen in the daily measurements in **Appendix 4**. Therefore unexpected impedance changes should be investigated further by performing repeat impedance measurements with the patient in different positions to determine whether the impedance change is due to lead fracture.

5.1.6 Implant measurements and implant difficulties

There was no statistical difference between the implant measurements for SE and NSE leads and therefore the differences observed at follow-up can be attributed to lead performance and are not associated with implantation factors.

The recommended acceptable lead measurements at implant (Medtronic 4965 technical manual, 1992) are as follows:
Maximum atrial and ventricular pacing threshold: 1.5 volts (at 0.5 msecs)
Minimum atrial amplitude (sensing threshold): 2 mV
Minimum ventricular amplitude (sensing threshold): 4 mV

The average implant pacing threshold for both SE (1.7v) and NSE (1.9v) leads did not meet these recommendations. This is likely to be due to various difficulties encountered during implantation which are relatively common, occurring in 23% of all epicardial lead implants. The average atrial and ventricular sensing thresholds did meet these recommendations.

For the leads where acceptable implant measurements were obtained, the rate of pacing and sensing threshold related complications was 20% compared to 22% for those leads with sub optimal implant measurements. This indicates that poor lead measurements at implant are not a predictor of increased occurrence of complications and lead failure during follow-up.

Some of the implant difficulties encountered were due to the epicardial surface being covered in fat, vascular adhesions or being fibrosed and in these cases a lead that penetrated the myocardium was required. Attempts to use an active (NSE) lead, rather than passive (SE) lead, to overcome this problem provided a short term solution of adequate pacing threshold values at implant but ultimately resulted in lead failure due to EB or HT during follow-up. The technique of cutting down to expose the healthier muscle fibres and burying the lead tip in the myocardium, gave good results in two cases and therefore this technique is recommended for the future.

5.1.7 Complications

5.1.7.1 Lead fracture

Previous epicardial lead studies report a variable occurrence of lead fracture ranging from 5.3% of 207 leads reported by Cohen *et al*. (2001), 7.6% of 79 leads reported by Horenstein, *et al.* (2003) through to 16.7% of 96 leads reported by Thomson, *et al.* (2004). The 15% occurrence of fracture in the 180 leads followed in this study is relatively high although similar to Thomson's study, which had a similar follow-up duration. Thompson's study had a higher proportion of bipolar leads (17% compared with 2.3% in this study), none of which fractured. Cohen's study had a higher proportion of leads implanted via the subxiphoid route (14% compared with 7% in this study), none of which fractured, but also had a greater median patient age at implant. Comparison with these studies highlights the possible reasons for the relatively high fracture rate seen in this study, which includes the use of unipolar leads and the fact that a relatively large number of leads were implanted by the thoracotomy route in early years. Bipolar leads have a diameter of 2.7 mm from the junction to the connector compared to the unipolar lead diameter of 1.5 mm. The bipolar leads would potentially have a reduced risk of lead fracture due to their greater mechanical strength although there have been no studies to specifically look at this theory. In some very small

patients placement of the two electrodes on the heart with a bipolar lead and fitting the lead within the pericardial cavity may prevent the use of these leads.

Although in this study the implant route was not a statistically significant predictor for detecting an increased risk of fracture, the Medtronic 4968 technical manual (2003) reports a 5 times greater risk of fracture with the thoracotomy route compared to subxiphoid and sternotomy, although this data is unpublished. Due to the low number of leads implanted by the subxiphoid route, the incidence of lead fracture with this method cannot be determined although the follow-up data to date suggests a low risk of fracture. This is supported by Cohen's study which had no lead failures in 29 leads implanted by the subxiphoid approach although this was also over a relatively short follow-up duration. (Cohen, *et al*. 2001). The long term success of the subxiphoid route in reducing the occurrence of lead fracture is yet to be determined as longer follow-up is needed.

The highest rate of lead fracture occurred in the second and third year post implant which is likely to be due to the high growth rate prior to this time and the activity level of the children at this age. Patients should therefore be monitored closely during this time period with regular chest x-rays and follow-up pacemaker checks. None of the patient, implant or lead related factors predicted an increased risk of lead fracture.

There was a wide variation in patient growth from implant to the time of lead fracture and therefore a change in the patient's stature did not predict when a fracture would occur. One patient was 7 days old at the time the lead was implanted and grew 75cm before the lead fractured. Another patient was aged 5.3 years at the time of lead implant and the lead fractured after 4 cm growth and in one patient the lead fractured after they were hit in the chest with a football. These cases indicate that factors other than patient growth contribute to stress on the lead resulting in lead fracture.

The measurement changes observed prior to lead fracture may be due to hairline fractures, not visible on x-ray, which result in variable lead function in the early stages of fracture. If the patient has an adequate intrinsic rhythm or their atrial lead fractures, this may not be detected until the fracture has progressed further. This highlights the need to perform thorough follow-up testing on these patients and to investigate any unexpected lead measurement changes.

5.1.7.2 Exit block and high threshold

This study confirms the findings of others that SE leads have a significantly lower incidence of EB or HT (5%) compared to NSE leads (57%). This is due to the elution of steroid from the lead tip which reduces the inflammatory response of the myocardium at the time of implantation. Steroid also reduces the formation of a fibrous cap at the point of contact between the lead and tissue which can impede current dispersion into the surrounding tissue.

Although the incidence of EB or HT with SE leads was low, this study confirms the findings of Beder's small study that these leads are not exempt from failure due to EB or HT (Beder, *et al*. (1997). Cohen's larger study had a 2.4% occurrence of EB with SE leads which is similar to this study.

Some of the leads developing EB or HT had sudden threshold changes while others showed a gradual threshold rise eventually leading to intervention. This indicates that the occurrence of EB or HT in this group of patients may be unpredictable and therefore the consequences unavoidable.

The comparison of pacing threshold in relation to ventricular function shows that for the limited number of measurements reviewed there was no relationship between ventricular function and capture threshold. Several cases of severe ventricular dysfunction had very low pacing thresholds. Both very low and very high thresholds were seen in patients who had normal ventricular function. Therefore pacing capture threshold is not an indicator of a change in ventricular function or the degree of ventricular dysfunction.

5.1.7.3 Sensing problems

Sensing complications occurred in 10% of leads although in all but one case the complication did not necessitate in surgical intervention. In all other cases sensing problems were relatively minor as they were able to be programmed around or did not result in symptoms requiring further action to be taken.

5.1.7.3.1 Loss of sensing

Loss of sensing resulting in inappropriate delivery of a pacing stimulus in competition with the intrinsic rhythm is a relatively rare complication occurring in only 3% of leads. Loss of sensing in some cases was related to difficulties finding good lead positions at implant. In this study loss of sensing only rarely involved further intervention and is not a major complication of epicardial pacing.

5.1.7.3.2 Oversensing

Oversensing of external electrical signals from muscle or signals external to the body can result in failure of the pacemaker to deliver a pacing output. If a patient has no underlying rhythm or a slow underlying rhythm this may result a period of no cardiac output and therefore patient symptoms of dizziness. Oversensing occurred in 4% of leads, all of which were unipolar. This was considered a minor complication as it did not result in lead replacement for any of the patients.

Occurrence of oversensing has been reported to be related to unipolar pacing (Secemsky, et al. 1982; Fetter, et al. 1984). In one case poor NSE lead function (sensing threshold) prevented reprogramming to resolve the oversensing, which was not the case with any of the steroid-eluting leads.

Oversensing was found during pacemaker clinic testing or on Holter monitor recordings which were performed for reasons other than to look for sensing problems. Holter monitoring was not performed on all patients and therefore the incidence of oversensing may be much higher than reported. In the infant age group the symptoms associated with oversensing are likely to be under reported due to the patient's inability to communicate.

5.1.7.3.3 Late sensing

Late atrial sensing resulting in loss of AV synchrony is likely to be due to the epicardial leads being located a relatively long way from the sinus node and therefore the time for the transmission of the impulse from the sinus node to the lead electrode is prolonged. As seen in the rare cases described, late sensing problems were partially resolved by reprogramming of the AV delay.

5.1.7.4 Twitch

Diaphragmatic stimulation (DS), via the phrenic nerve, or abdominal muscle stimulation (AMS) is considered a relatively rare and minor complication of epicardial pacing. In this study AMS or DS occurred in 13 of the 180 leads followed (7%). This is considerably higher than that reported in Cohen's study of 207 epicardial leads where there was a 1.4% occurrence of phrenic nerve or muscle stimulation.

NSE leads generally required higher output programming because of their higher thresholds giving an increased likelihood of twitching. The frequency of twitching was only slightly higher in NSE leads (13%) compared to SE leads (6%) although the patient outcome of the two lead groups was significantly different. The majority of non steroid-eluting leads required surgical intervention or cessation of lead use in order to solve the twitching problem where as the lower thresholds on the steroid-eluting leads enabled the problem to be resolved by reprogramming of the pacemaker to a lower output.

AMS is due to stimulation of the muscle in the region of the pacemaker and is more likely to occur with the unipolar current pathway from the lead tip to the pacemaker unit. In bipolar leads there is a small distance between the two electrodes for current to flow resulting in a reduced risk of AMS. All AMS occurred in unipolar leads but a comparison could not be made with bipolar leads since there were only 4 implanted.

5.1.7.5 Lead dislodgement

In this study dislodgement occurred in one lead (0.5%) which compares with an average of 3% in previous epicardial lead studies (Thomson, *et al*. 2004; Villain, *et al*. 2000; Esperer, *et al*. 1992). This study confirms that lead dislodgement with epicardial pacing is rare as would be expected since the SE leads are generally sutured on to the epicardium. As also seen in this study there is a risk of dislodging recently implanted epicardial leads during removal of temporary pacing wires.

5.1.7.6 Infection

Four of the five cases of infection were successfully managed by temporary removal of the pacing hardware and antibiotics. In one case initial treatment was by antibiotics only, which was unsuccessful and resulted in a further 5 pacing related operations, explanting and implanting various pacing systems over the following 12 months before the infection was finally eliminated. This case reinforces the point that an infection at the pacemaker site requires the whole pacemaker system to be explanted plus administration of antibiotics. Treatment by antibiotics alone is insufficient to resolve the problem. As seen in one case during this study, an early high threshold on a SE lead may be a result of an infection at the tip of the lead although this is a rare occurrence.

5.1.8 Outcome of back-up or lead only implants

Epicardial leads that were implanted in case they would be required in the future went on to be used in the majority of cases. Although only 56% of SE lead only implants went on to be used, the outcome for these patients was improved. Because of this practice, 11 patients were spared from having another surgical intervention for lead placement. Cohen, *et al*. (2004) also found that prophylactic epicardial lead implantation to be successful. Implantation of additional leads for possible use in the future increases the cost of the initial procedure, but the potential benefit to the patient and reduced cost of further interventions offsets the initial outlay.

5.1.9 Future considerations with epicardial pacing

5.1.9.1 Cardiac resynchronisation therapy

There is a growing need for epicardial pacing due to the expansion of biventricular pacing for heart failure in patients with a prolonged QRS interval. This is also known as cardiac resynchronisation therapy (CRT). Significant improvements in patient mortality and reduced hospital admissions have been reported with CRT and therefore the use of this technique to treat heart failure is escalating (Bristow, *et al.* 2004). Left ventricular pacing is typically achieved by placement of a specifically designed transvenous lead into a branch of the coronary sinus (CS). Possible problems with CS lead placement include high pacing thresholds, failed CS assess or repeated lead dislodgement. In situations where CS lead placement is not possible the alternative is to place this lead epicardially. Lead placement via a thorascopic approach avoids major surgical intervention although this technique can only be used with an active fixation lead. All active fixation leads are NSE and as seen in this study these leads have significantly higher pacing thresholds and failure rate. This growth area for epicardial pacing may encourage pacing lead manufacturers to invest more research and development into SE active fixation epicardial leads with higher impedances.

5.1.9.2 Pacing induced cardiomyopathy

Over recent years there has been a growing realisation of the negative effects of right ventricular apical pacing. Studies have reported RV apical pacing is associated with increased heart failure hospitalization and mortality due to deterioration of ventricular function (Wilkoff, *et al.* 2003). These findings have prompted the use of alternative pacing sites such as the RV outflow tract and an awareness of programming long AV delays in patients with intermittent or continuous AV conduction to ensure that ventricular pacing only occurs when needed. Lead placement is limited with transvenous leads whereas with epicardial lead placement the lead location is relatively unlimited. It is common practice at this institution (GLH) to perform pacemaker reprogramming at follow-up checks in order to minimize the percent ventricular pacing when patients have intact ventricular conduction.

At the time of lead implantation consideration should also be given to placement of the ventricular lead in a location where the depolarisation wave will be as close as possible to the normal conduction pathway. That is lead placement close to the upper inter-ventricular septum in order to obtain a narrower paced QRS complex. This issue is particularly significant for the paced paediatric population since they have often had cardiac corrective surgery which may reduce their ventricular function anyway and they are likely to require pacing throughout life.

5.1.9.3 Automatic threshold detection and output adaptation

The availability of automatic pacing threshold detection and output adaptation has now been adopted in various forms by the majority of pacemaker manufacturers. This feature enables the programmed output to be safely set to just above the monitored pacing threshold resulting in increased device longevity. This is particularly important in paediatric patients as pacemaker longevity is typically lower compared to that in adults. The reasons include their requirement to be paced at higher rates, the lower impedances of epicardial leads increasing battery current drain and possibly higher output programming to overcome higher thresholds. For these reasons and the fact that the patients are looking at a lifetime of pacing, therefore multiple unit replacements, the use of the automatic threshold and output adjustment may be an important attribute for pacing paediatric patients. The availability of this feature and compatibility with the polarity of the epicardial lead should be strongly considered at the time of device selection at implantation. However, consideration must also be made of the limited published data on the use of the automatic threshold adaptation feature with epicardial leads and therefore this needs to be carefully evaluated.

5.2 Recommendations

The use of epicardial leads is recommended in small patients and those with inaccessible cardiac chambers as this will allow the children's small veins to be able to grow and also be saved for future placement of transvenous leads.

NSE leads are not recommended for use in the future as they have a high failure rate compared to SE leads. They also have higher thresholds requiring higher output programming resulting in increased pacemaker current drain and reduced pacemaker longevity. Those NSE leads that are still in use should be replaced with SE leads particularly in patients with slow underlying rhythms.

The practice of cutting down to healthy myocardium before placement of the passive epicardial lead should continued to be utilized in these difficult cases to avoid the use of NSE leads. There is a need for lead manufacturers to develop a steroid eluting active fixation lead for situations where passive fixation epicardial leads are contraindicated.

Lead failure due to fracture is a significant risk in the paced paediatric population. The use of bipolar leads over unipolar may reduce the incidence of lead related complications such as fracture, oversensing and twitching. Therefore bipolar, passive fixation, steroid eluting epicardial leads should be used as a first choice where possible. To reduce the incidence of lead fracture it is recommended that the leads be implanted by the subxiphoid or median sternotomy route.

Monitoring of patient growth by measuring patient height at each follow-up pacemaker check should be performed, as leads fractured after an average patient growth of 30cm, although there was considerable spread around this value.

Where unstable lead impedance measurements are obtained at follow-up repeat impedance measurements should be performed with the patient in different positions in order to determine whether the impedance change is due to lead fracture. Where daily measurements are available these should be reviewed closely at each follow-up check. If a bipolar lead is in place, lead switch should be turned on if the feature is available.

For those leads showing a trend of increasing pacing threshold these patients should receive more frequent follow-up and where patients are pacemaker dependant consideration should be made as to whether to electively replace the lead.

The potential for late sensing due to distal atrial lead placement should be taken into consideration when epicardial leads are implanted. This may not always possible for the surgeon for following reasons: limited access to the atria with the subxiphoid approach, extensive adhesions or implantation in infants with small hearts. It is recommended that during follow-up of patients with epicardial leads the surface ECG should be carefully examined to ensure the P wave to V pacing interval is physiologic with the AV delays that are programmed.

It is recommended that Holter monitoring be performed in the early follow-up period for all patients with unipolar epicardial leads, particularly if the mode of pacing is AAI(R) as this will identify loss of sensing and oversensing.

A significant infection at the pacemaker site requires pacemaker system removal plus administration of antibiotics. Treatment by antibiotics alone is insufficient to resolve the problem.

Epicardial ventricular leads should be placed close to the upper inter-ventricular septum when possible in order to obtain a narrower paced QRS complex.

Pacemaker selection at the time of implantation should take into consideration the availability of automatic output detection and adjustment features.

Placement of back-up leads is recommended in patients who may be too small for initial DDD pacemaker units, where sustained AVB post surgery is envisaged or those with a history of complications.

5.3 Limitations of this study

The practice of cardiac pacing has changed significantly over the 28 years that this study covered. Pacemaker and lead technology has improved, surgical techniques were refined and knowledge in the field of pacing has advanced considerably since 1977 which is when the first lead in this study was implanted. These factors would contribute to the superior performance observed in the recently implanted leads over older NSE leads. The limitations described below were predominantly unavoidable and were not able to be overcome.

A relatively large number of patients and leads were included in this study at initial implant although the numbers available during follow-up were much smaller for a variety of reasons outlined in section 4.2.7. As seen in table 26 only 25% of the initial lead implants were still being followed at 5 years and by 7 years post implant this had reduced to 10%. The mean follow-up duration for all leads was 3.3 years which is relatively short. For those leads that ceased to be followed it is unknown whether they would continue to function or fail.

In the early years of pacing when only NSE leads were available, implanting one ventricular lead with a single chamber pacemaker was common practice as this provided the minimum requirements for achieving adequate pacing. For this reason a small number of atrial NSE leads were implanted during the study period and therefore atrial SE and NSE lead performance cannot be compared.

The subxiphoid route was first used for epicardial lead implantation in 2002 and therefore the number of leads placed by this method is small and their follow-up duration is relatively short. Although the early results of this implant route look promising a greater number of leads and a longer follow-up duration are required to determine the longer term outcome of this method.

A small number of bipolar leads were implanted during the study period. The long term performance of these leads in comparison to unipolar leads requires longer follow-up and greater lead numbers.

Due to incomplete medical records or documentation in pacing files there were cases of missing data in relation to patient characteristics or lead implantation details.

5.3.1 Variation in pacemaker testing procedures

As this was a retrospective study there were several limitations due to pacemaker models having varying measurement capabilities and techniques for performing lead testing.

During pacing and sensing threshold tests the increment adjustments will vary depending on the type of pacemaker. For example when testing the pacing threshold the output may be adjusted in increments of between 0.1V to 0.5 V for a voltage threshold. If an increment of 0.5volts is used the measured pacing threshold may vary by up to 0.5 volts either side of the measured value. This lack of precision causes a small error in the measurement although the magnitude of this error is not statistically significant.

Pacing thresholds were determined using either pulse width or voltage threshold methods. The voltage pacing thresholds were performed at a range of pulse widths. For these reasons pacing thresholds as recorded could not be compared and required application of the threshold conversion formula. Although this formula has a good correlation between measured and calculated its application will cause a small error in the threshold compared to an actual measured pacing threshold value.

Sensing thresholds may be measured by the pacemaker automatically adjusting the sensitivity value until the operator observes loss of sensing on the surface ECG at which time the test is stopped. If the intrinsic signal is above the measurement range of the pacemaker (i.e. >3.5 mV for a P wave) then the actual sensing value is unknown except that it is greater than the measurement range of the pacemaker. If the same patient receives a new pacemaker which has a different measurement upper limit (i.e. >5mV for a P wave) the atrial sensing threshold would appear to have improved from >3.5mv to >5mV but this observed change is due to the change in the pacemaker measurement capability not the patient or lead status.

5.3.2 Unobtainable lead follow-up data

Lead follow-up data was not able to be obtained at some follow-up checks for the following reasons:

Atrial pacing threshold and impedance was not able to be measured if the pacemaker could not be programmed to a rate faster than the sensed sinus rate. Sinus tachycardia is a normal occurrence in infants.

The ventricular sensing threshold could not be measured when there was no underlying rhythm to sense when the pacemaker rate was programmed to the minimum rate of 30ppm. In this case the patient is referred to as being pacemaker dependant. If the patient became symptomatic during the ventricular sensing threshold test they were considered pacemaker dependant and the sensing test was aborted with no result.

If the patient was uncooperative the tests were not able to be performed. On some occasions the patient either refused to have the programming wand placed near them or was moving and crying throughout the check which prevents visualisation of the ECG which is required to determine the pacing and sensing threshold test values.

If the patient's intrinsic ECG rhythm changed to atrial fibrillation or atrial flutter, the atrial pacing threshold could not be tested. Atrial fibrillation is rapid uncoordinated activation of the atria and atrial flutter is atrial depolarization at approximately 300bpm. Atrial capture via a permanent pacemaker is not possible during these rhythms.

If the patient's intrinsic rhythm was junctional rhythm with no atrial depolarization signal to sense, the atrial sensing threshold could not be performed.

Early pacemakers did not have telemetry capabilities and therefore lead function measurements could not be obtained from these devices.

If the position of the pacemaker within the abdomen changed so that a telemetry link with the programmer wand could not be achieved, lead testing could not be performed.

5.3.3 Follow-up data relating to complications

Follow-up intervals were typically every 6 months and therefore in cases where the patient was asymptomatic with a complication, this complication may have occurred any time within this 6 month period. Some patients did not have pre-complication follow-up checks because they did not attend their scheduled pacemaker check. In these cases the actual date that the complication occurred is unknown and the date that the complication was found was used as the date of occurrence.

In some cases where a lead was initially capped and later tested, this was the time that the lead failure was discovered. For others a lead fracture was observed on X-ray. In these cases the exact date of lead failure is unknown.

Patient symptoms in relation to lead complications are likely to be under-reported in infants and young children due to their inability to communicate. For example if a twitch is not visualised during a pacemaker check, the sensation of twitching must be communicated by the patient to the pacemaker technologist in order to identify this complication.

Height measurements were not always performed at the time of implant and lead fracture. It would have been valuable to more fully evaluate the effect of growth on lead fracture rate, comparing this leads which did and did not fracture. Echocardiography was not performed on the majority of patients who developed exit block or lead fracture.

5.4 Future research

In order to determine whether epicardial or transvenous lead placement gives the best outcome, assessment of the performance and survival of transvenous leads implanted at GLH is required. Consideration would have to be made for the fact that transvenous leads would have been placed in an older patient cohort.

Over more recent years the use of bipolar leads and the subxiphoid route has increased. It is expected that these changes in practice will result in a decreased incidence of lead fracture. Once a larger number of these implants have been performed and a longer follow-up time is available a future study to evaluate the outcome of these leads is required in order to determine the success of this practice.

A longer follow-up of SE leads will reveal whether EB or HT will continue to occur at later intervals post implant in this group.

5.5 Conclusions

- Steroid leads maintain lower pacing thresholds and have a reduced incidence of exit block compared to non-steroid leads.
- Development of steroid-eluting leads which can penetrate through the damaged or fatty epicardial surface is required. Meanwhile in situations where the use of current SE leads is contraindicated, alternative surgical techniques for SE lead placement should be attempted rather than resorting to the use of NSE leads.
- Lead fracture is a significant complication of epicardial pacing in paediatric patients. The use of stronger bipolar leads implanted by the subxiphoid route may reduce the risk of fracture.
- Medium term survival of epicardial leads is acceptable and therefore the continued use of these leads is recommended in young patients allowing their veins to be saved for transvenous leads later in their life.

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Appendix 1a

Health and Disability Ethics Committees

e-mail: *pat_Chainey@moh.govt.nz*
website: *http:/www.newhealth.govt.nz/ethicscommittees*

Northern X Regional Ethics Committee
Ministry of Health
3rd Floor, Unisys Building
650 Great South Road, Penrose
Private Bag 92 522
Wellesley Street, Auckland
Phone (09) 580 9105
Fax (09) 580 9001

15 March 2005.

Ms Karen Searby
Pacemaker Clinic
Auckland City Hospital
PB 92 024
Auckland.

Dear Karen,

Medium-term follow-up comparison of steroid-eluting and non steroid-eluting epicardial pacing leads

Thank you for your letter/application dated 11 February 2005 which has been reviewed by the Chairperson of the Northern X Ethics Committee under delegated authority.

The project is considered audit that does not require ethical approval as set out in the Operational Standard for Ethics Committees, Ministry of Health, March 12002.

Yours sincerely,

Pat Chainey
Administrator, Northern X Ethics Committee

Cc: Waitemata DHB

Appendix 1b

AUT
AUCKLAND UNIVERSITY OF TECHNOLOGY
TE WĀNANGA ARONUI O TAMAKI MAKAU RAU

MEMORANDUM

Academic Services

To: Elaine Rush
From: **Madeline Banda**
Date: 16 May 2005
Subject: Ethics Application Number 05/85 **Medium-term follow-up comparison of steroid-eluting and non steroid-eluting epicardial pacing leads.**

Dear Elaine

I am pleased to advise that the Auckland University of Technology Ethics Committee (AUTEC) approved your ethics application at their meeting on 9 May 2005. Your application is now approved for a period of three years until 16 May 2008.

I advise that as part of the ethics approval process, you are required to submit to AUTEC the following:

- A brief annual progress report indicating compliance with the ethical approval given using form EA2, which is available online at *http://www.aut.ac.nz/resources/research/ethics/ea2appendixg.doc* , including a request for extension of the approval if the project will not be completed by the above expiry date;
- A brief report on the status of the project using form EA3, which is available online at *http://www.aut.ac.nz/resources/research/ethics/ea3appendixh.doc* . This report is to be submitted either when the approval expires on 16 May 2008 or on completion of the project, whichever comes sooner;

You are reminded that, as applicant, you are responsible for ensuring that any research undertaken under this approval is carried out within the parameters approved for your application. Any change to the research outside the parameters of this approval must be submitted to AUTEC for approval before that change is implemented.

Please note that AUTEC grants ethical approval only. If you require management approval from an institution or organisation for your research, then you will need to make the arrangements necessary to obtain this.

To enable us to provide you with efficient service, we ask that you use the application number and study title in all written and verbal correspondence with us. Should you have any further enquiries regarding this matter, you are welcome to contact Charles Grinter, Ethics Coordinator, by email at charles.grinter@aut.ac.nz or by telephone on 917 9999 at extension 8860.

On behalf of the Committee and myself, I wish you success with your research and look forward to reading about it in your reports.

Yours sincerely

Madeline Banda
Executive Secretary
Auckland University of Technology Ethics Committee

Cc: Karen Searancke karen@adhb.govt.nz

From the desk of ...
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Appendix 2

Paediatric Epicardial Pacing Lead Study Data Collection Form

Pg 1: Demographics (1 page per patient)

Surname

First name

Previous surname

Hospital Number

Gender (M/F)

Ethnicity E = European, M = Maori, O = Other (state) _____

Date of birth ☐☐ • ☐☐ • ☐☐☐☐

Follow-up centre

Date of first epicardial lead implant ☐☐ • ☐☐ • ☐☐☐☐

Age at first epicardial implant ☐☐ Years ☐☐ Mths ☐☐ Days

Weight at first implant (Kg) ☐☐☐ • ☐☐

Implanting physician _____

Structural heart disease (Y/N)

- Heart disease classification _____

Indication 1 for implant _____

Indication 2 for implant _____

Previous cardiac surgery (Y/N)

- 1st Cardiac surgery & date _____
- 2nd Cardiac surgery & date _____
- 3rd Cardiac surgery & date _____

Implant at time of other cardiac surgery (Y/N)

Patient status (A = Alive D = Deceased)

Date of death ☐☐ • ☐☐ • ☐☐☐☐

Cause of death: _____

Comments: _____

Page 2: Lead Information (1 sheet / lead)

Lead chamber placement (RA, LA, RV, LV) | | |

Lead Model | | | | | | | |

Lead Polarity (Uni / Bi) | | |

Fixation Method (Active / Passive) | | | | | | | |

Steroid Eluting (Y / N) |

Implant Technique (Sternotomy / thoracotomy / subxyphoid) | | | | |

Lead Implant Date | | • | | | • | | | | |

Complications/Difficulties with lead implant (Y/N) |

- Comments on lead implant _____

Complications during follow-up (Y/N) |

- Complication 1 type _____

- Complication 1 date of occurrence | | • | | | • | | | | |

- Complication 1 _____

- Complication 2 type _____

- Complication 2 date of occurrence | | • | | | • | | | | |

- Complication 2 _____

Lead Follow-up Data

Follow-up Interval	Date	Pacing Threshold (V/ms)	Pacing Threshold (цJ)	Sensing Threshold (mV)	Lead Impedance (Ω)	Comments
Implant						
1day						
2weeks						
6weeks						
4.5months						
10.5mths						
1.5yrs						
2 yrs						
2.5 yrs						
3 yrs						
3.5 yrs						
4 yrs						
4.5 yrs						
5 yrs						
5.5 yrs						
6 yrs						

Follow-up Interval	Date	Pacing Threshold (V/ms)	Pacing Threshold (цJ)	Sensing Threshold (mV)	Lead Impedance (Ω)	Comments
6.5 yrs						
7 yrs						
7.5 yrs						
8 yrs						
8.5 yrs						
9						
10						
11						
12						
13						
14						
15						

Comments:

Appendix 3

Full data from the threshold conversion formula validation study.

Threshold # 1 (Measured)		Threshold # 2 (Measured)		Threshold #2 (Calculated)	Measured vs Calculated Difference
Voltage (V1)	PW1 (ms)	Voltage (V2)	PW2 (ms)	Voltage (V3)	V3 minus V1
2.5	0.5	5	0.06	1.40	-1.10
2.5	0.5	5	0.06	1.40	-1.10
1.25	1	0.5	1.5	0.64	-0.61
1.25	0.5	2.5	0.06	0.70	-0.55
1	0.4	1.6	0.06	0.51	-0.49
1.25	0.75	2.5	0.12	0.83	-0.42
1.25	0.75	2.5	0.12	0.83	-0.42
2.5	0.5	5	0.12	2.12	-0.38
2.5	0.5	5	0.12	2.12	-0.38
2.5	0.5	5	0.12	2.12	-0.38
2.1	0.4	1	1	1.73	-0.37
1	0.4	0.5	0.6	0.64	-0.36
1.5	0.8	1	1	1.14	-0.36
1.25	1	5	0.06	0.92	-0.33
1	0.45	0.5	0.75	0.68	-0.32
1.6	0.36	4	0.06	1.37	-0.23
1.5	0.4	1	0.6	1.28	-0.22
1.5	0.4	1	0.6	1.28	-0.22
1.25	0.5	2.5	0.12	1.06	-0.19
1.25	0.25	2.5	0.06	1.06	-0.19
1.25	0.25	2.5	0.06	1.06	-0.19
1.25	0.5	2.5	0.12	1.06	-0.19
1.25	0.5	2.5	0.12	1.06	-0.19
1.5	0.37	0.9	0.7	1.32	-0.18
0.5	0.4	1	0.06	0.32	-0.18
1.25	1	2.5	0.25	1.09	-0.16
1.25	0.75	5	0.06	1.10	-0.15
1.25	0.75	5	0.06	1.10	-0.15
0.8	0.54	1.6	0.12	0.65	-0.15

5	0.5	3.2	1	4.85	-0.15
0.8	0.8	1.6	0.18	0.65	-0.15
1.2	0.36	1.6	0.18	1.06	-0.14
1.5	0.6	1	1	1.36	-0.14
1.9	0.75	1.5	1	1.78	-0.12
0.8	0.48	1.6	0.12	0.70	-0.10
1.2	0.5	0.9	0.7	1.10	-0.10
1.6	0.42	2.5	0.18	1.50	-0.10
1.5	0.8	1.25	1	1.43	-0.07
1.5	0.37	0.9	0.8	1.43	-0.07
1.8	0.4	1	1	1.73	-0.07
1.6	0.54	2.5	0.24	1.54	-0.06
1.3	0.4	1	0.6	1.28	-0.02
1.3	0.4	1	0.6	1.28	-0.02
0.8	0.42	2.5	0.06	0.78	-0.02
1.2	0.37	0.9	0.58	1.18	-0.02
0.5	0.4	1.5	0.06	0.48	-0.02
0.5	0.4	1.5	0.06	0.48	-0.02
1.4	0.4	1.1	0.6	1.40	0.00
1.3	0.75	1.1	1	1.31	0.01
1.5	0.4	1	0.8	1.52	0.02
1.5	0.4	1	0.8	1.52	0.02
1.25	0.4	1	0.6	1.28	0.03
1.25	0.4	1	0.6	1.28	0.03
0.8	0.54	1.6	0.18	0.83	0.03
0.8	0.18	1.6	0.06	0.83	0.03
0.8	0.18	1.6	0.06	0.83	0.03
0.5	0.4	2.5	0.03	0.53	0.03
1.25	0.75	2.5	0.25	1.29	0.04
1.25	0.75	2.5	0.25	1.29	0.04
1.6	0.24	2.5	0.12	1.65	0.05
1	0.6	0.9	0.8	1.07	0.07
1.4	0.8	1.3	1	1.49	0.09
0.8	0.48	1.6	0.18	0.89	0.09
0.8	0.48	1.6	0.18	0.89	0.09

0.8	0.48	1.6	0.18	0.89	0.09
1.2	0.36	2.5	0.12	1.29	0.09
2	0.4	1.5	0.7	2.10	0.10
1.3	0.4	1	0.7	1.40	0.10
1.3	0.4	1.1	0.6	1.40	0.10
1.5	0.4	1.1	0.75	1.60	0.10
1.3	0.75	1.2	1	1.43	0.13
1.75	0.4	1.25	0.8	1.89	0.14
1.25	0.5	5	0.06	1.40	0.15
1.25	1	5	0.12	1.40	0.15
1.6	0.54	2.5	0.3	1.76	0.16
0.8	0.42	1.6	0.18	0.96	0.16
0.8	0.42	1.6	0.18	0.96	0.16
2	0.4	1.25	1	2.17	0.17
2	0.4	1.25	1	2.17	0.17
1.1	0.5	1	0.75	1.28	0.18
0.8	0.45	1.6	0.2	0.98	0.18
1.8	0.5	1.5	0.8	1.99	0.19
1.7	0.6	1.4	1	1.90	0.20
1.3	0.5	1	1	1.52	0.22
1.5	0.4	1	1	1.73	0.23
1.6	0.3	2.5	0.18	1.84	0.24
1.6	0.3	2.5	0.18	1.84	0.24
1.6	0.3	2.5	0.18	1.84	0.24
0.8	0.12	1.6	0.06	1.06	0.26
0.8	0.48	1.6	0.24	1.06	0.26
0.8	0.12	1.6	0.06	1.06	0.26
2	0.5	1.5	1	2.27	0.27
2.5	0.2	3.3	0.15	2.78	0.28
1.6	0.42	4	0.12	1.89	0.29
0.8	0.48	2.5	0.12	1.09	0.29
0.8	0.48	2.5	0.12	1.09	0.29
1.6	0.4	1.1	1	1.91	0.31
1.2	0.4	1	0.8	1.52	0.32
2	0.5	1.75	0.8	2.32	0.32

2.1	0.4	1.6	0.8	2.43	0.33
1.5	0.4	1.25	0.76	1.84	0.34
0.8	0.48	4	0.06	1.15	0.35
1.25	0.25	2.5	0.12	1.61	0.36
1.25	0.25	2.5	0.12	1.61	0.36
1.25	0.25	2.5	0.12	1.61	0.36
1.25	0.25	2.5	0.12	1.61	0.36
1.25	0.25	2.5	0.12	1.61	0.36
1.4	0.6	1.3	1	1.77	0.37
1.3	0.5	1.1	1	1.67	0.37
0.8	0.42	2.5	0.12	1.18	0.38
0.8	0.42	2.5	0.12	1.18	0.38
0.8	0.35	2.5	0.1	1.18	0.38
1.25	0.5	2.5	0.25	1.65	0.40
1.25	0.12	2.5	0.06	1.65	0.40
1.25	0.12	2.5	0.06	1.65	0.40
1.25	0.5	2.5	0.25	1.65	0.40
1.25	1	2.5	0.5	1.65	0.40
2.25	0.5	1.75	1	2.65	0.40
0.8	0.6	2.5	0.18	1.21	0.41
1.25	0.75	5	0.12	1.67	0.42
1.25	0.75	5	0.12	1.67	0.42
0.8	0.42	4	0.06	1.24	0.44
1.6	0.4	1.2	1	2.08	0.48
1.25	0.4	1	1	1.73	0.48
1.6	0.25	5	0.06	2.12	0.52
1.6	0.54	4.2	0.18	2.17	0.57
3.5	0.6	3	1	4.08	0.58
2.3	0.5	1.9	1	2.88	0.58
2.5	0.25	4.2	0.15	3.09	0.59
1.5	0.4	1.25	1	2.17	0.67
1.25	0.75	2.5	0.5	1.96	0.71
1.25	0.75	2.5	0.5	1.96	0.71
2.5	0.2	5	0.1	3.30	0.80
1.6	0.4	1.4	1	2.43	0.83

0.8	0.12	2.5	0.06	1.65	0.85
1.6	0.06	2.5	0.06	2.50	0.90
3.5	0.6	3.5	1	4.76	1.26
0.8	0.12	4	0.06	2.64	1.84

Appendix 4

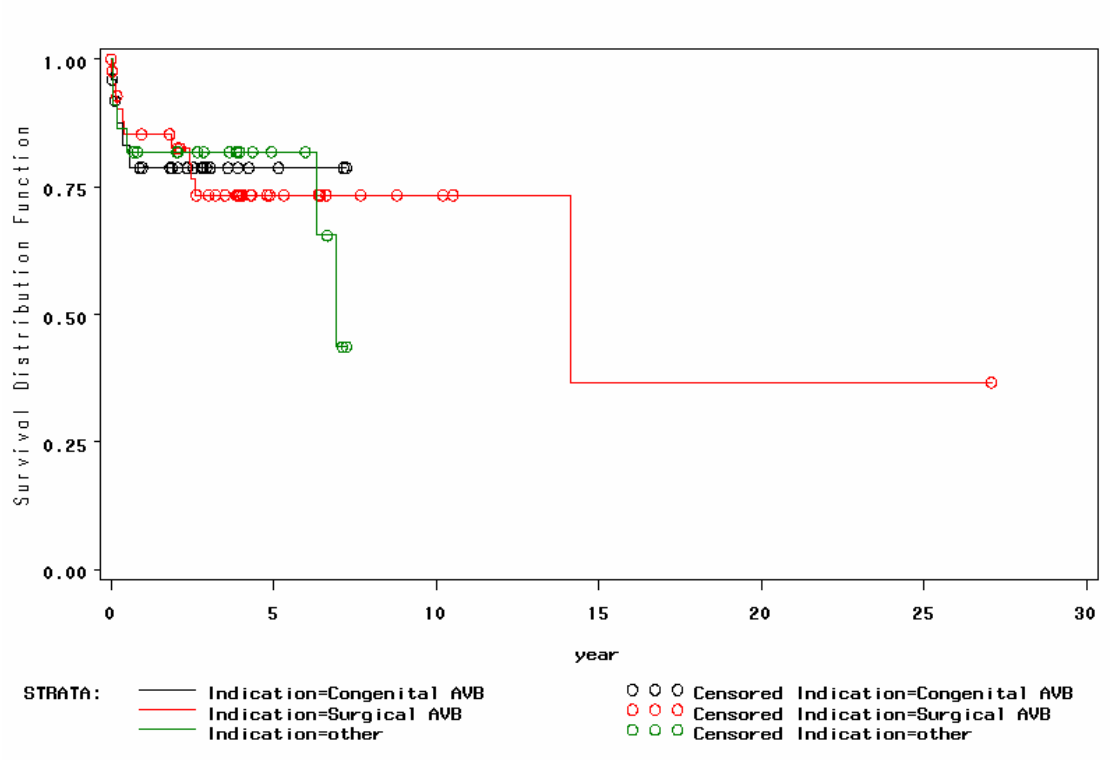
Daily measurement readings from a Guidant Discovery pacemaker

Daily Measurement - Data Table

Date	Atrial Amplitude (mV)	Atrial Impedance (Ω)	Ventricular Amplitude (mV)	Ventricular Impedance (Ω)
22-APR-2002	1.3	460	>9.0	540
21-APR-2002	2.3	470	>9.0	540
20-APR-2002	1.8	>2500	>9.0	550
19-APR-2002	>3.5	500	PACED	550
18-APR-2002	>3.5	>2500	>9.0	550
17-APR-2002	2.8	760	>9.0	550
16-APR-2002	>3.5	>2500	PACED	520
11-APR-2002	>3.5	1190	>9.0	550
04-APR-2002	1.8	1480	>9.0	520
28-MAR-2002	>3.5	2150	>9.0	550
21-MAR-2002	1.7	1150	>9.0	560
14-MAR-2002	>3.5	1500	>9.0	520
07-MAR-2002	>3.5	1820	>9.0	550
28-FEB-2002	>3.5	>2500	>9.0	550
21-FEB-2002	>3.5	880	PACED	550
14-FEB-2002	>3.5	500	>9.0	550
07-FEB-2002	>3.5	1820	>9.0	540
31-JAN-2002	>3.5	790	PACED	530
24-JAN-2002	>3.5	1520	>9.0	520
17-JAN-2002	>3.5	970	>9.0	540
10-JAN-2002	>3.5	2160	PACED	550
03-JAN-2002	>3.5	460	>9.0	520
27-DEC-2001	>3.5	2400	PACED	560
20-DEC-2001	1.0	1200	PACED	560
13-DEC-2001	>3.5	1180	PACED	550
06-DEC-2001	1.3	1220	>9.0	560
29-NOV-2001	>3.5	1520	PACED	550
22-NOV-2001	>3.5	880	PACED	580
15-NOV-2001	>3.5	880	>9.0	560
08-NOV-2001	>3.5	800	>9.0	580
01-NOV-2001	>3.5	1160	>9.0	550
25-OCT-2001	>3.5	840	>9.0	550
18-OCT-2001	>3.5	840	>9.0	560
11-OCT-2001	1.1	480	PACED	590
04-OCT-2001	>3.5	1150	>9.0	540
27-SEP-2001	>3.5	540	PACED	590
20-SEP-2001	>3.5	530	PACED	590
13-SEP-2001	1.6	850	PACED	600
06-SEP-2001	>3.5	500	PACED	610
30-AUG-2001	1.3	470	>9.0	600
23-AUG-2001	1.0	470	>9.0	620
16-AUG-2001	1.0	460	>9.0	610
09-AUG-2001	1.1	440	PACED	590
02-AUG-2001	1.1	440	PACED	600
26-JUL-2001	1.1	440	PACED	600
19-JUL-2001	0.9	440	>9.0	600
12-JUL-2001	1.0	430	>9.0	610
05-JUL-2001	1.0	430	PACED	560
28-JUN-2001	0.7	440	PACED	600
21-JUN-2001	1.0	410	PACED	590
14-JUN-2001	0.9	410	>9.0	610
07-JUN-2001	1.0	410	PACED	610
31-MAY-2001	1.0	410	>9.0	610
24-MAY-2001	0.9	400	PACED	600
17-MAY-2001	1.0	420	PACED	620
10-MAY-2001	0.9	400	PACED	600
03-MAY-2001	1.1	410	PACED	590

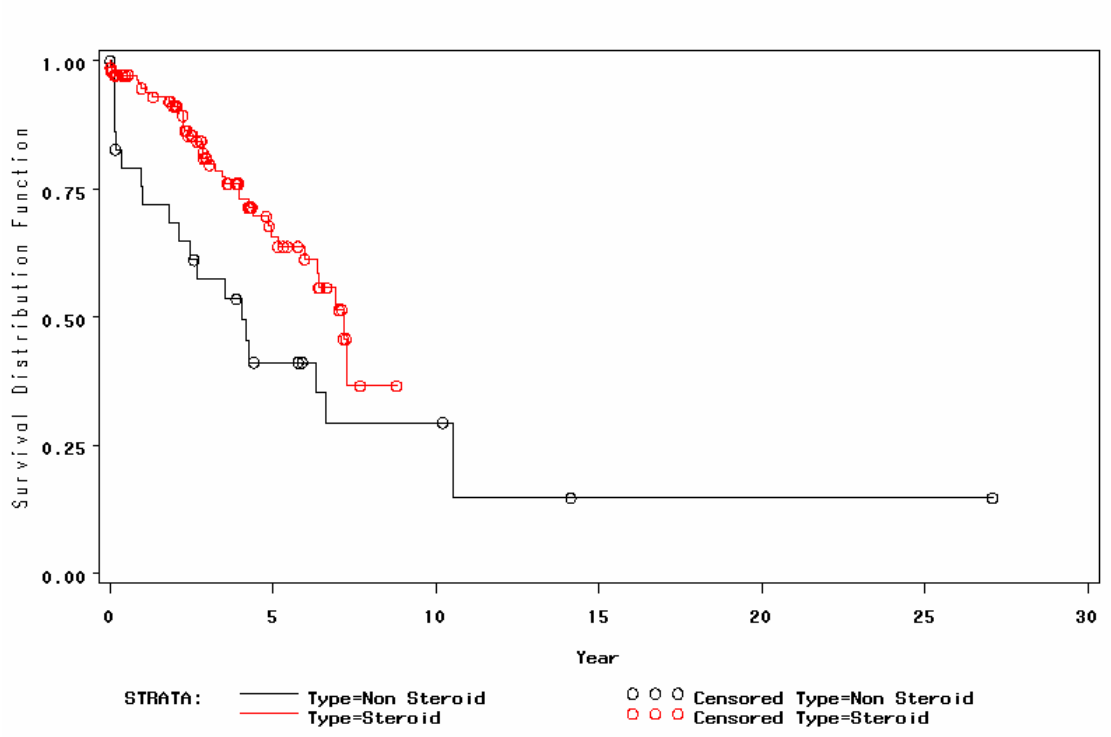
Appendix 5a

Mortality rate according to indication for pacing



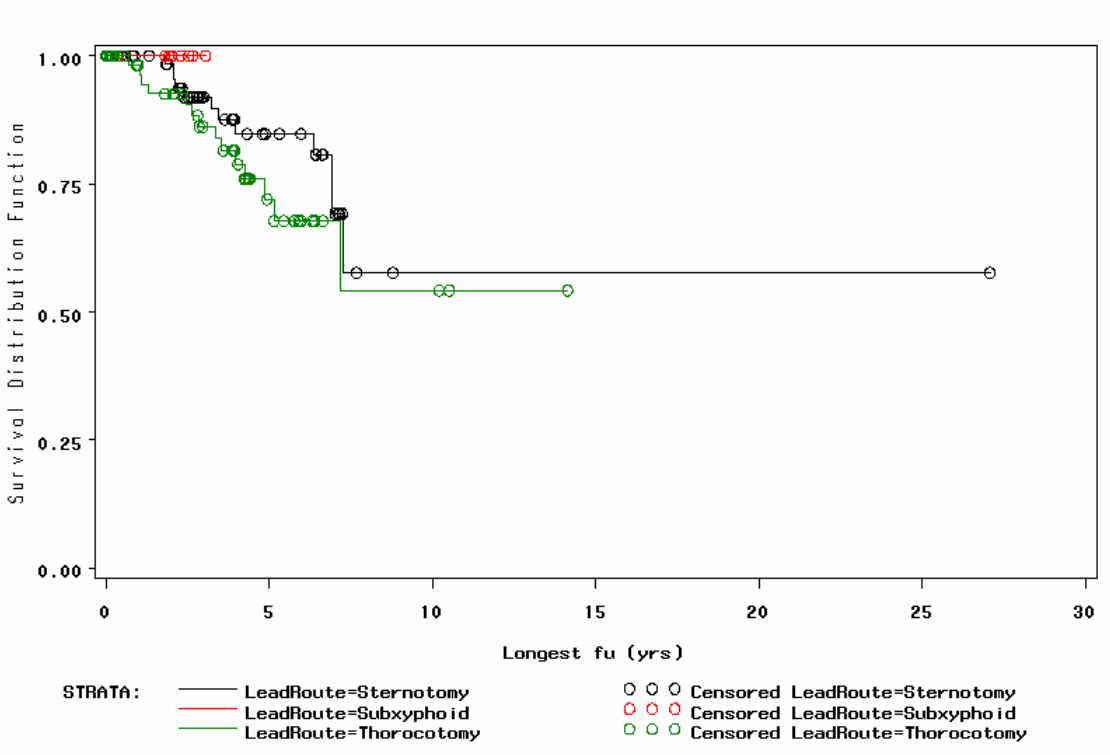
Appendix 5b

Comparison of lead failure (all causes) for steroid-eluting and non steroid-eluting leads



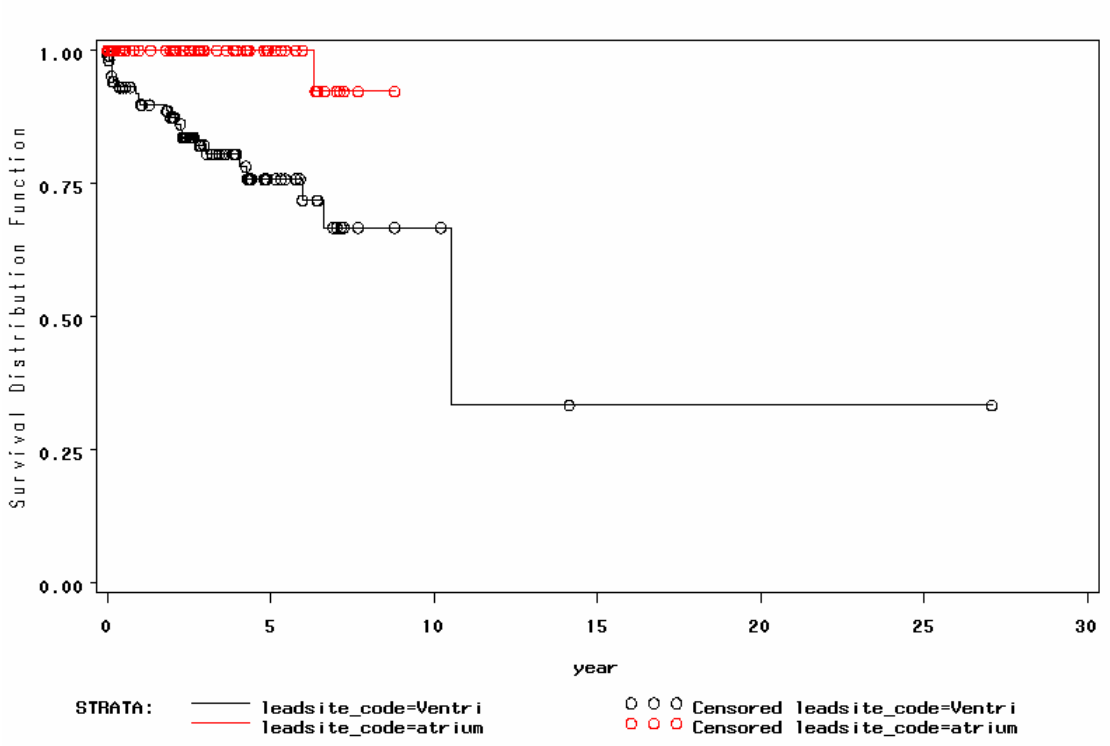
Appendix 5c

Comparison of lead failure (due to fracture) according to implant route



Appendix 5d

Comparison of lead failure (due to exit block or high threshold) according to lead site



Appendix 5e

Comparison of lead failure (due to exit block or high threshold) according to gender