CLINICAL ASPECTS OF CARDIAC PACING FOR BRADYARRHYTHMIAS

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KLINISCHE ASPECTEN VAN HARTSTIMULATIE VOOR BRADYARITMIEËN

PROEFSCHRIFT

TER VERKRIJGING VAN DE GRAAD VAN DOCTOR

AAN DE ERASMUS UNIVERSITEIT ROTTERDAM

OP GEZAG VAN DE RECTOR MAGNIFICUS

PROF. DR. C.J. RIJNVOS

EN VOLGENS HET BESLUIT VAN HET COLLEGE VAN DEKANEN.

DE OPENBARE VERDEDIGING ZAL PLAATSVINDEN OP

WOENSDAG 22 JANUARI 1992 OM 15.45 UUR

DOOR

JACOB HENDRIK RUITER

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Aan Margreet, Diederik en Gerbrand .
Aan mijn ouders.

U allen, die dit boek in handen neemt, groet ik recht hartelijk. Ik weet niet goed hoe te beginnen, maar ik moet iets zeggen, anders zult ge van dit boek niets begrijpen. Het is namelijk niet af.

Uit : Pieter Bas van Godfried Bomans.

Table of contents

Voorwoord

In de meeste cardiologische opleidingscentra blijft, wegens verschillende uiteenlopende redenen, de belanstelling voor en mede daardoor de kwaliteit van het onderwijs in hartstimulatie achter.

Mijn eerste ervaring met twee kamer stimulatie was in het najaar van 1980, toen een oudere collega mij vroeg, na het succesvol implanteren van vijf ventriculaire pacemakers, om bij een patient een DVI pacemaker te implanteren. Terwijl hij mij dit vroeg duwde hij mij de gebruiksaanwijzing van een atriale geleider in handen.

De interesse in meer fysiologische pacemakersystemen was gewekt vooral ook toen, met behulp van de productspecialist van de pacemaker firma, deze eerste twee–kamer stimulatie gelukte. De ervaring in twee–kamer stimulatie in Nederland was toen nog zo gering, dat ik reeds na enkele implantaties werd gevraagd op een pacemakertraining anderen van mijn ervaringen deelgenoot te maken. Sedertdien heb ik aan meerdere pacemakercursussen mijn bijdrage geleverd en kwam zo in aanraking met de vele vragen en praktische problemen van de aspirant–pacemakercardioloog.

In dit proefschrift heb ik getracht, puttende uit de eigen klinische ervaring en vanuit mijn kennis van de literatuur, op vele veel voorkomende vragen een antwoord te geven. Mijn promotor Prof. Dr. Jos R.T.C. Roelandt heeft mij in deze opzet van het proefschrift ten volle gesteund en ik dank hem voor de vele waardevolle adviezen. Jos, het was mede jouw idee om een hoofdstuk over de kosten–baten analyse van pacemakertherapie toe te voegen, jij en ik hebben het geweten, in het proefschrift betreft het hoofdstuk 9 een betere titel was geweest: versie 9. Ik weet nu pas echt goed hoe goedkoop een pacemaker is.

Mijn co–promotor Dr. Karel den Dulk heeft meerdere versies van het proefschrift doorgewerkt. Uit alle delen van de wereld, Zuid Afrika, Australie kreeg ik per express of per fax zeer waardevolle verbeteringen toegestuurd. Karel, naast je reislust bewonder ik je kennis van zaken en zeer systematische aanpak.

Mijn co–referenten Prof. Dr. Maarten L. Simoons en Prof. Dr. Piet Verdouw ben ik erkentelijk voor de kritische kanttekeningen bij enkele hoofdstukken van het manuscript.

Dr. Rob van Mechelen, toen ik als arts–assistent bij jouw in het St. Franciscus Gasthuis kwam werken, had jij reeds verstand van pacemakers en ik wist hoe je ze er in moest zetten. Dat deze samenwerking een succes moest worden

sprak haast voor zich. Door jouw wetenschappelijk inzicht, maar vooral ook door jouw vriendschap kreeg ook voor mij de pacemakerwetenschap gestalte.

Al mijn broeders en zuster in de pacemakerresearch, Hans de Boer, Drs. Malcolm Begemann, Drs. Jan Pieter Heemels, Dra. Hetty Wortel, Art Pilmeijer, en mijn pacemakertechnicus Dick Kee ben ik zeer dankbaar voor de vele uren van gezamelijke arbeid en hun aandeel in de publicaties.

Marijke de Zeeuw, nu al weer zes en een half jaar mijn voortreffelijke secretaresse; de snelheid en de accuratesse waarmee jij mijn hierogliefen in wordperfect weet om te zetten verbaast mij iedere keer weer. En ook voor je meeleven en voor de extra kopjes koffie tijdens het ochtend spreekuur, wanneer ik de voorgaande avond weer de tijd was vergeten, ben ik je dankbaar.

Het hoofd van de functie afdeling cardiologie Jos Buter, en alle daar werkzame verpleegkundigen echter in het bijzonder: Loes Weteling, Ingrid Voogd, en Anneke Janse–de Jonge ben ik erkentelijk voor de vakbekwame en zeer adequate steun bij de vele pacemaker implantaties bij soms ernstig zieke patienten.

Drs. Ewout Steyerberg van het centrum voor klinische besliskunde van de Erasmus Universiteit in Rotterdam wist het proefschrift op het laatste moment, in hoofdstuk 9, nog van enkele figuren te voorzien.

Barbara Gaynor of C.P.I Corporate Communications made many spelling corrections and puncuation changes and noted several inconsistencies in tables and headings. Thanks for spending many hours in editing and reediting the manuscript.

De laatste engelse correcties werden verzorgd door Wilma van Runt, mijn dank hiervoor.

Marianne S. Eicholtz verzorgde de vlotte afwikkeling van de "promotiezaken" met de Erasmus universiteit.

Hans de Boer en Cor de Bruin hebben mij wegwijs gemaakt in de mogelijkheden van desk–top publishing, jullie bleven mij trouw ook in weekend en avonduren om de laatste wijzigingen gestalte te geven. Ik begrijp nu wat een extra regel voor een ravage aan kan richten in een reeds gezette tekst.

De heer T. Ros ontwierp de fraaie omslag van dit proefschrift.

Mijn cardiologische vrienden en maten Dr. Charles de Beus, Cees Burgersdijk, Joost Henneman, Dr. Alf Arnold en Dr. Stan Reichert ben ik dankbaar voor hun kameraadschap in drukke tijden.

Je bent nooit te oud om je ouders te bedanken voor een, naar eigen inzicht,

geslaagde opvoeding, deze reeds wat rijpere promovendus ervaart het nog steeds als een voorrecht om "thuis" te mogen komen.

Lieve Margreet, de vele uren en dagen dat jij aan het proefschrift hebt gewerkt waren voor mij van onschatbare waarde. Het is toch eigenlijk wel het toppunt dat je zelfs dit dankwoord moet typen.

Ook mijn zoons Diederik en Gerbrand hebben daadwerkelijk mee geholpen zodat het proefschrift soms leek op een familiespel met honderden A4–tjes die liefst op de juiste volgorde moesten worden gelegd.

De pacemaker firma's Medtronic , C.P.I. en Intermedics dank ik voor hun genereuse financiëele bijdrage bij de tot standkoming van dit proefschript.

Rest mij nog mijn pacemakerpatienten te bedanken voor het in mij gestelde vertrouwen en hun inzet bij de pacemakerstudies.

Chapter I

HISTORY OF CARDIAC PACING

1.1. Electrical Stimulation

Biophysics is concerned with solving biological problems using the physical sciences. As such, cardiac pacing can be regarded as a very successful application of biophysics to cardiovascular medicine. The value of biophysical principles in medicine has long been recognized. Written descriptions of the salutary effects of electric forces are already found in ancient references. The electric catfish was pictured on tombs by the ancient Egyptians. An early "case report" describes relief of the pain of gouty arthritis in an Egyptian slave by stepping on an electric catfish. In ancient Greece and Rome the shocks of the electric torpedo fish were used as a cure for gout, headache and other maladies. Until the mid 19th century "electroichthyology" was considered by many physicians and particulary many charlatans as an important tool in the treatment for all kinds of disorders.

William Gilbert (1544–1603) is regarded by many to be the founder of electrical studies. In his principal work, " De Magnete, Magneticisque Corporibus et de Magno Magnete Tellure", the terms electric attraction and electrical force were first used. The word electric is deduced from the Greek word " electron ". which means beaming sun and amber. The power produced from amber by friction was named electrical force by Gilbert.

Early Christianity had an adverse affect upon medical progress, as diseases were regarded as a punishment for sin, and such chastening demanded only prayer, devotion and repentence. In addition, the human body was held secret and dissection was strictly forbidden. Perhaps the greatest services rendered to medicine by the church was a preservation and translation of the classical Greek medical manuscripts and the preaching of love of one's fellow creatures.

Until the theories of Galen (131–201 A.D.), the Greek physician who founded experimental physiology, there was no conception of a circular movement of the blood leaving the heart by the arteries and returning to it by the veins. Galen traveled to Italy and became chief physician for the gladiators in

Pergamum in 157 AD. He and his Roman colleagues were able to study the beating hearts of wounded gladiators. Galen proved that arteries contained blood and not a mixture of blood and air as was common knowledge. He still believed that air entered the right site of the heart and that the movement of the blood was governed by forces of ebb and flow. Without any doubt, the oscillatory movement of the pulse was recognized but he had no idea of its significance. One misconception was that each organ in the body had its own heart and depended on its own pulse rate. Until the invention of the metronome by Galileo (1581) in Pisa, it was not possible to compare the pulse rate of one patient to that of another. The golden standard until then was the physician's own pulse rate.

The first scientist who dared to differ from Galen's doctrines was Andreas Vesalius. In 1543, he published at the university of Padua " De Humani Corporis Fabrica," a fundamental work and the fruit of his own observations.

Gabriel Falopius, a disciple of Andreas Vesalius, suggested to his pupil, William Harvey, the idea of the circulation of blood in his work of the valves of the veins. It was William Harvey who demonstrated the function of the heart and the circulation. He published his brillant work, " De Motu Cordis " in Frankfurt, Germany in 1628. The only missing part was the capillary bed. Demonstration of its existence had to wait for the invention of the microscope.

The relation of electricity and biology became a subject of speculation in the 17 th century. Sir Isaac Newton, in the " Principia" (1687), wrote " a certain most subtle spirit with pervades and lies hidden in all gross bodies " and that" all sensation is excited and the members of animal bodies move at the command of the will, namely by the vibrations of this spirit mutually propagated along the solid filaments of the nerves." The first experiments of electrical stimulation of muscle were carried out by Abbe Beccaria in Turin, Italy and by Albrecht von Haller at Göttingen in the mid of the 18th century. However, it was Luigi Galvani (1737–1798) who opened the way to new research in the physiology of muscle and nerve and the entire subject of electrophysiology. His famous studies in the exposed muscle of the frog established for the first time that bioelectrical forces exist within living tissue. Galvani provided the major stimulus for his friend, but scientific opponent Volta, to devise the voltaic battery, a source of constant voltage in 1802.

Volta rejected Galvani's idea of an animal electric fluid as the electrical stimulus of muscular contraction. He thought that every electrophysiological

effect required two different metals as sources of current. In retrospect, Galvani and Volta were both partly right and partly wrong.

In an effort to prove Galvani's theory, Giovanni Galvani's nephew, Aldini and the French physiologist Marie Bichat conducted many electrical experiments on guillotinated victims 30–60 minutes after their execution, at the time of the French revolution. That time delay was probably the reason that they were not able to show the human heart response to Galvanic stimulation. Only the biceps and gastrocnemius muscles showed any reaction.

The first successful stimulation of the human heart post mortem was carried out by Vassali in Turin and Nysten in Paris. In Nysten's publication (1802) " Experiences sur le Coeur et les autres Parties d'un Homme decapite le 14 Brumaire, Au 11 ", he indicated that the ability to reactivate the arrested heart by electrical stimulation was first lost in the left, and subsequently for the right ventricle, the left auricle and the right auricle. Particular areas at the lower part of the superior vena cava (Sinus node!) were able to be reactivated long after cardiac arrest.

At that time, the earliest reports on reanimation by electricity were already published. Hunter (1776) advised that electrostimulation should be applied routinely as a last resort in death due to drowning. In the early part of the 18th century, Gerbezius (1719) and 40 years later, Morgagni (1761) recognized the association of a slow pulse with convulsive seizures. They concluded, however, that this form of epilepsy was caused from water in the brain. Adams (1827) believed that apoplexy was due to cerebral venous congestion secondary to a disease of the heart.

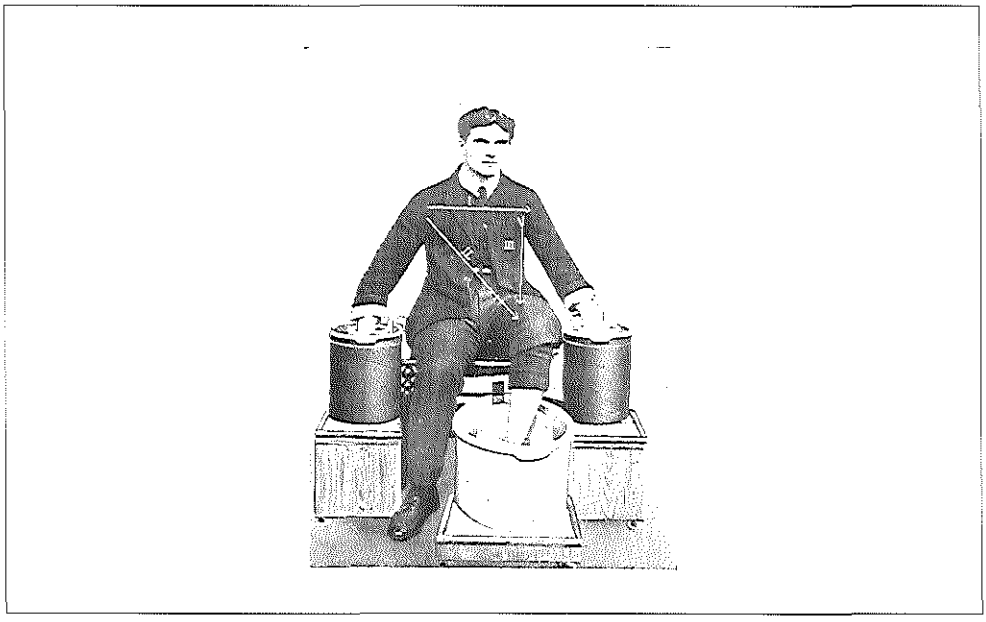
In the 19th century several case reports were published on bradycardia, asystole and syncope. In 1846, Stokes reviewed the literature on this subject and noticed the frequent correlation of syncope with aortic stenosis. He pointed out in his publication " Observations on some cases of permanently slow pulse" (1846) , that the apoplectic seizures were due to episodic deficits in the arterial blood supply to the brain.

In 1899, Huchard named the condition of slow pulse with apoplectic seizures after Stokes and Adams. In modern practise the names are ordered chronologically and often the name of Morgagni has been added.

The study of electrical potential was reactivated when Du Bois Reymond built an instrument to measure small potential differences in muscles, the galvanometer, in Paris in 1827.

In 1888, Gaskell described atrio–ventricular dissociation by damage of the A–V node region in the turtle heart. He named this condition heart block. He also postulated the existence of a conduction path between atria and ventricles. Earlier, Purkinje (1839) discovered the fibers which transmit electrical stimuli to the ventricular myocardium. Stanley Kent (1892) and Wilhelm His (1893) indentified the pathways between the atria and the ventricles. In 1907, Kent and Flack described the sinoatrial node and the following year Tawara revealed the last landmark of the specialized conduction system of the heart: the A–V node.

Using a galvanometer, Waller demonstrated that cardiac action currents could be recorded from the body surface. The first tracing was made from his own dog, Jimmy. However, clinical electrocardiography was born when Willem Einthoven in Leiden invented the string galvanometer. In his paper of 1906, a wide range of patient observations were reported including the earliest known recording of complete heart block. Einthoven coined the word electrocardiogram and he already standardized the recording method and the nomenclature (P,Q,R,S).



The string galvanometer of Einthoven

Earlier, Walshe (1858) suggested the importance of faradic stimulation of the nervi sympatici of the heart in treatment of cardiac arrest. Duchenne de

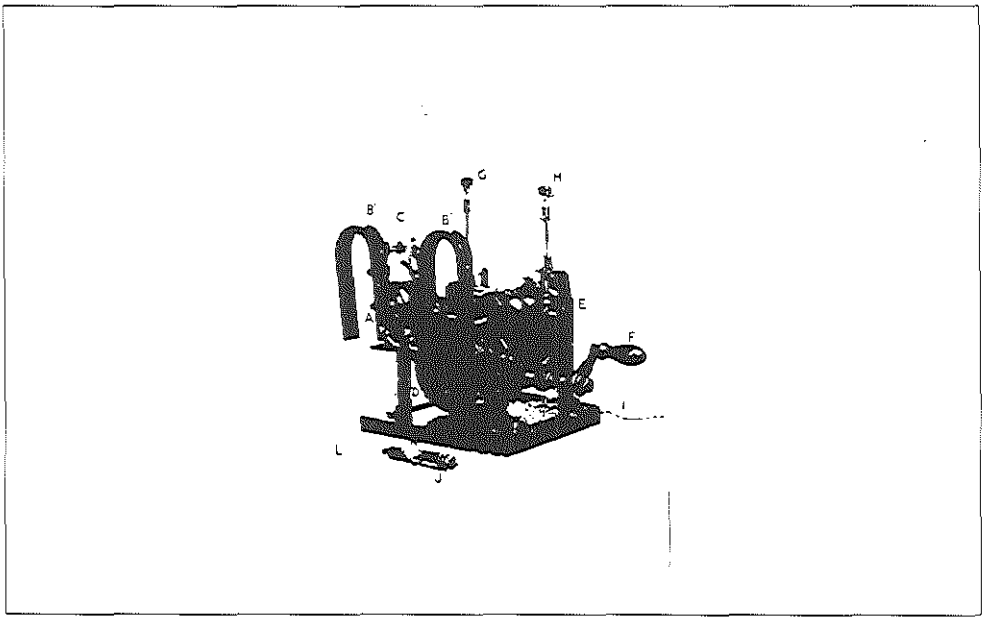
Boulogne (1870) used an induction coil to generate electrical stimuli which he applied over the precordial region to stimulate the heart.

1.2. Artificial Cardiac Stimulation

In 1880, the English physiologist John Mc Williams noted that, " Artificial excitation might be useful in arousing into action the heart that has been arrested by temporary cause." Hugo von Ziemssen (1882) carried out one of the earliest investigation involving electrical stimulation of the heart. He studied a young woman who had survived surgical removal of a bone tumor involving several ribs over the precordium and whose heart was covered only by skin. Application of electrodes to the precordium demonstrated in this patient that rhythmic stimulation by a sufficiently intense current at a rate above the intrinsic heart rate was possible. In 1900, Prevost and Batilli showed that electric currents could terminate ventricular fibrillation. These studies led to further investigations to stimulate the heart in ventricular standstill. However, it was not until 1927 that Marmorstein published the first report of endocardial stimulation of the heart. He conducted stimulation studies of the sinus node of the right and the left ventricle of dogs using unipolar, bipolar and tripolar electrodes.

The first pulse generator was designated by Gould (1929) in Australia. He used this generator with a unipolar, anodal, transthoracal pacing needle electrode.

The original work of Marmorstein and Gould remained almost totally unrecognized in the United States, as only Albert Hyman identified the potential value of these studies. In 1930, he described an external stimulator which stimulated the heart of a patient for several hours. Albert Hyman coined the term artificial cardiac pacemaker. In a 1932 publication, he described his ideal external pacemaker " small enough to fit into a doctor's bag, should have a common flashlight battery as current source, an interrupter mechanism, a timing device and a transthoracic atrial needle". The generator was driven by a spring motor and weighed over seven kilograms. To use it, a hand crank was turned, which activated the spring; as the spring wound back down, the device provided about six minutes of cardiac stimulation. Hyman was unable to interest anyone in the United States in his artificial pacemaker and finally in desperation gave it to a company in Germany where it was bombed by allied aircraft during World War II.

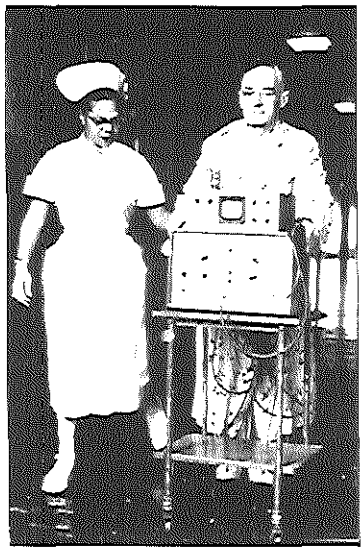


External Stimulator of Hyman

Hopps, Biglow and Callaghan in Canada (1949) unaware of the earlier work of Marmorstein, conducted a series of experiments in transvenous endocardial stimulation of the right atrium. Their attempts to resuscitate patients were often not successful because they did not recognize the importance of right ventricular pacing in the presence of atrioventricular block. The transvenous route was abandoned again. In 1952 Paul Zoll described resuscitation of the heart in ventricular standstill. He applied current pulses of 75–150V at 2 ms through metal paddles to the skin of the anterior chestwall. Zoll presented some of his successful cases of patients with Stokes–Adams Syndrome to the New England Cardiovascular Society in 1952. However, he was told that this external pacemaker was a marvelous toy but of no clinical value. Moreover, earlier external pacemakers were not without their problems: skin burns occurred, pacing was difficult in emphysematous patients and the pain of the chest muscle contractions with each pacemaker firing was not always tolerable.

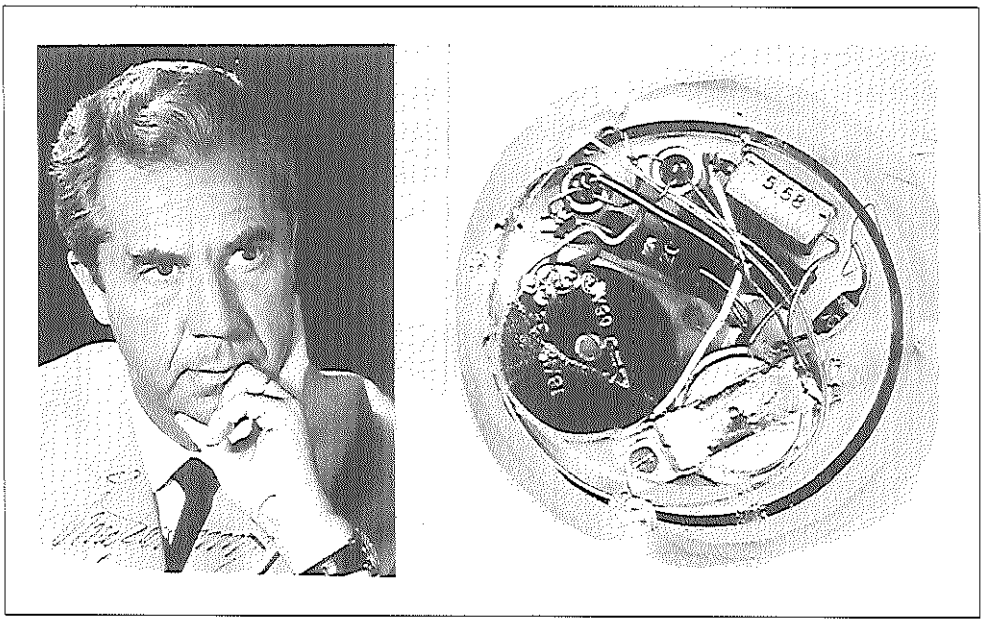
Lillehei in the USA and Weirich in Germany (1950) used epicardial wires to pace the heart temporarily when heart block complicated open heart surgery. Furman (1958) again raised the possibility of transvenous endocardial

pacing. The first clinical trial was in an eldery patient with chronic complete heart block undergoing colon resection for a carcinoma. The plan was to pace him only during surgery, but it turned out that the patient could not go without cardiac stimulation after surgery. The patient was then successfully paced externally for several days until sufficient intrinsic rhythm developed. This case proved that endocardial pacing was possible and probably reliable for the primary treatment of heart block with Stokes–Adams attacks.



The external stimulator used by Furman

Also in 1958, Earl Bakken, the founder of Medtronic (pacemaker company), invented the first portable external battery operated pacemaker which stimulated the heart through subcutaneous wires after cardiac surgery. The first pacemaker ever implanted in a patient was an externally rechargeable nickel cadmium powered Siemens–Elema generator. This implant took place in 1958 in Stockholm, Sweden were Senning placed a small electronic device on the surface of the patient's heart. The recipient was an electrical engineer who worked, together with Senning and Elmquist, on the development of a device "that would keep him from falling down".



First pacemaker ever implanted

Wilson and Greatbatch developed a battery–driven pacemaker that did not require external recharging and Chardack implanted the first prototype in New York (1959) that did not require external recharging. All of these generators were fixed–rate asynchronous devices that delivered their impulses without any consideration to any underlying spontaneous rhythm.

Noncompetitive–demand, or standby, pacing of the ventricle was introduced by Leatham (1956) and Nicks (1962) as an external instrument. For internal implants, Lemberg (1964), Goetz (1964), van der Berg and Thalen (1965) developed the first on–demand ventricular pacemaker. The first implantable atrial synchronous ventricular paced device was described by Nathan et al in 1963. This unit required an epicardial atrial sensing electrode as well as a pacing electrode to the ventricle. The pacemaker could only sense atrial activity and pace the ventricle. In the absence of regular sinus rhythm, the unit worked as a fixed–rate ventricular device with the possibility of competition with the intrinsic ventricular rhythm.

In the late 1960s, increasing numbers of patients were paced for sinus bradycardia. In patients with sinus bradycardia and intact A–V conduction, ventricular units were connected to atrial leads in an attempt to sense and pace the

atrium. Bifocal pacemakers were developed for patients with sinus bradycardia and heart block to provide atrioventricular sequential pacing.

The first universal dual–demand (DDD) was described by Funke in 1976 (Germany). This generator could pace and sense in the atrium and ventricle so offering the patient with heart block an optimal functional coordination of the atria and ventricles over a wide range of heart rates. Previously, technical problems related to atrial lead instability and the mercury zinc batteries had made clinical applications of the DDD generator impossible. The mercury zinc battery cells used initially lasted less than two years and were very bulky. They represented over two–thirds of the space and even more of the weight of the pulse generators. New power source technology was necessary.

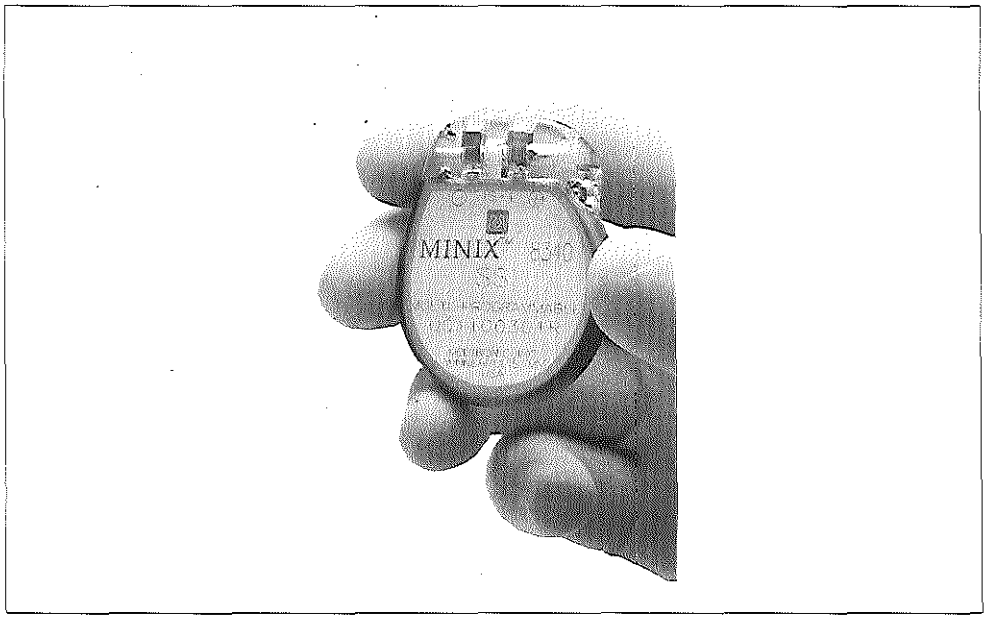
The first lithium–iodide powered units were implanted in 1972. This new battery technology was designed by Wilson Greatbatch. The generator longevity was expanded over 5 years. Atomic energy with a promise of a longevity of over 10 years had been used before (1964), but the cost, enviromental risk and nuclear restrictions limited their use.

As transvenous leads evolved it became obvious that they were easier and less traumatic to implant then those requiring a transthoracic approach. However lead dislodgment, perforation of the right ventricle and conductor fracture were major problems, severely limiting reliable long–term pacing. In the 1970s, lead design concentrated on problems with stable implantation and reliable long term use. The early leads had relatively high electrode areas, such as 50 to 80 mm^2 and more. It was recognized, that smaller higher current density electrodes were more efficient, reducing battery drain. Due to many innovations, smaller electrodes were developed with very low thresholds, low polarization (polarization increases the stimulation threshold) and much improved sensing. Reoperation rates decreased dramatically to a great deal also caused by the production of multiprogrammable pacemakers (Tarjan, 1972). Pacemaker programming technology started in 1962 (Kontrowitz), pacing rate and output could be changed by transcutaneousy insertion of a surgical needle into one of two self–sealing ports in the pacemaker enclosure.

The DDD pacemaker seemed to be the ideal solution for many clinical conditions in patients with a normal sinus node response to exercise or emotion. However, many pacemaker patients have sinus node disease and need a different sensor than the sinus node to meet the metabolic demand.

The first adaptive rate pacemaker, a pacemaker capable of altering the

paced rate on the basis of input from a sensor incorporated in the pulse generator, was proposed by Krasner (1966), used the respiratory rate as a sensor for exercise. The use of central venous pH to modulate pacing rate was suggested by Camilli in 1976, blood temperature by Weisswange in 1978, the Q–T interval by Rickards (1981), body motion by Humen and Anderson (1983), right ventricular stroke volume by Salo (1984), rate of change of right ventricular systolic pressure (1985), ventricular depolarization gradient by Walton (1985), minute ventilation by Alt (1985), and presystolic ejection interval by Chirife (1987). Since 1986, sensors are also built in DDD generators offering optimal rate increase and A–V synchrony. In a thirty year period, epoxy encapsulated implantable cardiac pacing has moved from a two discrete component photo flash battery–powered device to multiprogrammable and multifunctional micro–miniaturized chip technology in a titanium can.



Pacemaker anno 1990

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Chapter II

DEFINITIONS AND TECHNOLOGY IN CARDIAC PACING

2.1. Introduction

The cardiac pacemaker provides an effective and widely available life support system to patients who would otherwise suffer significant morbity and mortality. A pacemaker's mode of response to cardiac signals combined with its pacing and sensing function is termed its mode of operation. The various modalities of pacing may be viewed as three distinct groups: single chamber pacing, dual chamber pacing and rate modulated pacing.

2.2. Modes of Cardiac Pacing

Modes of cardiac pacing were described in 1974 using a three letter code developed by the International Intersociety Commission for Heart Disease resources (I.C.H.D.)[4].

1 The first letter indentifies the chamber(s) paced, as A (Atrium), V (Ventricle) or D (both).
2 The second letter indentifies the chamber(s) sensed, as A (Atrium), V (Ventricle), D (both) or O (none) for fixed mode pacemakers.
3 The third indentifies the mode as I (Inhibited), T (Triggered), or D (both).

This three letter code was expanded to a five letter code in 1981 to incorporate letter four for programmability and telemetry and letter five for antitachycardia functions. The most widly used code is the NASPE (North American Society of Pacing and Electrophysiology) and BPEG (British Pacing and Electrophysiology Group) " five position generic code "[5] (Table 1).

The first three positions are the same as in the ICHD code.

Position four incorporates R for rate modulation, replacing the asterisk used for this designation, and retains programmability and telemetry codes. Position five indicates the presence of one or more active antitachycardia functions whether automatically or manually initiated. The pacing modes are listed in section 2.4

Table 1 NASPE/BPEG Generic (NBG) Pacemaker Code[1]					
Position	I	II	III	IV	V
Catagory	Chamber(s) paced	Chamber(s) sensed	Response to sensing	Programmability, rate modulation	Antitachy–arrhythmia function(s)
Letters	O–None A–Atrium V–Ventricle D–Dual (A+V)	O–None A–Atrium V–Ventricle D–Dual (A+V)	O–None T–Triggered I–Inhibited D–Dual (T+I)	O–None P–Simple programmable M–Multiprogrammable C–communicating R–Rate modulation	O–None P–Pacing (antitachy–arrhythmia) S–Shock D–Dual (P+S)
Manufacturer's designation only	S–Single (A or V)	S–Single (A or V)			

[1] *Bernstein A, Camm AJ, Fletcher RD, et al: The NASPE/BPEG generic pacemaker code for antibradyarrhythmia and adaptive rate pacing and antitachyarrhythmia devices. PACE 1987; 10 (July): 795.*

2.3. Definitions

The following is a list of abbreviations and definitions which will be used throughout the next chapters.

P wave : a native atrial depolarization.

R wave : a native ventricular depolarization.

A : an atrial stimulus.

P–R interval : the interval from the moment of sensing of a P–wave to the onset of the ventricular complex.

A–V interval : the interval from an atrial stimulus or the point within the P–wave at which atrial sensing occurs to the synchronised ventricular stimulus.

A–R interval : the interval from an atrial stimulus to the onset of the native R– wave.

V–A interval : the interval from a ventricular stimulus to the retrogradely conducted atrial depolarisation.

A E I (V A I) : Atrial Escape Interval. The interval from a ventricular paced or sensed event to the next atrial output.

V E I : Ventricular Escape Interval. The interval from a ventricular paced or sensed event to the next ventricular output.

M T R I : Minimum Tracking Rate Interval. The minimal interval or the shortest time between two ventricular pulses.

M T R : Maximum Tracking Rate. The maximum rate at which 1:1 ventricular tracking of native atrial activity can occur.

M S R : Maximum Sensor Rate. The maximum pacing rate allowed as a result of sensor control.

A R P : Atrial Refractory Period. Atrial refractory period refers to the total atrial refractory period which consists of the A–V interval and the P V A R P

P V A R P : Post Ventricular Atrial Refractory Period beginning with a ventricular stimulus or sensed event.

V R P : Ventricular Refractory Period beginning with a ventricular stimulus or ventricular sensed event.

Blanking period : a brief period of ventricular sensing refractory coincident with an atrial stimulus.

L R L : Lower Rate Limit. The minimum paced rate in the atrium and ventricle in the absence of sensed atrial activity.

U R L : Upper Rate Limit. The maximum rate to which the ventricle will be allowed to track atrial activity only if T A R P is shorter than U R L interval.

2.4. pacing modes

A O O : atrial pacing at fixed rate; no sensing.

V O O : ventricular pacing at fixed rate; no sensing.

D O O : atrial and ventricular pacing at fixed rate separated by a period of time called the A–V interval; no sensing.

A A I : atrial pacing and sensing; inhibited mode (atrial demand).

A A I R : A A I pacing with sensor–based increases and decreases in paced atrial rate in response to changes in metabolic demand.

V V I : ventricular pacing and sensing; inhibited mode (ventricular demand).

V V I R : V V I pacing with sensor–based increases and decreases in paced ventricular rate in response to changes in metabolic demand.

A A T : atrial pacing and sensing; triggered mode.

V V T : ventricular pacing and sensing; triggered mode.

V A T : ventricular pacing, atrial sensing, tracking only; no ventricular sensing.

D V I : dual–chamber pacing, ventricular sensing; pacing no atrial sensing.

V D D : ventricular pacing, atrial and ventricular sensing; tracking and inhibited respectively (P–wave synchronous pacing); no atrial sensing.

D D I : dual–chamber pacing and sensing, inhibited mode without triggering of a ventricular response from the sensed P–wave.

D D I R : D D I pacing with sensor–based increases and decreases in paced atrial and/or ventricular rate in response to changes in metabolic demand.

D D D : dual–chamber pacing and sensing; inhibited mode and tracking atrium.

D D D R : D D D pacing with sensor–based increases and decreases in paced atrial and/or ventricular rate in response to changes in metabolic demand.

2.5. Pacemaker Technology[1–3,10–12]

The basic function of the pacemaker is the delivery of a stimulation pulse when required. In order to do this the pacemaker must be able to detect intrinsic cardiac activity, and deliver a stimulus which will give rise to a cardiac contraction, and time the delivery of the stimulus so that this is delivered at the correct moment or to inhibit the delivery of a stimulus if required. To perform these basic functions, the pulse generator system is comprised of three important components:

- The Power Source
- Cardiac Stimulation And Sensing Circuitry
- Electrode And Leads

2.6. The Power Source

The power source has two tasks; to provide electrical current to run the electric circuitry of the pulse generator and to stimulate cardiac tissue periodically through a lead.

The power source can be regarded as a reservoir of electric current. Its capacity is usually measured in units of charge (current X time in ampere hour) and it passes charge through an electric circuit in the form of current (charge per unit time) by converting chemical potential energy into electrical potential energy.

Pacemaker design, performance characteristics and longevity are profoundly affected by battery cell electrochemistry. The implantable pacemakers used in the 1960s had mercury zinc cells which suffered from high self–discharge currents, low energy density and low voltages[4]. The reaction by which mercury–zinc batteries function produces gas, which must escape or the cell will explode. The gas can permeate epoxy resin, but its production precludes the enclosure of the pulse generator in a hermetically sealed can. The introduction of lithium–based chemistries in 1973 resulted in a dramatic change in both pacemaker design and longevity[6–9].

Currently available lithium–cell pacing systems have under optimal settings an expected lifespan of 10 to 15 years[8,9]. The longevity of lithium batteries is only exceeded by nuclear power sources; recent data indicate that more than 80% of the plutonium 238 powered pulse generators survive more

than 15 years[7,9]. However, only a small number of patients need such a long life power source and considerable nuclear regulation contraints strongly limit their use.

In the lithium batteries, lithium serves as the anode with another element or compound as the cathode. Lithium cells have an increased energy density as compared with earlier cell chemistries and can be hermetically sealed. Within the familiy of lithium–based cells, there are substantial differences in battery longevity. Figure 1 shows the long term cumulative survival of pacemakers based on their lithium–cell chemistry. (Adapted from Billitch M. et al,7). The lithium–iodide cell and lithium–cupric–sulfide cell account for well over 90% of all lithium–based pacemakers on the market today.

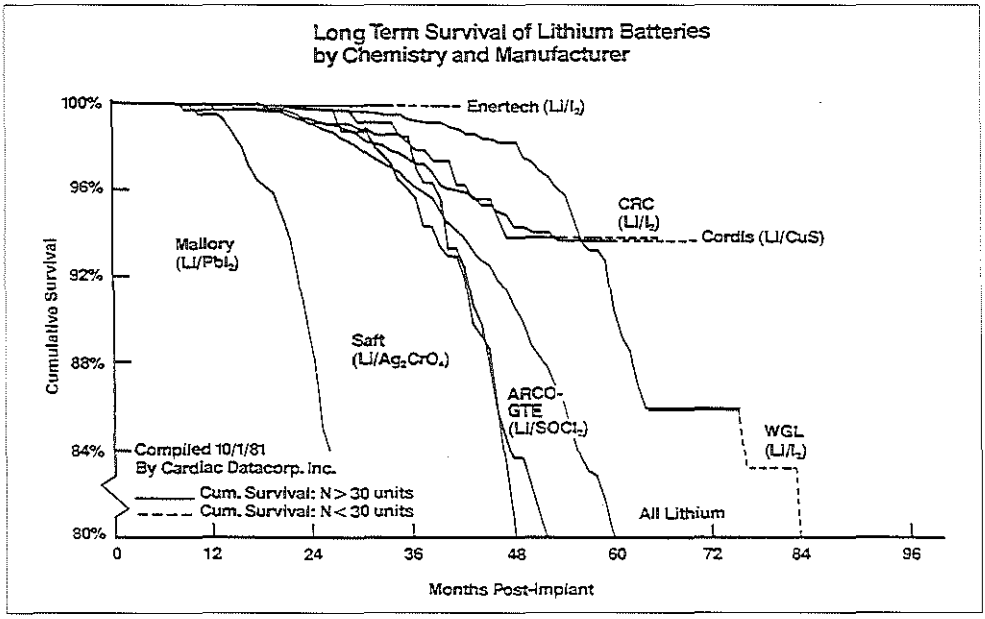

Figure 1. Cumulative survival of lithium cells.

The lifespan of the power source is a function of the capacity of the electronic circuit, the pacing rate, the output voltage or current, the pulse duration, the impedance of the lead, impendance of the lead tissue interface (stimulation impedance) and the resultant percentage time of pacing. The self discharge rate for the modern lithium–powered units is less than 1% per year.

The need for pacemaker reoperation has been significantly reduced with the application of the lithium battery[10–12]. Moreover, lithium chemistry pro-

vides a reliable end–of–life behavior, so that battery depletion is relatively simple to anticipate during pacemaker follow–up. An important characteristic of lithium batteries is the gradual decrease in voltage at the end of the battery's life. The cell slowly decreases in output voltage over its lifetime, for example, from its original nominal open circuit voltage of 2.8 Volts to an elective replacement time (ERT) of approximately 2.1 Volts (Figure 2).

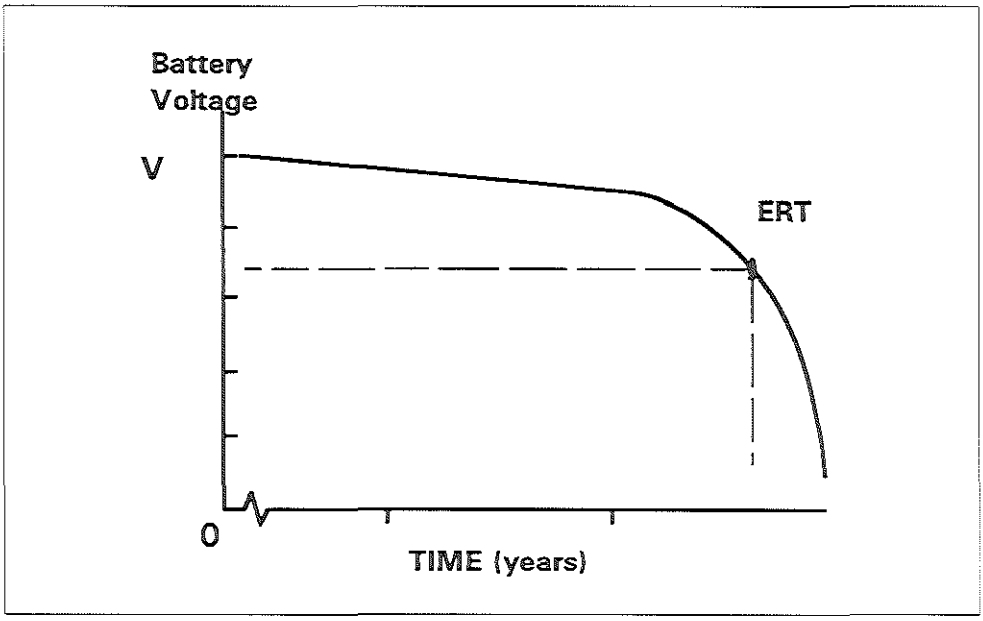

Figure 2. Output voltage over pacemaker lifetime.
ERT = Elective replacement time.
BOL = beginning of life.

The pulse generator's output voltage, however, remains constant throughout the entire pulse generator lifetime. Most pulse generators have an ERT indicator, which consists of a gradual linear reduction in magnet test rate from, for example, 100 ppm at beginning of life (BOL) to 90 ppm at ERT. Since this is a gradual linear reduction, the magnet test rate at any time between BOL and ERT can be taken as an approximate indicator of power source status. When the magnet test mode is enabled with an externally applied magnet, a reed switch within the unit converts the unit to a fixed rate, asynchronous mode and a pulse width of 1.0 msec. The programmer displays its measured magnet rate, the calculated battery status and, in some, units the actual battery voltage, in-

ternal and lead resistance and expected time until battery depletion. The pulse generator should be replaced when it reaches ERT. In most generators, at nominal settings, 100% pacing is available for a approximately 60–90 days after ERT has reached.

2.7. Cardiac Stimulation And Sensing Circuitry

Pacing and sensing present separate functions in a pacemaker and testing of the stimulation and sensing characteristics at implantation and during follow–up is essential to establish a reliable pacing system.

The cardiac stimulation threshold is defined as: the minimum amount of cathodial electrical energy required to produce consistent cardiac depolarizations given through an electrode and applied outside the cardiac refractory period. Stimulation threshold may be expressed in terms of voltage, current, energy or charge. The threshold of stimulation is determined by a number of factors related to the myocardium, the pulse generator and the lead electrode. Myocardial factors include distance to viable tissue (beyond fibrosis or scar tissue), time after implantation, cardio–active medication and electrolyte balance. Pulse generator–related factors are pulse duration and unipolar or bipolar stimulation configuration. Lead and electrode factors affecting threshold are type of lead insulation, electrode material and composition, electrode tip, surface area, distance from viable tissue and lead fixation mechanism.

The stimulus current density must be sufficiently high and have sufficient duration to depolarize a large enough group of cells to initiate myocardial depolarization.

The strength duration curve gives the typical relationship of the strength of the current, voltage and two derived functions – charge (current x time) and energy (current x voltage x time) versus pulse duration (Figure 3). As the pulse duration decreases, current and voltage requirements increase while the charge expended at threshold decreases. Energy at threshold is lowest at 0.5 to 1.0 msec pulse duration, increasing at shorter and longer durations.When pulse width is increased the current or voltage required for a response does not lessen for pulse durations longer than 1.0 msec. The energy relation resulting from the voltage x current x pulse width shows that the most efficient pulse width is in the 0.5 msec range (Figure 3).

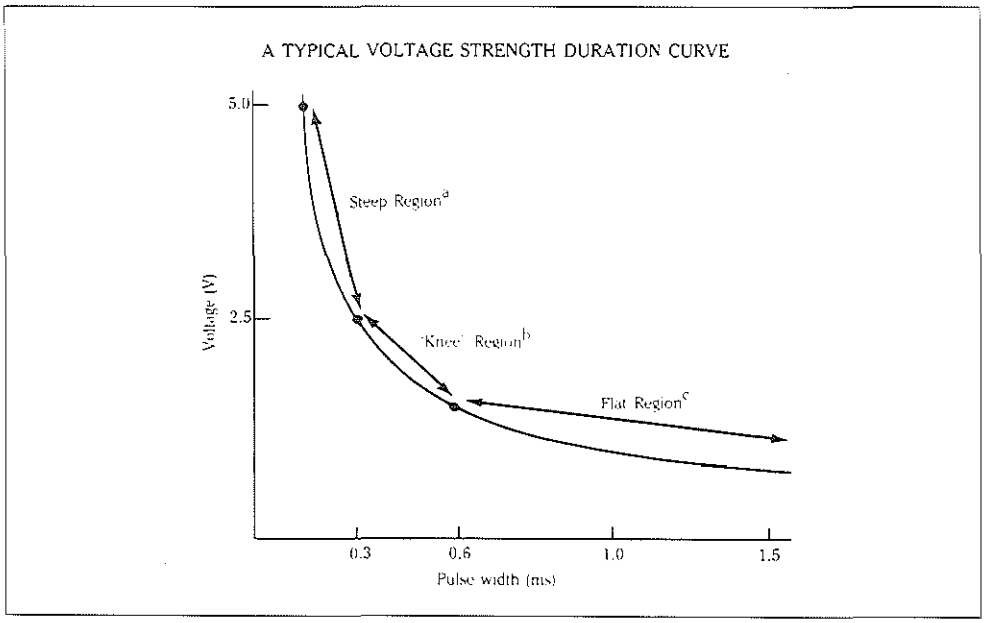

Figure 3. The strength duration curve.

The most common method for changing the output of a programmable pacemaker is to change the voltage or the pulse duration. On most generators, an automatic threshold testing feature is present to aid in determining the minimum ventricular and/or atrial pulse width at a particular impulse amplitude or the minimum pulse amplitude at a selected pulse width needed for capture. When doing an auto threshold test in some of the currently available pacemakers the programmer automatically steps down the pulse width or pulse amplitude while monitoring the ECG. Removing the programmer head or achieving the minimum available setting will immediately restore the original programmed settings.

2.7.1. Stimulation threshold

The voltage safety margin is defined as the ratio of the output voltage devided by the treshold voltage of the same pulse width.

The stimulation threshold may vary during daily activities, posture changes and during coughing, deep inspiration and due to medication use. However, the most important changes in stimulation threshold occur the first one to three weeks postoperatively due to mechanical irritation and myocardial scar

formation at the electrode tissue interface.

In some patients the threshold peak may be five times the voltage at implant. Typically the treshold will stabilize after 8–12 weeks post implant to 2–3 times the voltage at implant. The need of the voltage safety margin to ensure 100% capture during the lead maturation process has decreased significantly because of advances in both electrode design and the use of steroid eluting electrodes, which blunt the local tissue response. Soon after implantation, the initial output setting should be at least 5 times the threshold energy. A safety margin of 100% of threshold energy will provide adequate patient safety if the long–term threshold is stable (steady for at least six months after implant). The objective of cardiac pacing is to ensure 100% capture when the intrinsic cardiac rhythm fails. When the output of the pacemaker has been programmed at or just above stimulation treshold this objective will certainly not be achieved.

New lead technology makes it possible to program the the implanted pacemaker at an output of 2.5 V with a pulse width of 0.5 msec. This provides the patient with the same degree of safety that the old standard 5 V/0.5 msec output has provided since 1973. The pacing threshold in the atrium and ventricle are similar in principle and there is no difference between the two in determining threshold or setting output.

2.7.2. Safety margin and conserving energy

As a general principle, stimulus amplitude should be kept at 5 V and 0.5 msec stimulus duration in the first and second month post implant, except perhaps for the steroid electrode[15]. When the electrode has matured, stimulus amplitude should be reduced to a level equal to battery voltage after it has been demonstrated that sufficient safety margin is established. The reason is that circuitry used to obtain stimulus amplitudes higher than the battery voltage are energy inefficient. Doubling battery voltage gives us rise to a four–fold increase in stimulus energy and so is the energy taken from the battery. Relatively little energy is saved by reducing the stimulus amplitude below the battery voltage. As can be seen from Figure 3, the pulse width should be programmed no less than 0.4 msec for safety reasons. As far as battery consumption is concerned reducing pulse width will not prolong battery life significantely and will only increase the risk of losing capture. In Figure 4 safety margin is unacceptably small. The safety can only be increased to an acceptable level by increasing the pulse amplitude to 2.5 V and not by increasing the pulse width.

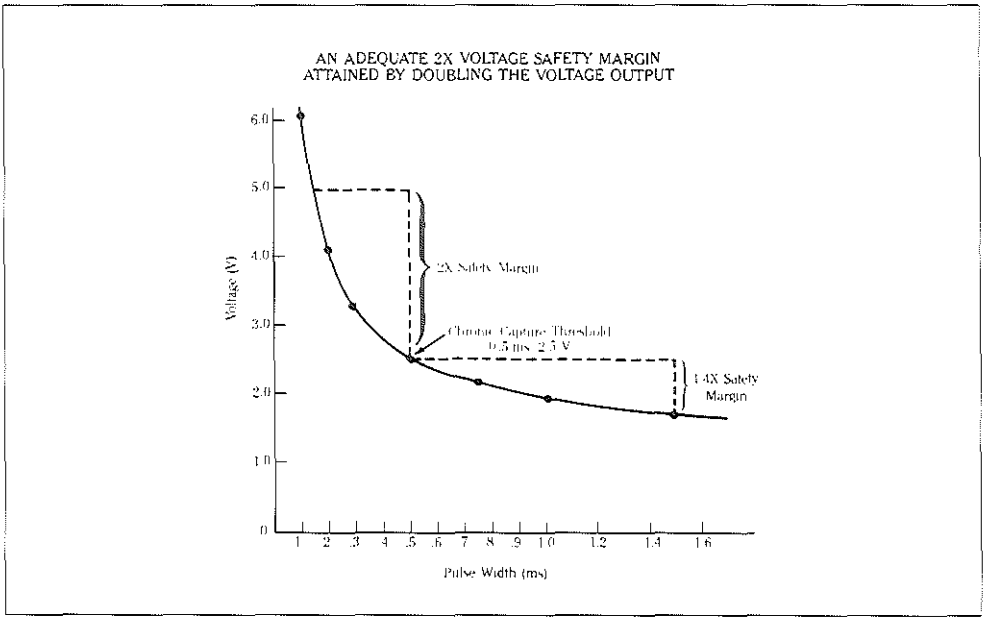

Figure 4. Voltage safety margin.

2.7.3. Sensing circuits

2.7.3.1. Introduction and definitions

The intended role of the sensing circuit of the pacemaker is the successful and continuous detection of spontaneous cardiac depolarizations. This process is complicated by the fact that all cardiac signals, whether depolarization or repolarization events and other non–cardiac electrical signals, can have a frequency spectrum which can produce a well recognized pattern for the sensing circuit of the pulse generator. The sensing circuit has two main functions: to detect (filter), and to amplify the incoming signal (Figure 5).

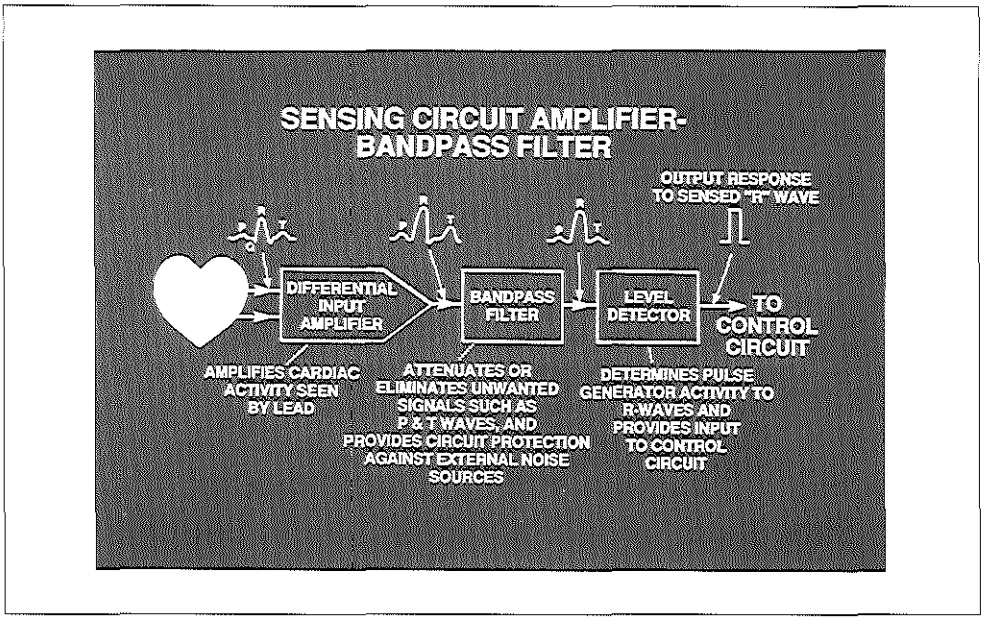

Figure 5. sensing circuit.

The sensing amplifier magnifies the voltage difference that appears across the anodal (positive) end and cathodal (negative) end of the sensing circuit. In a unipolar pacemaker system, the sensing circuit forms a relatively large electrical field between the cathodal end of the pacemaker lead in the heart and the can of the generator. In bipolar pacing systems, the electrical sensing field is small; it consists of the two distal electrodes of the pacemaker lead (Figure 6).

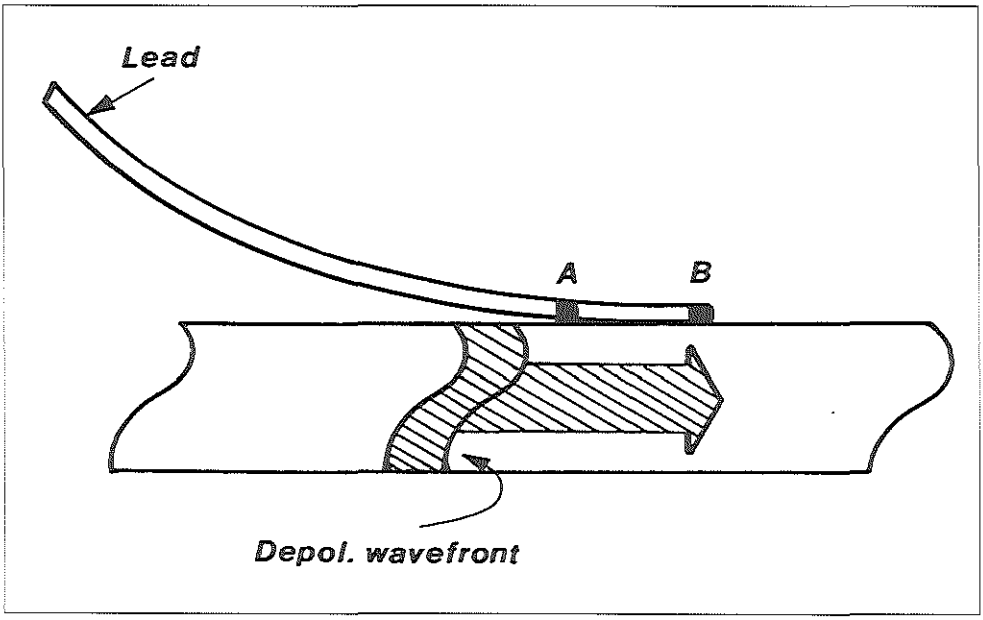

Figure 6. Uni – Bipolar pacing system.

The cardiac signals are picked up by the electrode(s) when a depolarization wave front travels through the heart. The greater the distance from the site of the activity, the smaller is the amplitude of the potential fluctuation at the electrode(s) site. It is the difference in potential between the two electrode sites that is amplified by the pacemaker. A different orientation of the electrical field (bipole) can result in a larger or smaller bipolar signal than the unipolar signal from either electrode. In bipolar sensing, the reflections occur at slightly different moments, and are not effected by subtraction of signals, as when recorded from two different electrodes at the same time.(Figure 7).

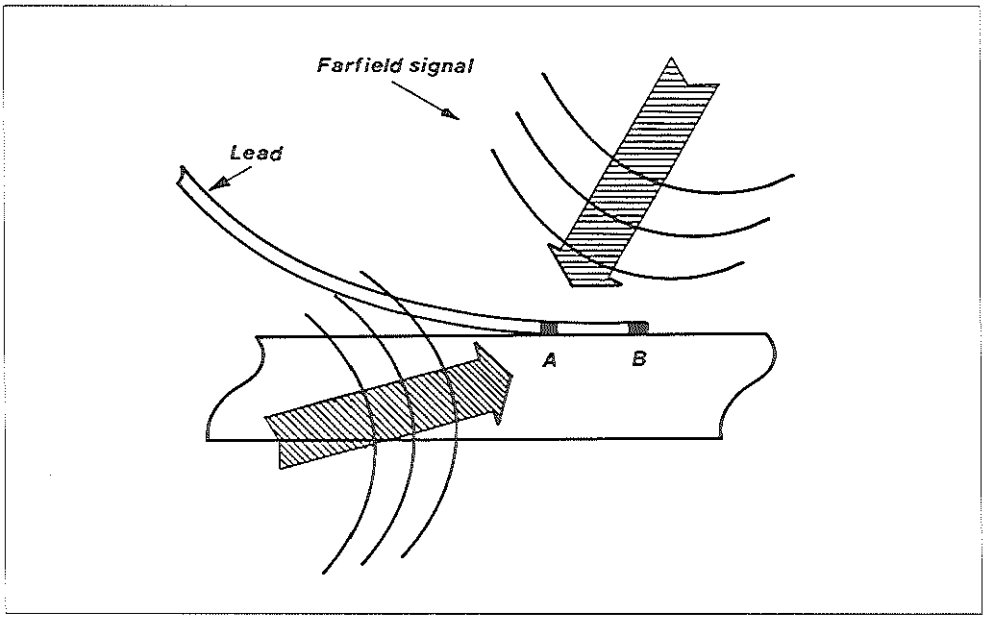

Figure 7. Bipolar sensing.

Signal detection of the sensing circuit is based on an electronic analysis of the myocardial depolarization signal it received. Signal level detection of the amplitude of the incoming signal is the main function of the band–pass filter. Once the frequency of the signal is determined, the amplitude must exceed a level defined by the band–pass filter for that frequency. If the amplitude is above the predetermined level, the signal will be processed further. This complex screening process is necessary to eliminate sensing undesirable signals from the heart, skeletal muscle, and external electromagnetic frequencies. However, the amplitude and frequency range of skeletal muscle myopotential signals overlap that of the R wave and can easily be picked up by the sensing amplifier (Figure 8).

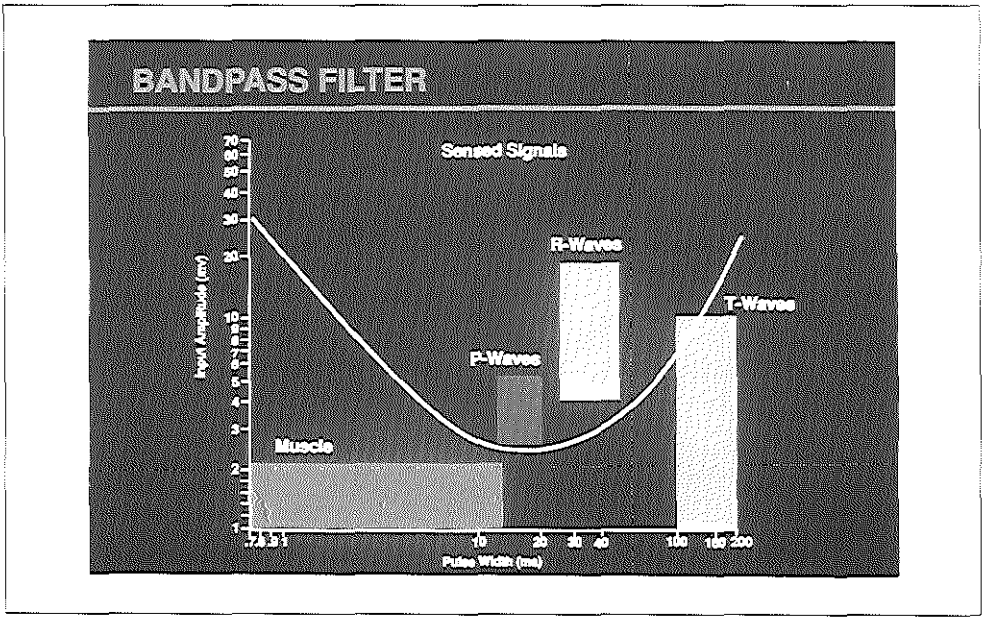

Figure 8. Band pass filtering of incoming signals.

Table 2 POLARITY DIFFERENCE: UNIPOLAR vs BIPOLAR		
	UNIPOLAR	BIPOLAR
Lead size	+	
Lead repair	++	
Stimulation threshold	0	
Myopotential sensing cardiac		+
Myopotential sensing skeletal		+
Farfield sensing		++
Crosstalk		+++
EM interference		++
Pectoralis stimulation		+++
Stimulus artefact size	+++	
Programming flexibility		+++
Special pacing systems		+++

EM = electro–magnetic. 0 = no difference. + = better, not significant. ++ = significantly better, not of clinical importance. +++ = significantly better and of clinical importance. (Adapted from Mond H.G, ref [32])

Unipolar pacing systems are, due to the large sensing field between the endocardial electrode and the pacemaker can, inherently susceptible to myopotential sensing. Further, bipolar sensing is advantageous because it is less susceptible to electromagnetic interference and atrial sensing of far–field QRS signals and other sensing artefacts that can give rise to self inhibition (Figure 9)(Table 1).

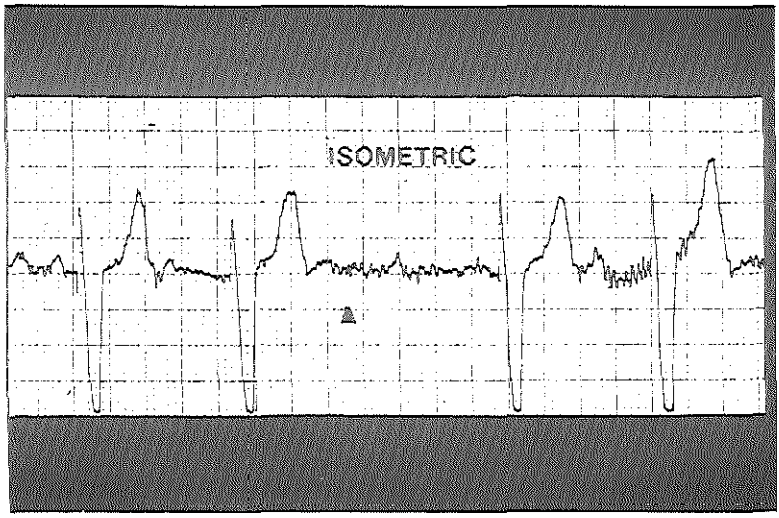

Figure 9. Self inhibition of VVI pacemaker by myopotentials.

Over the years, manufacturers have tested many different designs of band–pass filters in an effort to separate the intrinsic R–and P–waves from intracardiac repolarization phenomena and non–cardiac signals. The band–pass filters reject relatively slow moving signal components as well as very rapidly moving signal components and only accept signals that fall within the range selected. However, under the existing circumstances, a sensing amplifier designed to be optimal for all patients does not exist. In addition, natural changes in intracardiac wave form occur with time and the progress of disease in any given patient can influence intracardiac signals.

2.7.3.2. Intracardiac electrogram

Measurement of the endocardial signal available for sensing at the time of pacemaker implantation is a simple but important procedure. The characteristics of the intracardiac signal are its amplitude in mVolts and the maximum rate of change of the potential measured in mV per msec (slew rate) (Figure 10).

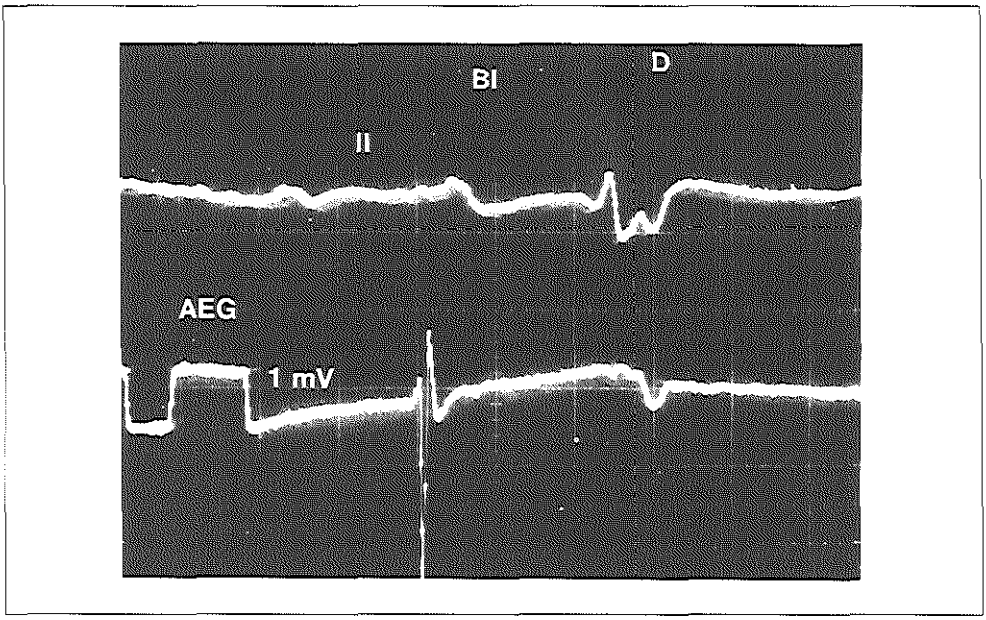

Figure 10. The characteristics of the intracardiac signal.

The two major components of the intracardiac–electrogram signal as seen by the sensing circuit of the pulse generator consist of a rapid deflection (the intrinsic deflection) and the slow deflection. These intracardiac events are different from the cardiac events seen on the surface ECG.

Electrocardiograms should be recorded on paper by connecting the V lead of an electrocardiograph to a unipolar electrode or, in case of a bipolarlead, connecting the right and the left arm leads to the distal and proximal electrodes of the pacing catheters. An examination of the morphology of the electrogram can disclose the potential of early sensing complications. A signal of at least 5 mV is needed for adequate long–term ventricular sensing. For stable acceptable chronical sensing in the atrium, the signal should exceed 2 mV. Analysis of the slew rate equires a high–speed physiologic recorder or an oscilloscope. The slew rate is important when intracardiac signals of marginal amplitude are

obtained. Minimal slew rate values for the ventricle and atrium are respectively 0.5 V/s and 0.35 V/s. At the time of pacemaker implantation, in most implanting clinics, the amplitude and slew rate signal will be measured by means of a commercially available pacing system analyser (PSA). Manufacturers usually design their PSAs to have the same sensing characteristics as their pacemakers. When the PSA and the pacemakers are made by different manufacturers, the recording of the intracardiac signals on ECG paper is even more important.

2.7.3.3. Sensing threshold

The sensing threshold or sensitivity of a pulse generator is the minimal intracardiac rapid deflection amplitude that will be detected at a given sensitivity setting to suppress the output of the pacing circuit. To assure chronic sensing efficiency, the intracardiac signal amplitude at implant should be at least 3–4 times the minimum sensitivity setting of the pacemaker channel. The three–fold safety margin applies primarily to acute lead measurements; as the lead matures, the measured signal amplitude may decrease significantly. The smaller the intracardiac signal at implant the higher the sensitivity setting (the higher the gain of the sensing amplifier) and the greater the risk of encountering problems with interference. Moreover, a safety margin is necessary to accommodate the variation in intracardiac signals during daily life. Standing up from lying down, or bicycle riding instead of sitting, can decrease the measured intra–atrial deflection in some patients by more than 50%[16,17]. These charges necessitate a reliable and large enough intracardiac signal at implantation.

When evaluating a chronic lead, a minimum two–fold safety margin should be demonstrated. The incorporation of a sensing circuit implies the risk of unwanted recycling of the generator.

In principle, every signal can be detected when its amplitude is superior to the nominal setting of the sensing circuit, the signal has an adequate frequency and steepness and it is delivered outside the cardiac refractory period.

2.7.3.4. Undersensing

Undersensing occurs when a pacemaker is unable to detect autonomous cardiac complexes. Undersensing of the cardiac impulse will result in failure to inhibit the discharge of a demand pacemaker and may also result in competi-

tion with the underlying rhythm. If the pacemaker fires during the vulnerable period of the cardiac cycle, the potential exist for the induction of a tachyar–rhythmia, although the latter occurs infrequently. The most common sensing defects observed in clinical practice are due to an insufficient amplitude and/or slew rate of the observed intrinsic cardial signal. Lead displacement is the most common cause of undersensing that occurs soon after implantation; fibrosis around the electrode tip may result in a similar problem later on.

2.7.3.5. Oversensing

Oversensing is almost exclusively a unipolar sensing problem and consists of the detection of signals other than the intrinsic P and/or QRS complexes. The most frequent causes are detection of myopotentials, detection of the intrinsic T–wave, and detection of after–potentials. Diagnosis is based on the presence of abnormally long cycles of variable duration that disappear after a magnet is placed over the pacemaker site.

In programmable units, changing of the sensitivity may result in correction of the abnormality; but the more serious problem of lead fracture must be excluded each time oversensing is observed.

2.8. Electrode And Leads

2.8.1. Introduction and definitions[12,18,19,20,29]

The pacemaker lead is the connecting link between the heart and the pulse generator. It consists of an electrode, the uninsulated ending of the lead which is actually in direct contact with the heart, the intervening conductor coil and a proximal terminal pin for connection with the pacemaker header (Figure 11).

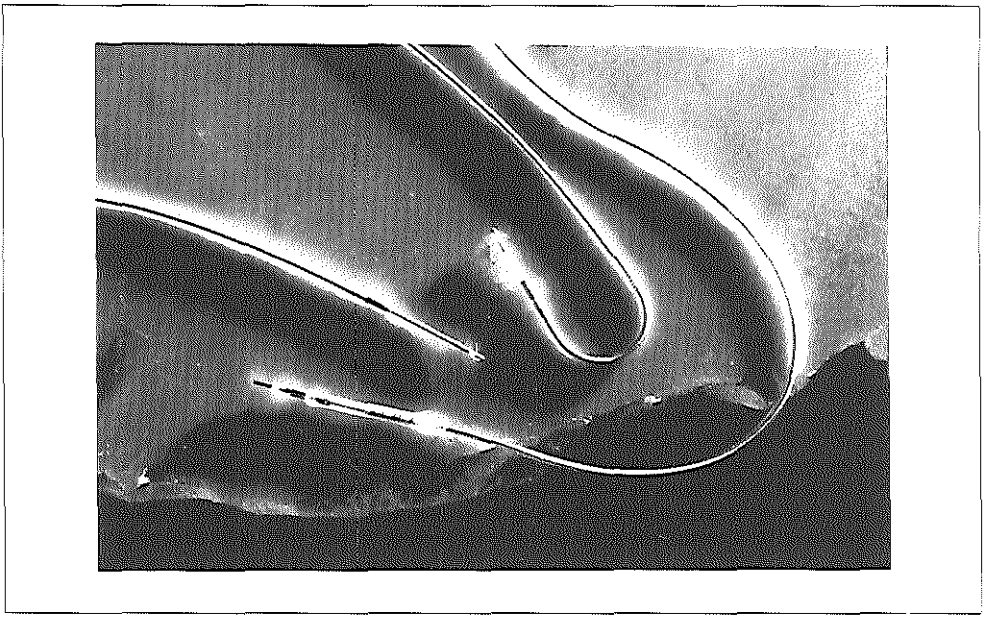

Figure 11. Pacemaker lead.

The entire lead is insulated from the connector to the electrode to ensure the efficient transfer of electrical energy from the pacing device to the heart. The major problems with the transvenous route have been the frequent displacements and the excessive threshold rise. These have resulted in a continuous search for more stable endocardial electrodes. Several methods have been tried to hook and stabilize the lead tip in the trabecules of the right ventricle or right atrial appendage. Fixation and stability are achieved by means of leads, which may be either passively or actively fixed in place. Passive (atraumatic) fixation leads are placed in position at the time of implant where they remain opposed to the endocardium, enmeshment facilitated by flanges, fins or tines in the trabeculae furnishes initial stability (Figure 12).

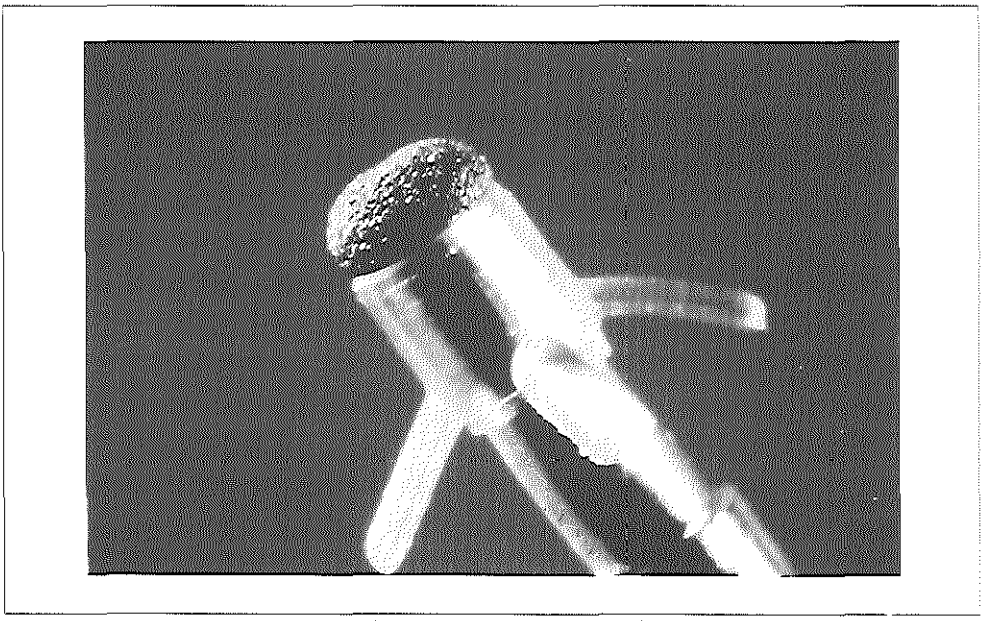

Figure 12. Fixation mechanism of electrode.

Fibrous growth from the endocardium around the lead tip eventually causes actual fixation of the lead.

Active (traumatic) fixation leads have a screw–like mechanism, which allows immediate fixation during implantation. The introduction of dual–chamber and rate–modulated pacing systems has tended to increase pacemaker current drain. Moreover, a trend toward smaller devices is made possible by the application of microelectronics in the pacing industry. These developments have stimulated new lead and electrode designs with an emphasis placed on saving energy[19–21].

Through introduction of porous and high microsurface area electrodes (platinum–iridium mesh, carbon), sensing characteristics have been improved and stimulation energy reduced[20,22]. A microsurface area electrode permits the ingrowth of fibrous tissue into the electrode improving electrode anchoring and increasing the effective surface area for sensing and pacing.

2.8.2. Electrode

At the present time, the most used electrodes are the carbon–ring electrode, the carbon–coated porous titanium electrode, laser porous dish electrode, and target tip electrode (platinum or platinized titanium). Particularly, target tip

electrodes show low polarization effects. Polarization voltage arises from the the potential difference at the electrode–tissue interface that occurs during the stimulation. This factor may be detrimental by contributing in major way to sensing (source) impedance. Large electrodes facilitate sensing because of low source impedance. Smaller electrodes deliver higher current densities which reduce stimulation thresholds. Studies[12,18,21] have shown that electrodes with a surface area between 6–10 mm^2 constitute the best compromise. Steroid electrode leads introduced in 1987 have been shown to save even more energy[13,14,23]. The corticosteroid is eluted from the electrode and dampens both the early and late affects of the inflammatory process on the rise of stimulation threshold after implantation. In 1988, Mond reported that the CapSure™ steroid eluting lead had exhibited very low constant stimulation threshold for the first 5 years postimplantation[22]. Klein et al[23] showed clinically favorable characteristics of steroid–eluting leads in comparison with platinum and laser–dish alternatives.

2.8.3. Leads

The stability of permanent transvenous pacing leads without an active or a passive fixation mechanism is poor. In the early 1970s, repositioning of the lead in the first several weeks after implant was reported at up to 30%. Implanting an atrial lead is still a major problem for many physicians resulting in the inappropriate low application of physiologic pacing systems by pacing the atrium.

The pacing industry, in cooporation with implanting physicians, have developed numerous stabilization devices to prevent lead dislodgement.

2.8.4. Passive fixation

Passive fixation devices use tines, flange, fins or conical protrusions. Since 1979, tined leads have become the most commonly used stabilization device. The tines hook behind the trabecules of the right ventricle apex or the right atrial appendage. Fibrous growth the endocardium around the tines causes the chronic fixation of the lead. Tined leads reduce reoperation for ventricular lead dislodgement to 1% or less and for atrial dislodgement to 5% or less[28,29]. The excellent ingrowth of these leads has a disadvantage, because removal of the leads from the atrium and ventricle is very difficult. Several reports mention the impossibility of extracting both atrial and ventricular tined leads[25,26].

A variety of reasons can exist for removal of leads, however only in pacemaker infection is removal imperative. Fortunately, pacemaker infections are uncommon; recent reports provide infection rates of 1–2% of implants[25,26].

2.8.5. Active fixation

Active fixation devices include springs, needles, pins, claws and screws. For the most part these leads have a screw–like mechanism that allows immediate fixation during implantation[24].

Theoretically, compared to tined leads, screw–in leads have the advantage of an easier removal procedure. Removal can usually be performed by reversal of the fixation screw. However, the traumatic fixation procedure may induce more cardiac trauma and fibrosis resulting in less optimal sensing and pacing characteristics. In some models the screw is retractable to facilitate introduction into the vein and advancement toward the heart. Yet, retractable–helix leads tend to be stiffer than fixed–helix leads and thresholds are not as low as they would be with most passive fixation leads. Recently, a fixed screw–in lead was put on the market with a mannitol coated tip over the fixed helix in order to ease insertion into the venous system[27]. The mannitol coating dissolves within several minutes in the blood stream allowing screwing of the helix into the endocardium, combining simple use and high electrical performance. Active fixation leads are especially useful in the atrium, where the early displacement rate is generally higher than in the ventricle, and for patients with dilated ventricles, severe tricuspid valve regurgitation and congenital heart disease. Particularly in patients who have undergone cardiac surgery with right atrial cannulation, atrial screw–in leads have been successfully employed.

2.8.6. Lead insulation

The purpose of the insulation material is to prevent leakage of current in the physiologic environment. Biocompatibility, lubricity, tensile strength, resistance to clot formation, capacity to sterilization and the absence of toxicity are essential for insulation material. Silicone rubber, introduced in the mid 1960s, is still in use and appears to have long integrity. However, silicone leads, especially bipolar ones, are relatively large because a thicker layer of silicone is necessary to provide enough tear and tensile strength. This is a disavantage, particularly in dual–chamber implants. Recently, a new high performance

platinum curred silicone has been utilized permitting a thinner insulating layer.

The newest material for insulating pacing leads is polyurethane and several formulations have been in use since 1979. Polyurethane leads are extremely tough and elastic and can be made smaller than silicone leads. They slide easily alongside one another, an advantage with the introducer implantation technique and in dual–chamber pacing. However, insulation failure began to appear described as microscopic surface cracking. Particularly, the extra cardiac vascular tie–down point and the J–curve of the atrial lead were vulnerable to insulation failure. Using other manufacturing processes and a different, harder polyurethane polymere, the pacemaker industry recently produced polyurethane leads with excellent clinical performance and durability[29]. However, in our opinion, silicone insulation should be preferred, particularly in the younger patient.

2.9. Conductors and connection

2.9.1. Conductors

The single wire coil (unifilar) had a very high early fracture rate. This was reduced to 1–2 % per year by the use of the use of tri– or quadrifilar coils [24,29]. Stainless steel was abandoned because of corrosion and replaced with a fatigue resistant alloy of nickel, cobalt, chromium, molybollenum and iron (Elgiloy).

2.9.2. Connectors

The connector is the proximal pin–plug combination of the lead that is inserted in the pacemaker header. Depending on uni or bipolar configuration, it can have single or double electrical contacts with the generator. Until recently, there was little uniformity of connectors among the various manufacturers. It was impossible to interchange generators of different manufacturers without the application of lead adapters. The first initiative to standardize the connectors was made in 1986[30]. However, disagreement arose over the location of the sealing mechanism for the connection of the lead with the header. In 1989, the international standard for the connector pin (IS–1 connector assembly) was applied throughout the pacemaker industry[31].

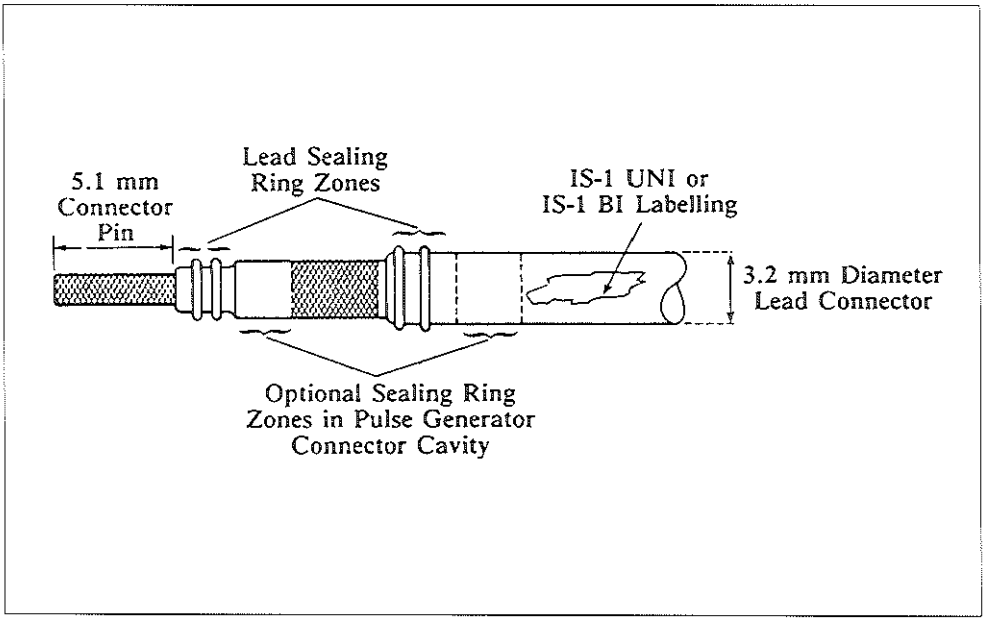

Figure 13. IS–1 connector.

Still, real compatibility does not yet exist; there are 3.2 mm connectors which are incompatible but, physically connectible with certain 3.2 mm leads. In his editorial in Pace (May 1990)[32], Furman concluded, " Just when we thought that it was save to connect any lead to any pulse generator, we find that this is not the case, and that it is difficult to get needed information. Surely the time has come for two events: real compatibility of leads and pulse generators, and real information ".

2.10. Pacemaker Programmability And Telemetry

2.10.1Programmability

Pacemaker parameters such as basic rate, output, pacing mode, etc. can be changed noninvasively by programming. Several programming systems have been developed. The systems are of two basic types: those employing a pulsed magnetic field to communicate between programmer and pacemaker and those employing a radiofrequency link. Pacemaker programmability provides a simple noninvasive way of dealing with certain clinical situations and allows better adaptation of the pacing system to the individual needs of the patient.

All modern pacemakers should be multiprogrammable for the following

reasons:

1. To optimize the pacing system in changing clinical conditions.
2. To troubleshoot pacemaker problems.
3. To noninvasively treat pacemaker complications.
4. To minimize/optimize output for an increased longevity.

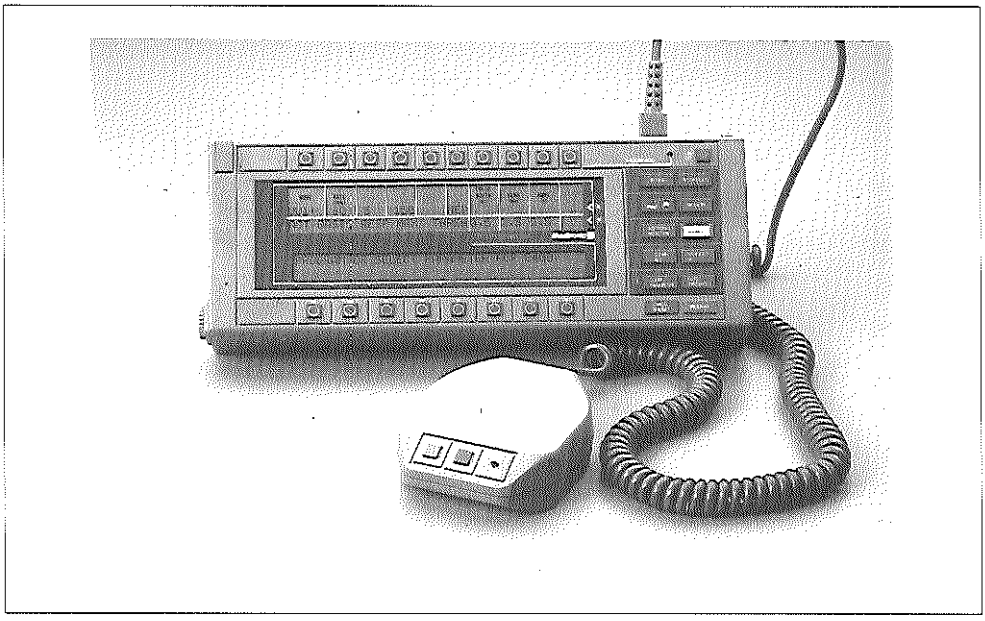

Figure 14. The programmer.

The programming technique must be precise to avoid the delivery of incomplete coded instructions that may lead to inappropriate pacemaker function. For this reason, all programmed parameters must be varified, interrogation capabilities are essential in this regard. Most generators emit a program confirmation indicator to signify receipt and acceptance of a permanent programming transmission. Moreover, upon command from the programmer, the pulse generator transmits for display and printout the permanent values for all programmable parameters. There is always the very small hazard of inadvertent reprogramming by external influences (magnet, electromagnetic interference, etc.). Some anecdotes report of spontaneous reprogramming of pacemakers but it should be remembered that often the physician or technician himself may be the phantom without recording the reprogramming. Meticu-

lous record keeping is essential. Unfortunately, there is no uniformity between programmers of different manufacturers and even the same manufacturer often requires several different programmers or memorymodules for their own different models. Recently, there is a tendency to use desk top computers for programmers; hopefully this will lead to uniformity and simplification of pacemaker programming.

Parameter	
Modes	DDDR, DDD, DDIR, DDI, DVIR, DVI, VVIR, VVI, AAIR, AAI, VVT, AAT, DOOR, DOO, VOOR, VOO, AOOR, AOO, ODO
Lower rate	40, 45, 50, 55, 60, 70, 80, 90 ppm (Activity modes)
Upper rate	80-180 ppm in 10 ppm increments (DDD and Activity modes)
AV Interval	30 - 350 ms (10 ms steps)
Upper rate timing	Atrial and ventricular (atrial derived from ventricular)
Tracks	Sensor or sinus in DDDR mode; sensor in DVIR, DDIR, AAIR, and VVIR modes

Parameter	
VSP	Same as Symbios and Synergyst II
Sensitivity	
Atrial	0.5, 1.0, 1.5, 2.0 2.5, 3.0, 3.5, 4.0 mV and async
Ventricular	0.5, 1.0, 1.5, 2.0 2.5, 3.0, 4.0, 5.0, 6.0, 8.0 mV and async
Amplitude	0.8, 1.6, 2.5, 3.3, 4.2, 5.0 V
PVARP	160-500 ms in 10 ms increments
Polarity	Uni or Bipolar Pacing Atrial Sensing and Ventricular Sensing independently programmable to uni or bipolar

Table 2. The programmable parameters of a DDDR pacemaker

Table 2 shows the programmable pacemaker parameters of a rate–responsive DDD pulse generator released on the market the end of 1990. This pacemaker offers about 1 trillion different program settings, enough for more than 100.000 years of uninterrupted programming. Fortunately the basic changes in program settings are mostly confined to rate, output, A–V delay and refractory periods and take routinely not more than one hour in a pacemaker generator's life. Moreover, in the near future, many of the adjustments of program setting will be an automatic function of the pacemaker. On the basis of measured telemetrics on generator and lead function, the pacemaker can adapt its function to changing conditions and optimize output and sensitivity.

2.10.2Telemetry

Telemetry is the communication link from the implanted pacemaker to one or more external receiving devices, such as programmer or ECG recorder.

Both physiologic and hardware data can be transmitted. Hardware identification and the programmed pacemaker settings can be given as well as measured pacemaker stimulation data, including voltages, current drain and impedance. Diagnostic data, including event counters, rate histogram, sensorgram and intracardiac electrograms, can be of value for routine analysis of pacemaker function as well as for troubleshooting malfunctions.

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Chapter III

INDICATIONS FOR CARDIAC PACING THERAPY

3.1. Introduction

Episodes of syncope, with or without convulsive seizures, in patients with a slow heart rate or asystole during the attacks, have become known as the Morgagni–Stokes–Adams syndrome. The electrocardiographic correlate of this syndrome, namely third–degree A–V block, was the first indication for permanent pacemaker insertion. The first permanent pacemaker was implanted in 1958. In the initial years of cardiac pacing the state of art was mainly concerned with preventing patient mortality due to ventricular asystole. This was achieved in the early 1960s but carried with it a very large morbidity and mortality. However, before pacemaker therapy became available, the first year mortality of acquired complete heart block was over 50%[1,2]. Initially, only patients at very high risk were paced. As reliability improved and available techniques became more widely appreciated, a higher proportion of patients received implanted pacemakers at an earlier stage of their heart disease.

Friedberg et al reported in 1964 a first–year mortality of 55% in a population with medically–treated complete heart block compared to a 10% first–year mortality in a population matched for age and underlying disease treated with a pacemaker[1–4].

The progressive advances in electronic technology, surgical techniques and pacemaker follow–up methods allowed a wide extension of the indications for permanent cardiac pacing. The indications for bradyarrhythmia cardiac pacing have widened to include partial or intermittent heart block, intraventricular conduction defect, sinus node dysfunction, hypersensitive carotid sinus syndrome and bradycardia–induced tachycardias (Table 1).

Table 1

Rhythm And Conduction Disturbances
+ Atrioventricular block
+ Sinoatrial dysfunction
+ Intraventricular conduction defects
+ Carotid sinus hypersensitivity
+ Tachyarrhythmia

All of these conditions may result in symptomatic bradycardia in which syncope, dizziness, light–headedness and fatigue are directly attributable to the slow heart rate (Table 2).

Table 2

Symptoms Of Bradycardia
+ Stokes–Adams Syncope
+ Presyncope
+ Dizziness
+ Congestive heart failure
+ Fatigue, lassitude, weakness
+ Tachyarrhythmia
+ Angina
+ Visual disturbance
+ Seizure disorder
+ Stroke
+ Memory loss, "negative story"

In recent large pacemaker surveys, complete A–V block, formerly the only pacing indication, has been mentioned in less than 40% of the cases[5–7]. Data derived from the Data Bank of the Dutch Working Group on Cardiac Pacing, covering more than 95% of all pacemaker implantations and replacements in the Netherlands, are given for the years 1986 to 1990 in Table 3[17].

Table 3

Implantations And Replacements In The Netherlands 1986–1990			
Year	**Implantations**	**Replacements**	**Total**
1986	3354	925	4279
1987	3202	871	4073
1988	3359	906	4265
1989	3492	914	4406
1990	3466	935	4401

A spectacular growth in the rate of pacemaker implantation was noticed in some countries. In the United States, health insurance companies had indications reviewed before approval was given to pay for the device[8–10].
In response to this problem, the American College of Cardiology/American Heart Association (ACC/AHA) Task Force on assessment of cardiovascular procedures issued a report from a subcommittee on pacemaker implantations, dated May 1984[11]. This report covered the Guidelines for Permanent Cardiac Pacemaker Implantations and was updated July 1991[12]. From 1981 to 1986, the average number of first implants per million population has decreased by about 1/3 in the USA (from 516/million to 359/million). In 1986, Germany (F.R.) and France were the "leading" countries in the world with 421/million and 413/million new implants, respectively (the Netherlands 265/million). Ector et al reported for the Belgian Pacemaker Registory the number of first implants from 1981 to 1989. An increase of first implants was noted from 235/million to 540/million, the highest implant rate of the world in 1989[7].

3.1.1. Evaluation of the potential pacemaker patient[13–16,18]

It is obvious that clear indications for pacemaker implantation should be defined. It is mandatory to establish a clear relationship with electrocardiographic documentation between the slow heart rate and the symptoms. This direct relationship cannot always be determined. It remains important to exclude other cardiac and non–cardiac etiologies (mainly neurological)
(Table 4, 5).

Table 4

Cardiac Syncope	
+ Rhythm and conduction disturbance	
+ Ischemic heart disease	
+ Aortic stenosis	– valvular – subvalvular (= IHSS = ASH)
+ Atrial myoxma or Ball thrombus	
+ Congenital heart disease	– Eisenmenger's complex – Tetralogy of Fallot
+ Pulmonary hypertension	– idiopathic – thromboembolic
+ Constrictive pericarditis	
+ Dissecting aortic aneurysm	

Table 5

Noncardiac Syncope	
+ Vasovagal	
+ Posttussive	
+ Postmicturation	
+ Orthostatic hypotension	
+ Cerebrovascular disease	
+ Epilepsy	
+ Migraine	
+ Pulmonary embolism	
+ Carcinoid syndrome	
+ Pregnancy	
+ Neuropsychiatric	– hysteria

In the evaluation of a potential pacemaker patient, after history, physical examination and the 12–lead electrocardiograms, ambulatory monitoring, exercise testing and an electrophysiology study can be essential to relate symp-

toms to bradyarrhythmia (Table 6).

Table 6

Evaluation
+ History
+ Physical examination
+ Electrocardiogram
+ Carotid sinus massage
+ Ambulatory monitoring
+ Exercise test
+ Electrophysiology study
+ Temporary pacing

The electrocardiogram gives, together with the acquired history, important information about the reliability of an escape rhythm and the need for immediate temporary pacing. Sometimes this is not obvious from the electrocardiogram and other noninvasive or invasive methods are needed to localize the site of the conduction block. Exercise testing can also give clues in this respect and is also of value when pacing system selection is considered. In patients with intermittent symptoms in whom documentation of a relationship between symptoms and dysrhythmia is sought, ambulatory monitoring is the evaluation technique of first choice. However, in some cases, especially in patients with paroxysmal sinus arrest, all noninvasive tests and even an invasive electrophysiologic investigation can be normal. In these cases, clinical evaluation with temporary pacing can be required. Careful examination of associated diseases, professional or social aspects have to be completed before the decision is made to implant a pacemaker. Electrophysiologic investigation can be of importance in the decision–making process of pacemaker therapy. During such an investigation an attempt is made to reproduce the symptoms and to localize the disorder in the conduction system, and subsequently helps determine the best medical or electrical therapy.

Disagreement about pacemaker indications is due in part to the widespread use of ambulatory ECG monitoring which documents abnormalities including bradycardia, pauses, or partial A–V block in patients who are either asymptomatic or whose symptoms are not clearly related to the recorded rhythm disturbances. Largely due to serious medical–legal consequences, par-

ticularly in the United States and Western Germany, some pacemaker physicians were implanting pacemakers for defensive reasons. In the Netherlands, the implants are stable for more than 10 years: the average number of first implants is± 230 per million population.

3.1.2. AHA/ACC Task Force Guidelines

The American committee on pacemaker implantation[11] reported indications for permanent pacemakers grouped according to the following classifications:

Class I: Conditions for which there is general agreement that permanent pacemakers should be implanted.

Class II: Conditions for which permanent pacemakers are frequently used but for which there is divergence of opinion with respect to the necessity of their insertion.

Class III: Conditions for which there is general agreement that pacemakers are unnecessary.

This classification has been adopted throughout the pacemaker community.

3.1.3. Section I. Pacing in Acquired Atrioventricular Block in Adults[19,20]

The diagnosis of permanent second or third degree A–V block can be easily documented by surface ECG and intermittent block can be disclosed by Holter monitoring. The anatomic location of the lesion should be assessed in order to separate patients with nodal block from those with Hisian or infra–Hisian block. Nodal block can be suspected by surface ECG in the first–degree A–V block when no intraventricular conduction defect exists. Second– degree A–V block of the Wenckebach type is usually nodal and third–degree block is commonly nodal when the QRS morphology is narrow and normal. In patients with type II second–degree A–V block or advanced second–degree A–V block (two or more consecutive P waves blocked), the conduction is affected into or infra–Hisian. In type III A–V block in the presence of a broad QRS escape rhythm, the conduction block is located infra–Hisian. Hauser et al (1985) mentioned that type III A–V block is acquired in more than 90% of the cases. Other causes are surgical (8%) and congenital (2%). Symptomatic and asymptomatic subjects with complete A–V block and those with type II second–degree

block or advanced block have better survival with pacing[2–4,10].

3.1.3.1. Class I: Indications

A. Patients with complete heart block, permanent or intermittent, at any anatomic level, associated with any one of the following complications:
   1. Symptomatic bradycardia. In the presence of complete heart block, symptoms must be presumed to be due to the heart block unless proved to be otherwise.
   2. Congestive heart failure.
   3. Ectopic rhythms and other medical conditions that require treatment with drugs, that suppress the automaticity of escape pacemakers and result in symptomatic bradycardia.
   4. Documented periods of asystole of 3.0 seconds or longer, or any escape rate of less than 40 beats/min in symptom–free patients.
   5. Confusional states that clear with temporary pacing.
   6. Post A–V junction ablation, myotonic dystrophy.

B. Patients with second–degree A–V block, permanent or intermittent, regardless of the type or the site of the block, with symptomatic bradycardia.

C. Patients with atrial fibrillation, atrial flutter or rare cases of supraventricular tachycardia with complete heart block or advanced A–V block, bradycardia and any of the conditions described under IA. The bradycardia must be unrelated to digitalis or drugs known to impair A–V conduction.

3.1.3.2. Class II: Indications

A. Patients with asymptomatic complete heart block, permanent or intermittent, at any anatomic site, with ventricular rates of 40 beats/min or faster.

B. Patients with asymptomatic type II second–degree A–V block, permanent or intermittent.

C. Patients with asymptomatic type I second–degree A–V block at intra–His or infra–His levels.

3.1.3.3. Class III: Indications

A. Patients with first–degree A–V block (see section IV on bifascicular and trifascicular block).
B. Patients with asymptomatic type I second–degree A–V block at the supra–His (A–V nodal) level.

3.1.4. Section II. Pacing in A–V Block Associated with Myocardial Infarction[21–23,26–32]

Patients with acute myocardial infarction, who develop infranodal A–V block, present bad prognosis owing to high incidence of sudden death, although this is often due to ventricular arrhythmias.

Management of various degrees of A–V block and intraventricular blocks with temporary pacing is discussed in the next paragraph. First–degree and Wenckebach I second–degree A–V block is usually a transient abnormality associated with inferior wall infarction and rarely progressive to complete heart block.

Mobitz type II block is more frequently associated with extensive anterior wall infarction and often progresses to complete heart block. In these patients, a high mortality is associated with severe left ventricular failure and permanent pacing may not make a difference in long–term survival.

Lie et al[30] could identify a high incidence of progression to çomplete A–V block in cases displaying recent bifascicular block and prolonged H–V (infra–Hisian) interval. Although the H–V duration is correlated with the severity of myocardial damage, incidence of sudden cardiac death is increased if bifascicular or trifascicular block is accompanied by complete A–V block.

Permanent pacemakers in infarct survivors with bundle branch block and transient Mobitz type II or third–degree block reduced the incidence of sudden death during the first year of follow–up from 65% to 10% in one study[31].

Many cardiologists favor permanent cardiac pacing in most patients with a complicated anterior wall infarction requiring a temporary pacemaker.

3.1.4.1. Class I: Indications

A. Patients with persistent advanced second–degree A–V block or complete heart block after acute myocardial infarction with block in the His–Purkinje system (bilateral bundle branch block). Decision for implantation of pacemaker should be made before discharge in this group of patients.
B. Patients with transient advanced block at the A–V node and transient associated bundle branch block.

3.1.4.2. Class II: Indications

A. Patients with persistent advanced block at the A–V node.

3.1.4.3. Class III: Indications

A. Patients in whom A–V conduction disturbances are transient in the absence of intraventricular conduction defects.
B. Patients with transient A–V block in the presence of isolated left anterior hemiblock.
C. Patients with acquired left anterior hemiblock in the absence of A–V block.
D. Patients with persistent first–degree A–V block in the presence of bundle branch block not demonstrated previously.

3.1.5. Section III. Pacing in Bifascicular and Trifascicular Block (Chronic)[25,33–38]

Infra nodal A–V conduction defect may affect the His bundle or one of the bundle branches (right or left) or the right bundle plus one of the two left bundle branches (bifascicular block).

First– and second–degree A–V block may appear in association to right or left bundle branch block (trifascicular block).

Determination of A–V conduction can be of interest in all these cases since prognosis is good in the absence of infranodal conduction defect[13, 14]. On the other hand, bad prognosis is reported in patients with bi– or trifascicular block and severe prolonged H–V interval (> 80 msec) and in patients with alternating bundle branch block[13, 14,15]. In these last two patient groups, permanent pacing is advocated even in the absence of bradycardia–induced symptoms.

3.1.5.1. Class I: Indications

A. Patients with bifascicular block with intermittent complete heart block associated with symptomatic bradycardia.
B. Patients with bifascicular block with intermittent type II second–degree A–V block without symptoms attributable to the heart block.

3.1.5.2. Class II: Indications

A. Patients with bifascicular or trifascicular block with syncope that is not proven to be due to complete heart block, but other possible causes for syncope are not identifiable.
B. Patients with markedly prolonged HV interval (>100 msec.)
C. Patients with pacing–induced infra–His block.

3.1.5.3. Class III: Indications

A. Patients with fascicular blocks without A–V block or symptoms.
B. Patients with fascicular blocks with first–degree A–V block without symptoms.

3.1.6. Section IV. Pacing in Sinus Node Dysfunction [29,50]

Sinus bradycarda, sino–atrial block, sinus arrest and the bradycardia – tachycardia syndrome are grouped together under the popular term "sick sinus syndrome"[39,40].

The incidence of symptomatic bradyarrhythmias in patients with the sick sinus syndrome ranges from 25 to 70%. When syncopal episodes are unquestionably correlated with a slow heart rate, the indication for permanent pacing is beyond doubt. When the brady–tachy syndrome is present, although the incidence of syncope is as high as 59%[43], evidence is required that the symptoms are related to the "brady" component of the syndrome before insertion of a pacemaker.

Particularly the patient with the brady–tachy variant and those with long sinus pauses carry a worse prognosis compared to those who present sinus bradycardia alone[45,46]. Their survival rate can be improved with atrial or dual–demand pacing due to a lower incidence of systemic embolism and preventing detoriation of cardiac function[47–49]. An important reason for pacing in the brady–tachy variant is often the necessity of antiarrhythmic therapy resulting

in a further slowing of the heart rate during sinus rhythm. Sclero–degenerative heart disease can often affect both sinus node and A–V node; combined nodal disease is reported in 20% of the pacemaker population[47].

3.1.7. Class I: Indications

A. Sinus node dysfunction with documented symptomatic bradycardia this will occur in some patients as a consequence of long–term essential drug therapy of a type and dose for which no acceptable alternative exists.

3.1.7.1. Class II: Indications

A. Sinus node dysfunction, occurring spontaneously or as a result of necessary drug therapy, in patients with heart rates below 40 beats/min when a clear association between significant symptoms consistent with bradycardia and the actual presence of bradycardia has not been documented.

3.1.7.2. Class III: Indications

A. Sinus node dysfunction in asymptomatic patients, including those in whom substantial sinus bradycardia (heart rate less than 40 beats/min) is a consequence of long–term drug treatment.
B. Sinus node dysfunction in patients in whom symptoms suggestive of bradycardia are clearly documented not to be associated with a slow heart rate.

3.1.8. Section V. Pacing in Hypersensitive Carotid Sinus Syndrome and Neurovascular Syndromes[51–56]

Carotid sinus hypersensitivity can cause syncope through three mechanisms :

a. Cardioinhibitory reflex because of increased vagal tone causing sino–atrial exit block.
b. Vasodepressor response causing systemic hypotension.
c. Combined form.

Cardiac pacing is only effective in the first group, sometimes partially effective in the third group. Documentation of sinus arrest and/or A–V block should be assessed during gentle and brief massage of carotid sinus area. When pacemaker insertion is considered, the arterial pressure should be measured during the carotid sinus massage. Avoid this maneuver in patients with a history of embolic cerebro– vascular disease.

3.1.8.1. Class I: Indications

A. Patients with recurrent syncope associated with clear, spontaneous events provoked by carotid sinus stimulation, in whom minimal carotid sinus pressure induces asystole of greater than three seconds in the absence of any medication that depresses the sinus node or A–V conduction.

3.1.8.2. Class II: Indications

A. Patients with recurrent syncope without clear, provocative events and with a hypersensitive cardioinhibitory response.
B. Patients with syncope with associated bradycardia reproduced by a head–up tilt with or without isoproterenol or other forms of provocative maneuvers and in which a temporary pacemaker and a second provocative test can establish the likely benefits of a permanent pacemaker.

3.1.8.3. Class III: Indications

A. Asymptomatic patients with a hyperactive cardioinhibitory response to carotid sinus stimulation.
B. Patients with vague symptoms, such as dizziness and/or light–headedness, or both, and with hyperactive cardioinhibitory response to carotid sinus stimulation.
C. Patients with recurrent syncope, light–headedness, or dizziness in whom the vasodepressor response is the cause for symptoms.

Parsonnett (1986) reported over questionable indications for pacemaker implantation. Misinterpreting of the ECG was one the most frequent mistakes [57,58]. He listed the most encountered ECG errors (Table 7).

Table 7

Ecg Misinterpretation
– Non–conducted atrial premature beats
– Concealed extrasystoles simulating A–V block
– 2 : 1 A–V block is always type II second–degree A–V block
– Accelerated idioventricular rhythm
– Correlation rest ECG with activity
– Artificial asystole

Hasty decision–making and incomplete clinical evaluation was frequently seen, also, the arguments, " let's be safe and put in a pacemaker, " and " I don't decide, I just put them in, " were frequently noted. These reports prove the importance of a very careful decision–making before pacemaker insertion.

Even after a complete evaluation of the potential pacemaker patient, decision–making can be hard. The question of or when to implant a pacemaker in cases of syncope of unknown origin, in sinus bradycardia with complaints of fatigue or in carotid hypersensivitiy is often difficult to answer. Particularly in difficult cases, factors other than the present rhythm or conduction disturbance may influence the decision to implant a permanent pacemaker. In Table 8, several cardiac and noncardiac factors influencing the decision to implant a permanent pacemaker are summarized.

Table 8

Cardiac And Noncardiac Factors	
Cardiac	Fixed or recurrent reversible conditions
	Presence of associated underlying disease that may be adversely affected by bradycardia
	Need for medication that may depress escape rhythm or cause A–V block
Extracardiac	Age
	Overall physical and mental state of the patient
	Concomittant diseases which may result in a limited prognosis for life
	Patient occupation (pilot, bus driver)
	Remoteness of medical care
	Significant ischaemic cerebrovascular disease with risk for cerebral hypoperfusion
	Other psychosocial factors

3.2. Temporary Cardiac Pacing

Introduction

Artificial temporary cardiac stimulation was introduced in 1952 by Zoll, utilizing intermittent transthoracic electrical discharges[59]. First clinical application of transvenous temporary pacing was achieved by Furman in 1958[61]. Ever since, this technique is the choice for management of bradyarrhythmias with extended use as prophylaxis and treatment in varied clinical settings.

The frequency of use of external pacemakers has yet to be quantified. In the Mayo clinics, according the Hynes et al[62], 10–15% of the patients admitted to the coronary care unit will recieve temporary pacemakers. In non–teaching hospitals this figure will probably be lower. In our institution less than 5% of the CCU patients are temporary paced. There has been much controversy on indications for temporary pacing[63,64]. Therapeutic and prophylactic applications will briefly be adressed.

3.2.1. Therapeutic Indications

Any bradyarrhythmia that is associated with symptoms or causes hemodynamic deterioration must be treated.Temporary A–V seqential pacing is the preferred pacing mode in patients with evidence of left and/or right ventricular failure during acute myocardial infarction.

Symptomatic bradyarrhythmias in:
- Acute myocardial infarction
- Sinus node disease
- A–V nodal disease
- Carotid sinus hypersensitivity
- Intraventricular conduction defects
- Hypervagotonic state
- Pacemaker replacements

Isoproterenol and atropine can be useful while awaiting temporary pacing.

Tachyarrhythmias unresponsive to drug management or when anti–arrhythmic drugs are contraindicated.
- Atrial tachycardias
- Atrial flutter
- A–V nodal reentry tachycardias
- Ventricular tachycardia.

,Torsades de pointes
– Repetitive ventricular premature contractions with hemodynamic deterioration

3.3. Prophylactic indications

Since pacing systems placed during emergency situations have the highest complication rates, it is desirable to be able to determine which patients are at highest risk for the development of a significant bradycardia. In these conditions a prophylactic pacing lead can be placed.

- Bifasicular block during acute myocardial infarction
- To support cardioversion in patients with cardioactive drug intoxication
- Cardiac catheterization in patients with intraventricular conduction defects
- Percutaneous transluminal angioplasty
- Following open heart surgery

3.3.1. Diagnostic procedures.

3.4. Types of Temporary Cardiac Pacing Systems

3.4.1. External (transcutaneous) cardiac pacing[59,60,68]

External cardiac pacing is cardiac stimulation by passage of current through the heart using electrodes placed on the surface of the chest.

However, the high current densities at the skin electrodes required to capture the heart resulted in painful stimulation of the cutaneous nerves and underlying skeletal muscles.

Recent improvements in the design of external pacemakers allow the device to be reasonably well tolerated by the majority of patients. Due to lower current densities by virtue of long pulse durations of 40 msec and by the use of two large external electrodes, less painful muscle stimulation will occur.

3.4.2. Transesophagial pacing[65,66]

Because placement of esophagial pacing leads is both easy and noninvasive, there has been a renewed interest in this pacing modality. Transesophagial pacing is particulary useful in the diagnosis and treatment of tachyarrhythmias.

3.4.3. Transvenous pacing[62–64,67]

Unlike external and transesophagical pacing, myocardial stimulation thresholds are much lower using transvenous leads in direct contact with the endocardium. A second advantage is the ability to place catheters in both chambers of the right side of the heart and permitting A–V synchronous sensing and pacing.

Transvenous pacing is used in 95% of all temporary cardiac pacing. There are several types of temporary transvenous pacing catheters:

- Traditional bipolar catheter
- Ballontip catheter
- Thermodilution catheter with side port for ventricular electrode
- A–V sequential lead
- Atrial J lead

3.4.4. Transthoracic pacing

The insertion of a transthoracic lead requires puncture through the chest wall and through the adjacent myocardiac ventricle wall.

Cardiac tamponade, myocardial laceration, coronary laceration and pneumothorax are reported. Given the potential gravity of the attendant risks, this technique should only be used in truly emergent situations.

After prolonged and unsuccesful resuscitation efforts, the efficacy of transthoracic pacing will be marginal.

3.4.5. Epicardial pacing[69]

Epicardial leads are used in the management of patients after cardiac surgery in the treatment of postoperative brady or tachyarrhythmias. Epicardial electrodes can also be used to maintain or improve hemodynamics in the postoperative period.

3.5. Comparison of different modes of temporary cardiac pacing

In Table 9 the advantages and disadvantages of different modes of temporary cardiac pacing are given.

Table 9

Comparison Of Different Temporary Pacing Modalities					
	Invasive	Rapidly placed	Safe	Bifocal	Pro-longed Use
Transvenous	+	–/+	+	+	+
Transesopha-geal	–/+	–/+	+	–	–
Transthoracic	+	+	–	–	–
Epicardial	+	–	+	+	+
External	–	+	+	–	–

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Bifascicular Block During Acute Myocardial Infarction

A Guideline For Temporary Pacing

J.H. Ruiter, C. Burgersdijk, H.S. Elings.

Ned. Tijdschr. Cardiol. 1988; 2:18–22.

(Summary)

The occurrence of a bundle branch block or bifascicular block during acute myocardial infarction indicates a poor prognosis because this usually occurs in the presence of an extensive myocardial infarction.

Short–term and long–term mortality is high in this group of patients due to severe pump failure, ventricular tachyarrhythmias and the development of complete heart block[2–4].

The possible role of temporary and permanent pacemaker treatment in preventing sudden death due to total A–V block, in this high risk group, had been suggested[2,4]. Extensive attempts have been made to determine which conduction disorders are most likely to lead to complete heart block.

The present study was designed to validate in our patient population a simplified method developed by Lamas et al to predict the occurrence of complete heart block during acute myocardial infarction[3]. A "risk score" for the occurrence of complete heart block was obtained by Lamas by giving one point for each of the following categories of conduction disorder: first degree A–V block, type I second degree A–V block, type II second degree A–V block, fascicular block, right bundle branch block and left bundle branch block.

The risk of progression to complete heart block was directly proportional to the "risk score."

In pooled patient data of Lamas, the risk of complete A–V block with scores of 0, 1, 2 and 3 or more was 1.2%, 7.8%, 25% and 36.4%, respectively.

In our population of 810 patients with acute myocardial infarction 33 patients developed an intraventricular conduction defect. Progression to complete A–V block was seen in 8 patients.

The development of complete A–V block could be correctly predicted using the Lamas score. With the Lamas score 0, 1, 2 and 3 or more the risk of progression to complete A–V block was respectively 1.1%, 18%, 22% and 40%. These data were in accordance with earlier studies[1–7].

It is concluded that patients with inferior (posterior) infarction and a risk score of 2 are well suited for the stand–by use of an external noninvasive car-

diac pacemaker. These patients have usually a reliable nodal escape rhythm and are hemodynamicly stable. However, patients with a risk score of 2 in the setting of an anterior (lateral) myocardial infarction should undergo prophylactic temporary transvenous pacing.

All individuals with a score of 3 or more are at high risk (greater than 40%) of developing high grade A–V block; temporary pacing is mandatory.

Het Bifasciculair Hartblok Tijdens Het Acute Hartinfarct

De noodzaak van tijdelijke pacemaker applicatie.

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Ned. Tijdschr. Cardiol. 1988;2:18–22

(Samenvatting)

Wanneer het ontstaan van een bundeltakblock of bifasciculair block als complicatie bij een acuut hartinfarct optreedt is er meestal sprake van een groot voorwandinfarct. De hoge vroege mortaliteit in deze patientengroep wordtvooral bepaald door een irreversibele pompfunctie stoornis van de linkerhartkamer. Recent onderzoek suggereert echter een verbetering in de overlevings
kans bij deze patienten wanneer prophylactisch een tijdelijke pacemaker wordt ingebracht. Het snel kunnen opvangen van een totaal AV block door adequate pacing voorkomt kennelijk bij sommige patienten onherstelbare haemodynamische schade.

Een methode om voor de individuele patient het risico op verdere progressie van de ontstane geleidingsstoornis naar een totaal AV block in te schatten wordt besproken. Dit risico bedraagt bij een bifasciculair block ruim 25%; applicatie van een prophylactische tijdelijke pacemaker wordt geadviseerd. De toepasbaarheid en betrouwbaarheid van diverse tijdelijke pacing–systemen worden onder de loep genomen.

Inleiding

Het plotseling optreden van een totaal AV block tijdens een acuut voor–wandinfarct is een ernstige complicatie. Wanneer er niet van overlijden sprake is, wordt de toch al sterk gecompromiteerde haemodynamiek verder aangetast door het meestal te langzame ventriculaire escape–ritme.

Bij plaatsing van een tijdelijke pacemaker is dan ook haast geboden. In veel klinieken is dit vooral in de nacht– en avonddiensten niet goed mogelijk en kost het teveel tijd voordat een tijdelijke pacemakergeleider is ingebracht. Daarbij kan de procedure ernstig bemoeilijkt worden door Adams–Stokes–aanvallen van de patient, bij een zeer traag of zelfs afwezig escape ritme. Bovenstaande overwegingen hebben er dan ook toe geleid dat op de meeste hartafdelingen profylactisch een tijdelijke pacemakergeleider wordt ingebracht bij een patient die geacht wordt een hoge kans te hebben om een hooggradig of totaal AV block te ontwikkelen. Welke patienten krijgen nu een totaal AV block en hoe groot is het risico bij een bifasciculair block op verdere progressie naar totaal AV block. In dit artikel proberen wij op deze vragen een antwoord te geven door een beschouwing van de literatuur gegevens, in het bijzonder wordt een risico–stratificatiemethode behandeld. Tevens wordt de incidentie van nieuw ontstane intraventriculaire geleidingsstoornissen besproken in een eigen populatie patienten met een hartinfarct. De risico–stratificatie–methode wordt ook op het eigen patientenmateriaal toegepast.

Patienten En Methoden

Definities

De diagnose acuut myocardinfarct wordt gesteld, als typisch precordiale klachten en enzymstijgingen aanwezig zijn. De diagnose linker–bundeltak-block (L.B.T.B.) en rechter–bundeltakblock (R.B.T.B.) zijn gebaseerd op de gebruikelijke criteria. (1) Linker anterior–hemiblock (L.A.H.) is aanwezig bij een as deviatie in het frontale vlak van > –30 graden en linker posterior–hemi-blok (L.P.H.) bij een as deviatie in het frontale vlak van > +120 graden bij afwezigheid van rechter–kamerhypertrofie. De combinatie van R.B.T.B. met L.A.H. of L.P.H., of de aanwezigheid van L.A.H. of L.P.H. bij een L.B.T.B. wordt beschouwd als een bifasciculair block. Hooggradig A.V. block wordt gedefinieerd als type II 2e–graads A.V. blok of 3e–graads A.V. block. Van alternerend bundeltakblock (A.B.T.B.) wordt gesproken als bij een patient afwisselend een R.B.T.B. of L.B.T.B. aanwezig is, of als bij een R.B.T.B. afwis-

selend een L.A.H. of L.P.H. optreedt.

Patienten

Van januari 1986 tot oktober 1987 namen wij op de hartbewaking van het Medisch Centrum Alkmaar 810 patienten met een acuut hartinfarct op. De gemiddelde leeftijd bedroeg bijna 66 jaar; er werden 317 voorwand (en laterale), 252 onderwand– (en achterwand–) en 241 "non–Q–wave"–infarcten gezien.

Methoden

Risicostratificatie

Welke patienten die tijdens de acute fase van het hartinfarcteen geleidingsstoornis ontwikkelen zijn nu "at risk" voor verdere progressie van de intraventriculaire geleidingsstoornis tot hooggradig A.V. block. Verschillende onderzoeken hebben getracht op deze vraag een antwoord te geven. [2,3,5–8]Op elegante en klinisch goed toepasbare wijze heeft Lamas [3] de gegevens van de Multicenter Investigation of Limitation of Infarct Size (M.I.L.I.S. study) gebruikt voor het ontwikkelen van een puntentellingssysteem om het optreden van een compleet hartblock te kunnen voorspellen bij patienten met een acuut-hartinfarct. De volgende geleidingsstoornissen bleken een voorspellende waarde te hebben. Het eerstegraads A.V. block, het tweedegraads A.V. block volgens Wenckebach, tweedegraads A.V. block Mobitz II, L.A.H., L.P.H., R.B.T.B en L.B.T.B. (tabel 1). Iedere geleidingsstoornis kreeg de score van 1 punt, bij voorbeeld een R.B.T.B. met eerstegraads A.V. block zou de score van 2 punten krijgen. Zijn Complete Heart Block score verkregen uit de databank van de M.I.L.I.S. patienten werd getest aan patienten uit eerder verschenen oderzoeken. [4–9]

Methoden tot tijdelijke pacing

In onze hartbewaking wordt meestal aan het bed via een arm–vene of de V subclavia een ballontip catheter ingebracht. Sinds kort beschikken wij echter over de noninvasieve tijdelijke pacemaker volgens Zoll. [10,11]

Tijdelijke pacing wordt verkregen via twee grote huid–elektroden, geplakt op de borst en de rug. Via deze elektroden worden gelijkstroompulsen afgegeven met een grotepulsebreedte van 40 mseconde, meestal wordt stimulatie van het hart verkregen met een stroomsterkte tussen 40 – 100 mAmpère.

Tabel 1

Geleidingsstoornisscore naar Lamas [3]	
Geleidingsstoornis	Score
Geen	0
Eerstegraads A.V. block	1
Tweedegraads A.V. blockWenckebach	1
Tweedegraads A.V. block Mobitz II	1
Hemiblok	1
Rechter bundeltakblock	1
Linker bundeltakblock	1
Bij de individuele patient worden de scores opgeteld. Bij een bifasciculair block is de score dus 2.	

Resultaten

In onze populatie van 810 hartinfarctpatienten trad bij 33 patienten (4%) (26 voorwand–, 7 onderwandinfarct) een bundeltakblock op als complicatie van het infarct. Van hen ontwikkelden 14 (1.8%) een bifasciculair block, 7 (0.9%) ook nog een 1e graads A.V. block en 2 (0.2%) een A.B.T.B. Bij 14 patienten werd een tijdelijke pacemaker ingebracht, 8 patienten (1%) ontwikkelden een totaal A.V.block, 4 van hen overleden ondanks pacing, de andere 4 (0.4%) kregen voor ontslag een permanente bifocale (D.D.D.) pacemaker. De incidentie van intraventriculaire geleidingsstoornissen bij onze 810 hartinfarct patienten en het optreden van een totaal A.V. block in deze groep is samengevat in tabel 2.

Het relatieve risico op het krijgen van een totaal A.V. block varieerde tussen de 18% en de 50%, afhankelijk van de ernst van de voorafgaande geleidingsstoornis. De geleidingsscore volgens Lamas had een goede voorspellende waarde. (tabel 2). De geleidingsscore werd door Lamas getoetst aan eerderverschenen onderzoeken. [4–9]

De volgende resultaten werden verkregen: een patient met een score van 2 of meer punten in deze schaal heeft een kans van 25% en hoger om een totaal A.V. block te krijgen. (tabel 3). In de context van het bifasciculair block betekent dit een risico van dus ook minstens 25%. Als hier ook nog een eerstegraads A.V. block bij ontstaat, is het risico tenminste 36%.

De ziekenhuissterfte van onze patienten met nieuw ontwikkeld bundeltakblock of bifasciculair block bedroeg ruim 35% (11 van de 31 patienten).

tabel 2

De incidentie van intraventriculaire geleidingsstoornissen en progressie naar A.V.–block bij een totaal aantal van 810 patienten met een acuut hartinfarct.				
Type geleidings stoornis	*Aantal patienten*	*Aantal patienten met progressie naar C.H.B.*	*Relatief risico van C.H.B.*	*Geleidings stoornisscore*
B.T.B.	17	3	18%	1
B.T.B. +L.A.H. of L.P.H.	9	2	22%	2
B.T.B. +L.A.H. of L.P.H. + 1e graads A.V.–block	5	2	40%	3
A.B.T.B.	2	1	50%	2
Voor de afkortingen zie de definities				

tabel 3

Geleidingsstoornisscore en het risico van een compleet hartblock	
Geleidingsstoornisscore	*Risico van een compleet hartblock* %
0	4.0
1	9.1
2	27.5
>3	36.5
Percentages zijn gemiddeld over de onderzoeken [1,2,4–7]Bij een score $\geq$ 2 wordt een tijdelijke pacemaker geadviseerd.	

Discussie

Het ontstaan van een bundeltakblock of bifasciculair block tijdens de acute fase van het hartinfarct is vrijwel altijd het gevolg van aanzienlijke myocard–schade. Meestal betreft het een groot voorwandinfarct veroorzaakt door een afsluiting proximaal in de ramus descendens anterior van de linker coronairar-

terie voor afgifte van de eerste septale tak.

Echter 25% van de acute infarcten met een nieuw bundeltakblock worden veroorzaakt door een afsluiting in een dominante rechter coronairarterie bij een uitgebreid septum infarct van het onder–achterwand. [2,4,5] Dit wordt veroorzaakt doordat de rechter coronair arterie in deze gevallen het proximale deel van de rechterbundeltak van bloed voorziet. Een acuut rechterbundeltakblock is dan het gevolg.

De ziekenhuissterfte van patienten, getroffen door een bundeltakblock gecompliceerd hartinfarct, is hoog. Hindman rapporteerde een vroege sterfte van 30% bij het voorwand–infarct en van 17% sterfte bij het onder–achterwandinfarct, terwijl uit zijn populatie de patienten in cardiale shock waren weggelaten. [4]

Mullins [2] vindt bij zijn infarctpatienten in 6% van de gevallen een nieuw ontstaan bifasciculair block en in 7% een bundeltakblock, veel hogere percentages dan die in onze populatie. In zijn populatie is de vroege mortaliteit onder deze patienten ruim 45%.

De onderzoekingen van Hindman en Mullins zijn echter al respectievelijk 10 en 12 jaar oud, ruim voor het "tijdperk" van de actieve thrombolyse technieken tijdens het acute hartinfarct. Onze infarctpatienten werden in 1986 indien verantwoord, intraveneus of intracoronair behandeld met streptokinase en in 1987 werd meegedaan aan de European Co–Operate Study for Recombinant Tissue–Type Plasminogen Activator (rt–PA).

Uiteraard kunnen deze methoden van actieve thrombolyse het voorkomen van ernstige geleidingsstoornissen ten gunste hebben beinvloed. Wanneer zich toch een ernstige intraventriculaire geleidingsstoornis ontwikkelde, bleek ook in onze patientenpopulatie een hoge vroege mortaliteit te bestaan. Deze hoge vroege mortaliteit werd voornamelijk bepaald door een ernstige pompfunctie stoornis van de linkerkamer. Echter, in zijn inmiddels klassiek geworden onderzoek over de klinische betekenis van het bundeltakblock bij het acute myocardinfarct, noemt Hindman in 7% van de sterfgevallen het plotseling ontstaan van een totaal atrioventriculair block de directe oorzaak van het overlijden. Het ontstaan van een totaal atrioventriculair block bij het voorwandinfarct en onderwandinfarct beinvloedt dus de mortaliteit, onafhankelijk van de pompfunctiestoornis. Dit bleek vooral het geval in de patientengroep met een relatief weinig beschadigde linkerkamerfunctie. Dit is verklaarbaar omdat bij het plotseling verbreken van de atrioventriculaire geleiding ter hoogte van de bun-

deltakken een laag ventriculaire escape ritme ontstaat dat vaak erg traag of zelfs afwezig is. (4)

Niet zelden is er cardiopulmonale resuscitatie noodzakelijk wegens Adams–Stokes aanvallen met voor de patient bedenkelijke levenskansen. Dergelijke calamiteiten moeten vermeden worden door reeds prophylactisch een tijdelijke pacemaker in te brengen bij de patienten die risico lopen op het krijgen van een totaal A.V. block.

Als risico lopend moeten worden beschouwd patienten die een geleidings–risicoscore hebben van 2 of hoger. Op goede gronden moet dan ook geadviseerd worden tot het plaatsen van een profylactische uitwendige pacemaker bij het bifasciculair block in de acute fase van het hartinfarct, ongeacht of het een voorwand– of onderwand infarct betreft, zeker als zich ook nog een 1e graads A.V. block ontwikkeld. In het bijzonder geldt dit ook voor het acute hartinfarct met een alternerend linker– en rechterbundeltakblock.

Bijna de helft van deze patienten krijgt een totaal hartblock in het verdere vroege ziektebeloop. (10)

tabel 4

Tijdelijke pacing–systemen en hun bruikbaarheid.

Route	Doorlichting	Betrouwbaarheid
Transveneus		
–Rigide catheter	Ja	Uitstekend
–Flexibele balon–tipcatheter	Neen	Redelijk–goed
– Swan–Ganz met extra lumen voor stimulatie–catheter	Neen	Redelijk
Transthoracaal	Neen	Slecht
Transcutaan		
– Non–invasief (methode volgens Zoll)	Neen	Nog onbekend (grote series ontbreken)

In tabel 4 worden enkele pacing systemen besproken. In onze kliniek bestaat de meeste ervaring met de ballontipcatheter, die meestal eenvoudig aan

het bed op de hartbewaking kan worden ingebracht. In die gevallen waarbij ook haemodynamische bewaking vereist was, werd een Swan–Ganz–catheter gebruikt met extra lumen voor stimulatie–catheter.

De betrouwbaarheid van pacing met dit systeem nam vaak na 1–2 dagen door dislocatie af, doordat de tip van de dunne pacing–geleider vrijwel nooit in de rechter ventrikelapex terecht kwam. Sinds kort gebruiken wij ook de transcutane pacemaker volgens Zoll.[11]

Een nadeel van deze methode zijn echter de meestal pijnlijke borst– en rugspiercontracties. Vaak zijn de spiercontracties goed te verdragen na valiumtoediening, soms is echter morfine i.v. noodzakelijk.

In noodsituaties zorgt de externe non–invasieve pacemaker voor een urenlange betrouwbare pacing. Indien nodig kan in alle rust een tijdelijke transveneuze geleider worden ingebracht. Onze eigen ervaring met de Zoll–pacemaker is nog beperkt.

Tenslotte moet nog worden gewezen op het hemodynamisch voordeel van tweekamer pacing bij in het bijzonder het grote onder–achterwandinfarct met uitbreiding naar de rechterkamer.

De reeds profylactisch ingebrachte ventriculaire pacing–geleider kan dan beter worden uitgebreid met een tijdelijke atriale geleider, als het hooggradig hartblock van meer langdurige aard is.

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CHAPTER IV

MODES OF CARDIAC PACING

4.1. Introduction

The preimplantion evaluation of a prospective pacemaker patient is focused upon decisions regarding pacing need and the selection of the proper pacemaker for implantation. The guidelines in the selection and use of a pacemaker system are discussed in chapter V.

The flexibility of today's multiprogramable, implantable pacemaker provides the physician with the ability to select a device and adapt that device to specific patient needs. There are many pacing modalities and options to optimize the hemodynamic and electrical situation.

It is important to recognize that in any given patient there may well be a need to change pacing mode to maintain efficacy and to optimize the hemodynamic benefit of pacing therapy.

The availability of versatile pacemakers has brought with it the need to understand the many options and modes of pacing and how and when to apply them. It is important to realise that pacing modes that aim to restore natural cardiac function will be optimal in principal for all patients. Pacing modes that will restore A–V synchrony and heart rate response on stress or emotion will be regarded as physiologic[37]. The various modalities of pacing may be viewed as three distinct groups:

- Single–chamber pacing
- Dual–chamber pacing
- Rate–modulated pacing

4.2. Single–Chamber Pacing

- Atrial Pacing
- Ventricular Pacing

4.2.1. Atrial Pacing

The reasons for selecting a mode involving the atrium are:

1. To re–establish rate and rhythm.
2. To re–establish A–V synchrony.

Permanent atrial pacing was first introduced by Silverman in 1968 in a pa-

tient with an inadequate sinus function[1].

Its early use was limited by the reliability of atrial leads and physician concern that atrioventricular block or atrial fibrillation might develop with time [2,3,9,10,13].

Since the late 1970s, atrial leads have become more reliable, and leads with active fixation mechanisms facilitated the implantation procedure[4–7].

Electrophysiologic testing has allowed more accurate assessment of A–V conduction. In patients in whom atrioventricular block of any type develops at atrial paced rates less than 120 bpm, atrioventricular dysfunction is probably present and AAI pacing would not be appropriate[10–12]. What percentage of patients who receive permanent atrial pacing will later demonstrate symptomatic atrioventricular conduction disease? Several large studies of long–term atrial pacing have been reported; the incidence of distal conduction disease were in the range of 1.6 – 18%[13–16,22,25]. In chapter V, the value of the A–V Wenckebach test will be discussed in more detail.

In a small subset of patients with frequent attacks of paroxysmal atrial fibrillation, atrial pacing is sometimes used to stabilize the atrial rhythm [17,18,20]. Coumel[17] reported long–term prevention of vagal atrial arrhythmias by atrial pacing at 90 bpm. By preventing atrial bradycardia, no recurrency of atrial flutter or fibrillation were given. More generally, in the context of atrial tachyarrhythmias, rate–mediated pacemakers are of more value by stabilizing the atrial rhythm during stress or emotion as well[19,20]. However, during antiarrhythmic treatment, particularly with B–blocking agents the atrioventricular delay cannot be controlled. In these situations, the atrioventricular delay may prolong or demonstrate Wenckebach block at high pacing rates [21].

There are four major contraindications to permanent atrial pacing:

1. Chronic atrial fibrillation.
2. Co–existent atrioventricular conduction disease.
3. Unsatisfactory atrial sensing or stimulation thresholds.
4. Associated carotid hypersensitivity.

In the patient with sinus node dysfunction and normal A–V conduction, AAI(R) pacing is the most physiologic way of pacing. However, a limited number of patients may require a reoperation if chronic atrial fibrillation or symptomatic atrioventricular block develops. The ability to predict which patients will be at risk of developing these problems is still not perfect[22–25].

4.2.2. Ventricular Pacing

In the first decade of cardiac pacing the only indication of implanting a pacemaker was a life threatening bradycardia or ventricular arrest, as such, ventricular pacing was very successful[26–29]. Before pacemaker therapy was available, the first year mortality of acquired complete heart block was 50% [30–32] and not to mention the distressing symptoms of temporary ventricular arrest.

The impressive favourable effects of ventricular pacing on prognosis and the significant relief of patients led many physicians to accept the hemodynamic shortcomings of this mode of pacing.

There were no acceptable alternatives in these early years of pacing. Interest increased in understanding the hemodynamic role of atrial contraction. Gilmore et al[33] wrote in 1963 "When the atrium and ventricle contract at or about the same time instead of sequentially, the ventricle is deprived of the atrial contribution to ventricular filling, mean atrial pressure rises in relation to left ventricular end–diastolic pressure, the end–diastolic pressure is lower, and the ventricle produces less external work."

In the same year, Nathan et al[34] developed the first VAT pacemaker, however, pacemaker and lead technology had still a long way to go to satisfy these clinical demands.

If we accept the hypothesis that cardiac pacing should restore A–V synchrony and adjust the pacing rate in relation to metabolic demands, then VVI pacing will seldom be the pacing mode of choice.

The major indication for VVI pacing is the management of A–V block complicating chronic atrial fibrillation. Another reason for single–chamber ventricular pacing is the inability to obtain an adequate atrial signal or a stable position for the atrial electrode.

In our view, the argument to implant a ventricular system for "just in case" (the pacemaker is only for prophylactic protection) is not valid. First, it is impossible to predict the patient's pacing need for the future. Further, to implant a permanent pacemaker for prophylactic protection can only be justified when in the near future there will be a high change of pacing need. The subsequent course of intermittent or infrequent peripheral conduction problems after pacemaker implantation is unpredictable. The conduction disorder may remain infrequent, but on the other hand the patient may become totally pace-

maker dependent. In these limited cases, often patients with bifascicular or trifascicular intraventricular conduction defects, the most suitable pacing system for the anticipated heart block should be implanted.

It is regrettable that the advent of rate–mediated pacing gives many physicians the opportunity to ignore the importance of A–V synchrony. Indeed, a rise in heart rate is the main contributor for the rise in cardiac output during physical or emotional stress, but a pacemaker syndrome in rest will not disappear or be less symptomatic during exercise[36,37,50]. It should also not be forgotten that the heart rate in most of the pacemaker recipients is below 100 beats per minute for the majority of the day.

Still, we have to realise that the majority of pacemaker patients are elderly and will not fully benefit from physiological pacing. Many have concomittant other diseases, such as cerebrovascular disease, peripheral vascular disease, arthritis or other affictions, that limit their exercise capability.

For many patients with bidirectional A–V nodal block a simple VVI (R) pacemaker can suffice. However, symptomatic intermittent pacemaker syndrome can still occur in the absence of retrograde conduction. The presence of concomittant non–complaint cardiac disease is frequent in the eldely, (hypertension) and makes them particularly sensitive for the loss of the atrial contribution.

4.3. Dual–Chamber Pacing

4.3.1. Introduction

By definition this pacing mode requires the implantation of two leads, one for the atrium and one for the ventricle. Such a mode of pacing is beneficial only when the atria can effectively augment ventricular function and the sinus node or the atrium is a reliable source of P–wave signals. The objective of dual–chamber pacing is to re–establish heart rate response and to re–establish A–V synchrony by compensating for or correcting the particular conduction system disorder. This means that every atrial depolarization sensed by the atrial channel of the pacemaker triggers an atrioventricular delay where the ventricular channel delivers a pulse if no intrinsic ventricular potential has been detected. The QRS–complexes are synchronised to the P–waves. There are seven modes of dual–chamber pacing: VAT, DVI, DDI, DDIR, VDD, DDD and DDDR.

VAT was the first and became obsolete when improved technology made adding of sensing at the ventricular level possible giving rise to the VDD mode. In DVI pacing, the atrium and ventricle are paced at a minimum rate without atrial sensing. The absence of rate response and the probability of competitive atrial stimulation limits its use.

4.3.2. DDD pacing

The next step was a DDD pacing system which has the ability to sense and to pace in both the atrium and ventricle with a programmable A–V delay[40]. Initially, DDD pacing systems were described as fully automatic, universal and even sinus rhythm in a can[39,40]. Particularly the occurrence of atrial tracking during atrial tachyarrhythmias and pacemaker mediated tachycardias, also called endless loop tachycardia or pacemaker circus movement tachycardia, prompted the pacemaker community to realise that DDD pacing was not yet universal and certainly not fully automatic[41–44].

4.3.2.1. Pacemaker circus movement tachycardia (PCMT)

As the name suggest, pacemaker circus movement tachycardia (PCMT) is very similar to circus movement tachycardia in patients with Wolff–Parkinson– White syndrome (WPW)[41,45]. The retrograde arm of the circuit is by way of retrograde conduction of the ventricular paced events, while the antegrade arm is provided by A–V synchronization of the pacemaker to the sensed retrogradely conducted atrial events (Figure 1).

Similar to circuit movement tachycardia in patients with WPW, this is caused by atrial or ventricular premature beats. Other mechanisms are synchronization of ventricular paced events to pectoral muscle artefacts sensed as P–waves by the atrial amplifier in unipolar DDD pacemakers, and ineffective atrial stimulation allowing the ventricular paced events to be conducted retrogradely to the atrium. PCMT was a problem in the first generation DDD devices, but this is no longer the case if the device is programmed appropriately[45–47].

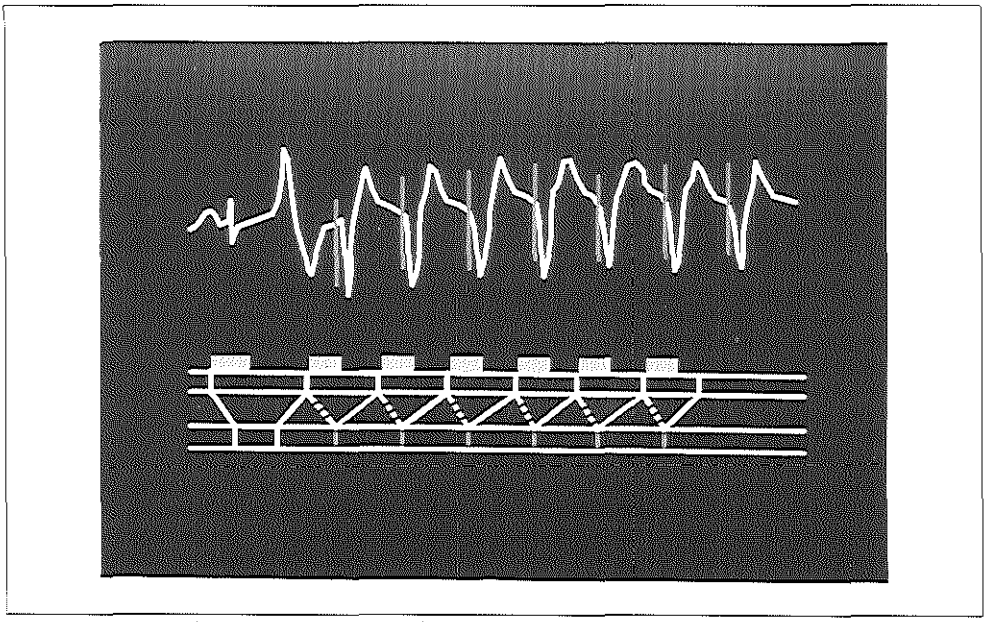

Figure 1. Pacemaker circus movement tachycardia.

4.3.2.2. Hemodynamics

Numerous studies have confirmed that in all patients the loss of A–V synchrony results in a decrease in blood pressure and cardiac output in rest and during exercise[48–52,54–57]. This decrease in cardiac output is less pronounced in patients with dilated left ventricle and more important in those with a normal or hypertrophied left ventricle[55,56,58–60,63]. In this respect, the findings of Benchimol et al[61,62] are in contradiction; he reported that atrial systole significantly improves cardiac function in patients with heart disease whereas it has little hemodynamic effect in normal subjects. Samet et al[68] using the same sequential atrioventricular pacing technique could not confirm these findings. For many years the opponents of dual–chamber pacing used the "Benchimol" studies to prove that dual–chamber pacing is only advantagous in a limited number of patients.

Since conflicting results have been published on the hemodynamic comparison of DDD and VVIR pacing during exercise, the relevance of atrial systole during physical stress is still under question[48,57,65–69,87]. However, these comparisons were made using either treadmill testing or bicycle ergometry to assess hemodynamic function. Sulke et al[70] compared the heart rate

response of patients with seven different types of rate–mediated pacemakers, both dual and single–chamber, with the natural chronotropic response of the normal sinus node in a group of healthy people. The comparison was made during various standard daily activities during graded exercise treadmill test and during mental stress at rest. They conclude that the simulation of natural chronotropic response during daily activities is generally poor in patients implanted with VVIR pacemakers. The dual–chamber pacemakers in VDD, DDD and DDDR modes gave the best form of rate response in terms of heart rate during everyday activities.

In a double blind crossover comparison of the effect of DDD and VVIR pacing on neuroendocriene variables, exercise performance and symptoms in patients with complete heart block, Oldroyd et al[71] found no significant differences in symptom scores of dyspnoea, fatigue and mood disturbances. Also the exercise time, maximal oxygen consumption and plasma catecholamines were not different. However, plasma concentration of atrial natriuretic peptide were raised in patients with complete heart block and were restored to normal by DDD pacing, but not by VVIR pacing.

A potential disadvantage of ventricular pacing is the increased incidence of the development of atrial fibrillation with its attendant risk of thromboembolism[72–78]. In theory it is less of a problem in patients with retrograde atrioventricular block, and would particularly refer to patients with sinus node disease [75–78]. Until now there are no comparative studies over the incidence of atrial fibrillation in physiologic or ventricular paced patients with bidirectional A–V nodal disease.

4.3.3. DDDR pacing

The most recent pacing mode is DDDR[80–83]. These devices are implanted in patients with A–V block and sinus node dysfunction with a poor acceleration of the sinus node with exercise or emotion. When the sinus node fails, the sensor takes over; further the sensor can be used to validate an atrial acceleration and discriminate between physiologic and pathologic atrial rate increases[79].

Although widely accepted as an effective method of dealing with rapid atrial rates in a DDD pacemaker, Wenckebach type and multiblock–type upper rate behaviour cannot be regarded as physiologic by creating A–V dissociation[41,42,44]. Sensor information based pacing can smooth the upper rate be-

haviour of the DDDR pacemaker, avoiding Wenckebach or multiblock.

A major concern with the introduction of DDDR pacing is that the engineering capacity of pacemaker companies will outship the capacity of current power sources[81,83]. Rate responsive cardiac pacing is energy expensive. The dual–chamber, rate–modulated units have three inputs, atrium, ventricle and the sensor with the more complex logic required to tie the three together. In patients with an active life style, the heart is paced at fast rates frequently during the day. If sensor energy requirements are excessive, then rate–modulated pacemakers and especially DDDR units will have limited implant times. Coupled with the present trend towards small pulse generator size, only limited battery capacity can be contained in the unit.

Steroid–eluting leads and automatic threshold detecting devices, which allow the voltage output to be maintained near threshold, are essential to provide DDDR systems of an acceptable durability. An acceptable durability for these units would be between 7 and 9 years, almost equal to the mean life expectancy for the typical pacemaker patient at implant, requiring only one pulse generator in a lifetime[85].

4.3.4. DDI(R) pacing

The DDI mode was introduced as an improvement to the DVI mode because it avoids competitive pacing in the atrium[88].The use of atrial ventricular sequential pacing with intact atrial sensing (DDI) has been propagated in patients with the bradycardia–tachycardia variant of the sick sinus syndrome[88]. It seems ideally suited for maintenance of A–V synchrony when atrial tracking , as will occur in DDD pacing during atrial tachyarrhythmias[18,19], is neither required or desirable.

It may also prove to be a valuable mode when there is a relative contraindication to a significant increase in heart rate, such as with coronary artery disease[86,88]. The DDI mode might be functionally thought of as an atrial or A–V sequential unit when the atrium is paced while being a simple single–chamber ventricular unit in the presence of a pathological atrial tachyarrhythmias.

An additional concern in the DDI mode is that of retrograde V–A conduction[89]. Retrograde P–waves are able to induce a sustained inhibition of the atrial output channel if the retrograde P–waves are sensed. This would result in single–chamber ventricular pacing or even the pacemaker syndrome. The majority of patients with sinus node dysfunction are capable of conducting retro-

gradily through the A–V node. Thus it is imperative to measure the V–A conduction interval and program the PVARP sufficiently long to preclude sensing of retrograde atrial activity.

Recently the **DDIR** mode was introduced, particularly for patients with the bradycardia–tachycardia variant of sinus node disease with a chronotropic incompetence of the sinus node during exercise[18,88].

4.3.5. Single Lead VDD Pacing

Atrial synchronous ventricular pacing is the elective electrical treatment of patients with advanced A–V block and normal sinus node function. A limitation of a dual–chamber mode is that it requires the introduction of two leads. The availability of single leads that are able to sense atrial and ventricular activities and to pace the ventricle should overcome this difficulty. The atrium cannot be paced and this is a potential limitation because A–V dissociation is created when only the ventricle is paced.

Antoniolli (1979) observed that a floating unipolar electrode positioned in the middle or middle–high part of the right atrium can record small, but high quality atrial signals that are able to drive a dedicated atrial synchronous ventricular paced pacemaker[90,91].

Due to the necessity of high sensitivity settings of the atrial amplifier, even with the usage of bipolar sensing signals, false inhibition or synchronization to myopotentials can be observed[92,93,95]. Percode et al[93] reported three cases of myopotential–induced electrical interference in a group of 24 patients with VDD pacemakers with bipolar sensing circuits.

A second problem can arise in the variability of the atrial signal during daily life. Fröhlig et al[94] demonstrated in a group of 19 patients with DDD units during exercise a systematic decrease of the atrial signal of the peak–to–peak amplitude of 0.1 to 1.6 mV (3–30%). These variations of the P–wave amplitude can be expected to be much larger in a floating atrial sensing electrode. In a clinical study of 107 VDD units during a follow–up of 18 months[95], four patients with loss of atrial sensing and five patients with occasional atrial nonsensing were reported.
After 12 months there was a 90.2% VDD mode survival[95].

Furman et al[96] mentioned a mean fluoroscopy time for implantation the single–pass VDD lead of 8.0 minutes, similar to implanting two separate leads in dual–chamber pacemakers in the same institution.

The risks associated with the single lead VDD pacing are:

First: for the patient presenting sick sinus syndrome with chronically slow sinus rates, the system will be unable to maintain the atrial rate and A–V synchrony will be lost. VVI pacing will also occur when the sinus rate falls under the programmed lower rate of the device during intermittent sinus bradycardia, sinus arrest or atrial malsensing.

Secondly: paroxysmal atrial arrhythmias, particularly atrial flutter or fibrillation, are a contraindication for the system.

Thirdly: the positioning of the atrial electrode in the superior vena cava can compromise efficient atrial sensing. When atrial sensing is inadequate or lost, the device will function as a VVI system.

4.4. Rate–Modulated Pacing

4.4.1. Introduction

Rate–modulated pacing can be defined as cardiac pacing by which the escape interval is varied through measurement of a physiologic indication of metabolic demand.

The concept of a non–atrial synchronous, rate–modulated ventricular pacing is more than 25 years old[97]. Camilli (1977) implanted the first rate–modulating pacemaker in a patient and used the venous pH as an input to control the heart rate[98]. The term used to describe this form of cardiac stimulation was "Rate–Responsive Pacing." This is however a misnomer in that the pacemaker is not responding to changes in rate but rather it is responding to changes in sensor input[99–101].

Parsonnet[99] suggested in 1987 the term adaptive–rate pacing or rate – adaptive pacing, others used the terms rate–mediated or rate–modulated pacing[100,103].

Since the development of rate–modulated and dual–chamber pacing, VVI pacing may no longer be considered the most hemodynamically optimal mode of pacing therapy in patients with the sick sinus syndrome or complete heart block.

4.4.2. Physiology

The goal of "Physiologic Pacing" is to restore the natural adaptive hemodynamic physiology of the intact cardio–vascular system by controlling heart

rate, atrioventricular synchrony and the speed of atrioventricular conduction [101–103].

Dual–chamber pacing systems restore the atrioventricular synchrony and can possess the ability to adapt the atrioventricular interval to higher heart rates. A physiologic heart rate response however only occurs in patients with a normal sinus node function. A significant subset of pacemaker patients have inadequate or inappropriate sinus node function due to sinus node disease, atrial tachyarrhythmias or atrial standstill. Rickards[103] estimated that, in up to 50% of all patients undergoing pacemaker implantation, the sinus node may not be suitable for a physiological adaptation of the pacing rate to the metabolic need of the patient. In large pacemaker patient surveys[104–106], the clinical indication for cardiac pacing the sick sinus syndrome or binodal conduction disease is reported in 42–60% of the cases.

Early studies[97,107] showed already the importance of rate regulation for the efficiency of the paced heart. Considering the normal physiological stimulation of the healthy heart, increases in cardiac output up to 4 or 5 fold with exertion and even up to 9 fold in athletes can be documented[101,102,108].

The marked increase in cardiac output is mediated by both rate and stroke volume, as cardiac output is the product of stroke volume and heart rate.

In the average not particularly trained heart, rate may increase by a factor of 3 and stroke volume by a factor of 1.5, adding up to overall increase of cardiac output during excercise of $3 \times 1.5 = 4.5$.

Several studies [102,103,107], in the normal heart and in pacemaker patients, suggest that with exercise the chronotropic response of the heart is the major determinant of the increase in cardiac output and that the ventricular filling effect of atrial systole is less important. If heart rate cannot be raised in otherwise normal hearts, some compensation by a further increase in stroke volume is possible. However, in those patients with a fixed small stroke volume due to myocardial disease, the only determinant of cardiac output will be heart rate.

4.4.3. Sensors

Clearly, a sensor as rate controller must mimic the function of the natural sinus node, increasing the rate when the patient needs it and decreasing it when the patient does not need it[101].

Among the most important features of a sensor driven pacemaker the fol-

lowing are the most indispensable[101,103,108,109].

1. Close parallelism between the signal and normal sinus rate under cardiocirculatory challenges.
2. Rapid response, since most episodes – like climbing stairs, walking – happen quickly.
3. Long–term reliability.
4. Signal not affected by artificial (paced) or pathological rate increase (arrhythmias).
5. Signal responsive to catecholamines and sympathetic tone.
6. The sensor itself should consume negligible current.
7. The sensor itself should be hermetically sealed or in some way immune to corrosive effects of the body.

The role of the alternative sensor should be to compare the detected cardiac rate, if available, against the independent estimate of metabolic demand (exercise or emotion). If the intrinsic rate is too slow, the pacing rate algorithm of the device will be governed by the sensor.

Ideally the sensor should not be subject to feedback effects, so that the act of changing heart rate should not itself produce an apparent change in metabolic demand as detected by the sensor[109].

If a feedback loop does exist, then the pacemaker algorithm must be able to discriminate between those variables which affect sensor response.

4.4.4. Sensor classification

Rickards[103] grouped the possible metabolic sensors according to their physiological basis.

Table 1

Metabolic sensors adapted from Rickards[103]		
Primary	:	Blood catecholamines
		Neural sympathetic activity
Secondary	:	Atrial rate
		QT interval
		Pre–ejection interval
		End systolic volume
		Right ventricle dP/dt (Changes in pressure)
		QRS duration
Exercise sensors		
Direct	:	Respiration rate
		Muscle noise
		Temperature
Indirect	:	Mixed venous O2 saturation
		Blood pH
		Right ventricular stroke volume
		Right ventricular pressure
		Blood flow velocity

Rossi developed another division of rate–mediated sensors[101], he recognized as most important a close relationship of the indicator with the O2 uptake in the body. He defined exercise or emotion as an hypermetabolic state.

Table 2

Metabolic sensors adapted from Rossi (101)	
Indicators of the **prime** order: (linear relationship to the hyper–metabolic state)	– volume of oxygen uptake – rate of oxygen uptake
Second order (linear relationship to the prime order indicators)	– cardiac output – A–V oxygen difference – minute ventilation
Third order (linear relationship to the second order indicators)	– stroke volume – heart rate – respiratory rate
Fourth order (direct relationship to the hypermetabolic state, catacholamine level (sympathetic tone)	– QT interval – pre–ejection interval – depolarisation gradient
Fifth order Indirect relationship to the hyper-metabolic state, catecholamine level (sympathetic tone)	– mixed venous pH – mixed venous lactate – mixed venous temperature – atrial pressure – body activity (motion)

Various rate–adaptive pacing systems were introduced in clinical practice or are still in clinical evaluation. These systems are listed in Table 3, with the date of introduction and the necessity of a special lead. It is important to realise that the sensor classification with regard to physiology, can easily underestimate the important contribution of the activity sensor to rate–modulated pacing.

The concept is simple, reliable and the activity device functions well, particularly in the elderly population. At present, almost every pacemaker manufacturer uses body vibrations as input for rate–modulated pacing.

Table 3

Rate–adaptive pacing systems				
	Standard Pacing Lead		**Special Pacing Lead**	
Clinical	Activity		Temperature	1988
	Piezoelectric	1985	Respiratory rate	1984
	Accelerometer	1990		
	QT interval	1981	Minute ventilation	1984
	QRS gradient	1988		
Preclinical			R.V. stroke volume	1989
			R.V. pre–ejection period	1989
			R.V. O2 saturation	1983
			R.V. dP/dT	1987
Troublesome			P–wave averaging	1981
			Central venous pH	1977
			Mean right atrial pressure	1984

R.V. = Right ventricular, O2 = oxygen, R.V. dP/dt = Changes in right ventricular pressure.

In the physiological evaluation of rate–adaptive systems, sensitivity, specificity, long–term stability and reliability must be evaluated for each system [101,103,108,109].

Sensor sensitivity is defined as the capacity of the sensor to react on changes of the physiological variable, expressed as percentage of true negative. Sensor specificity is the capacity of the sensor to react only on changes of the physiologic variable, expressed as percentage of true positive. Sensor stability is defined as the maintenance of the specificity level. Sensor reliability refers to the sensor stability and longevity. In Table 4 the sensors are listed with regard to: stability, specificity, sensitivity and reliability[82,101,103,108].

Table 4

Physiological evaluation of metabolic sensors					
	Sensor	**Stability**	**Specificity**	**Sensitivity**	**Reliability**
1	Activity				
	Piezo electric crystal	++	–	–	++
	Accelerometer	+	–	+/–	+
2	Respiratory rate	+/–	–	+	+/–
3	Minute ventilation	+	+/–	–	+
4	pH	–	–	+	–
5	O_2 saturation	–	+	–	–
6	RV dP/dt	–	+	–	–
7	RV stroke–volume	+/–	–	+/–	+/–
	RV dV/dt (the speed of volume changes)	+/–	–	–	–
8	Pre–ejection interval	+/–	+/–	+	+/–
9	A–R interval	+	+/–	+	?
10	Q–T interval	+	+/–	–	+/–
11	QRS gradient	+	+/–	–	+

4.4.5. Combined sensors[108–111]

None of the present generation of rate–adaptive pacemakers shows an optimal heart rate control, some sensors lack specificity (activity, respiration), others have a slow onset of action (pH, QT interval, temperature). By combining sensors via a control algorithm, the deficiency of one system can be overcome by the other. In clinical evaluation today are pacemakers combining activity and QT interval[114] or activity and central venous temperature[112]. Activity can be used to prime the pacing system at the onset of exertion but once exercise is established the temperature or the change in the QT interval will further

regulate the heart rate.

By measuring right ventricular impedance, three physiologic variables are obtained: pre–ejection period, stroke volume and right ventricular contractility. A practical possibility would be to combine this different information. However, these measurements are closely related and the possibility to obtain important additional useful information will be small.

Two different sensors must be preferred, impedance measurements can easily be combined with the information of QRS gradient or QT interval.

Pacemaker companies have rushed to patent all aspects of pacemaker technology, even when the rate controlling principles are based on earlier non–pacing related physiological work[100]. Probably it is not possible for a pacemaker company the achieve the best sensor combination without the very expensive purchase of patents or without cross licensing of technology. It will certainly not be in the interest of the pacemaker patients and the pacemaker "community" when the legal industry gets the opportunity for money consuming warfare.

4.5. Recent Sensor Applications

4.5.1. Adaptation of the A–V delay

In the normal heart the P–R interval shortens as the heart rate increases. On the basis of measured sensor values the pacemaker can shorten the A–V interval as the heart rate increases.

4.5.2. Prevention high–rate tracking of atrial arrhythmias

A DDD generator is designed to track the atrial rhythm. In the presence of atrial tachyarrhythmias, a DDDR unit must track the atrial signal but it has to track the sensor as well. However, during an atrial arrhythmia or pacemaker tachycardia the sensor value will remain low, giving the opportunity to discriminate between exercise or emotion–induced sinus tachycardia and pathologic atrial rate increase[79,81].

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Prevalence Of Retrograde Conduction In Heart Block After DDD Pacemaker Implantation

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Am. J. of Card. 1986;57;797 – 801

Summary

Electrophysiologic studies were performed before DDD pacemaker implantation in 50 patients with symptomatic heart block. The patients were separated into 2 groups. Group I consisted of patients with intact retrograde conduction and group II consisted of patients with blocked retrograde conduction. After pacemaker implantation, postventricular atrial refractory periods in patients in group I were programmed at 50 to 100 ms, in excess of the retrograde conduction times measured during electrophysiologic studies. In group II patients, postventricular atrial refractory periods were routinely programmed at 300 ms. During follow–up, patients visited the outpatient clinic at 3–month intervals for noninvasive assessment of the prevalence of retrograde conduction, and to test the inducibility of pacemaker–mediated tachycardias.

The mean follow–up of group I (15 patients) was 27 ± 10 months, whereas the mean follow–up of group II (35 patients) was 19 ± 19 months. The mean number of noninvasive tests performed during follow–up was 8 ± 3 per patient for group I and 5 ± 3 per pàtient for group II. In group I, retrograde conduction remained intact in 12 patients ($P < 0.01$).

In 29 of 31 patients in group II, retrograde conduction remained absent ($P < 0.01$). In 4 patients in group II, chronic atrial fibrillation occurred during follow–up. Chronic atrial fibrillation did not occur in any patient in group I. During serial electrophysologic testing, no pacemaker–mediated tachycardias could be induced in any patient in group I or II.

These results suggest that electrophysiologic studies performed before pacemaker implantation reliably predict the prevalence of retrograde conduction during follow–up of patients with symptomatic heart block and that adjusted atrial refractory periods of the pulse generator at implantation prevent the induction of pacemaker–mediated tachycardias during serial electrophysiologic testing.

Pacemaker–mediated tachycardias in patients with DDD units can be pre-

vented by adjusting the postventricular atrial refractory period.[1–5] However, an adjusted atrial refractory period may become ineffective in avoiding pacemaker–mediated tachycardias when the functional properties of the atrioventricular (AV) conducting system for retrograde conduction change during follow–up.

We studied retrograde conduction invasively before and noninvasively after DDD pacemaker implantation to find out if the electrophysiologic studies performed before pacemaker implantation would reliably predict the prevalence of retrograde conduction during long–term follow–up, and if selected postventricular atrial refractory periods at implantation would prevent pacemaker–mediated tachycardias during serial electrophysiologic testing.

Methods

Patients: DDD units were implanted in 50 patients with symptomatic second– or third–degree AV block. All patients were physically active before the onset of conduction disorder.

Electrophysiologic studies: After informed consent was obtained, patients underwent an incremental ventricular pacing study to assess the prevalence and persistence of retrograde conduction. For both stimulation and recording, 3 catheters were placed at the lateral high right atrial wall, tricuspid valve ring and the right ventricular apex. Incremental pacing at steps of 10 beats/min was initiated at a beginning rate that was slightly faster than the spontaneous sinus rate, up to a pacing rate at which second–degree ventriculo–atrial block occurred. Each pacing period lasted 1 minute.

Retrograde conduction time was defined as the interval from the ventricular spike to the onset of atrial activation at the high right atrial electrogram. Measurements were made at a paper speed of 100 mm/s.

Pulse generators: In all patients, DDD units were used with programmable postventricular atrial refractory periods. In patients with intact retrograde conduction during electrophysiologic studies (group I), a postventricular atrial refractory period was selected 50 to 100 ms in excess of the measured retrograde conduction time at electrophysiologic studies.

In patients with retrograde block (group II), a postventricular atrial refractory period of 300 ms was programmed.

Patient follow–up: Patients were prospectively followed in the outpatient clinic at intervals of 3 months. Holter recordings were performed in all patients

during the first 6 weeks after hospital discharge and thereafter when history suggested transient brady– or tachyarrhythmias. The noninvasive assessment of retrograde conduction was divided into 2 parts:

Prevalence of retrograde conduction: By programming the pulse generator from the DDD to the VVI pacing mode at a rate 10 to 15 beats/min faster than the spontaneous sinus rate, either AV dissocation or retrograde conduction was present. When spontaneous P waves were still present on the electrocardiogram, it was concluded that AV dissocation was present (Fig. 1). However when P waves disappeared or when P waves with a different polarity were visible in every ST–segment of the ventricular paced beats, it was inferred that retrograde conduction was present (Fig. 2).

Prevention of pacemaker–mediated tachycardia: In patients with intact retrograde conduction, the pulse generator was programmed in the VDD pacing mode at a minimal rate of 10 to 15 beats/min faster than the spontaneous sinus rate. When ventricular pacing at the programmed minimal rate was observed, the postventricular atrial refractory period was adequate in preventing pacemaker–mediated tachycardia (Fig. 3).

When ventricular pacing occurred at a rate faster than the programmed minimal rate, pacemaker–mediated tachycardia was present and the postventricular atrial refractory period had to be prolonged to prevent sensing of retrograde P waves (Fig. 4).

Statistical analysis: Comparisons between groups were made using Fisher's exact test for unpaired data. All data are presented as mean $\pm$ standard deviation.

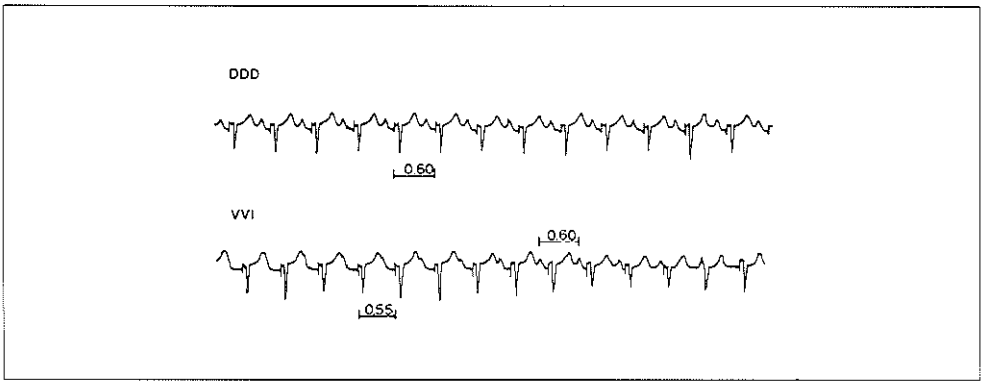
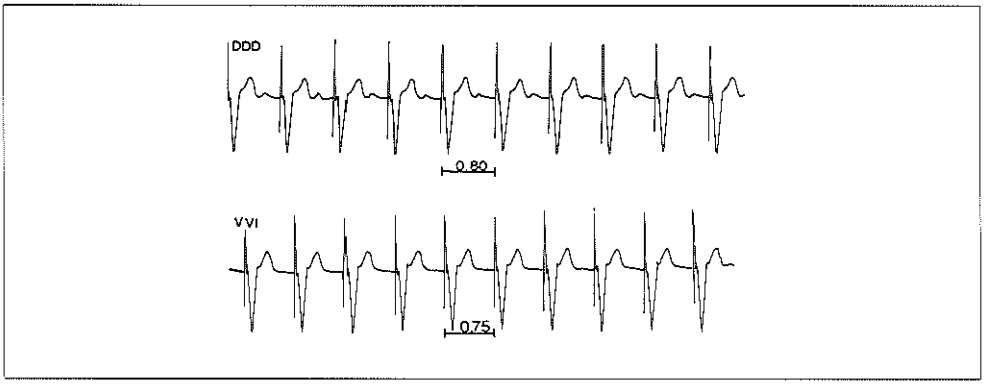


Figure 1.



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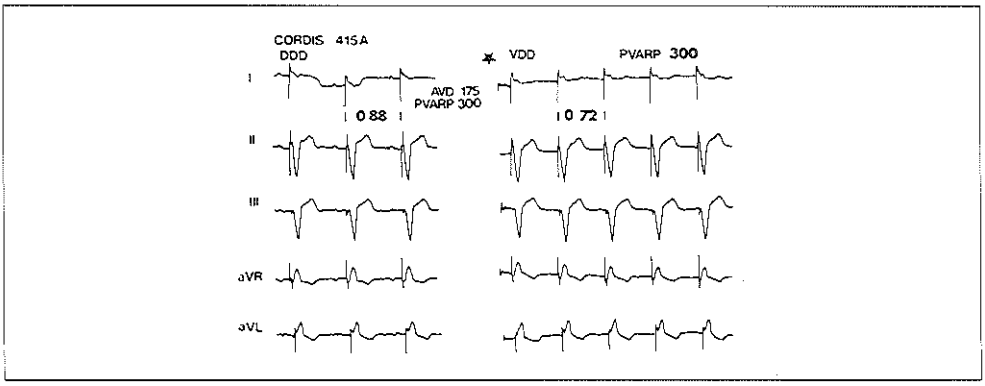

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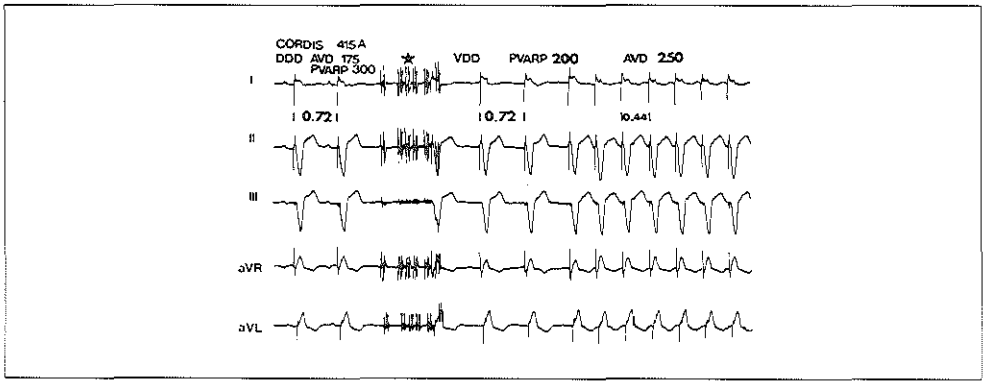
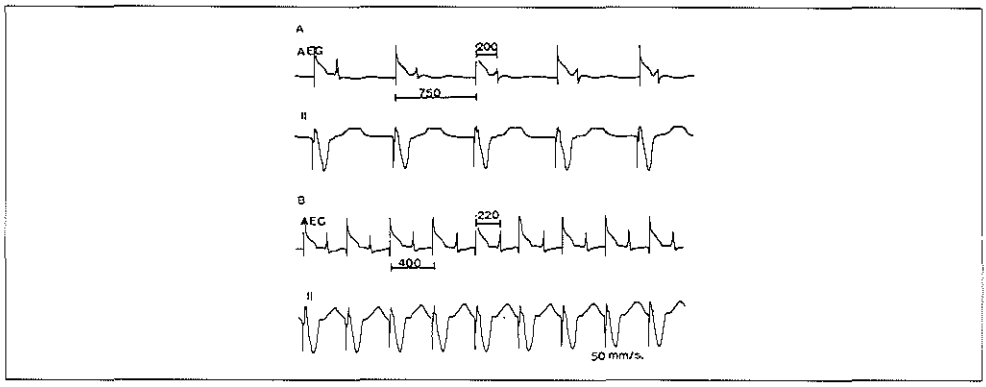


Figure 4



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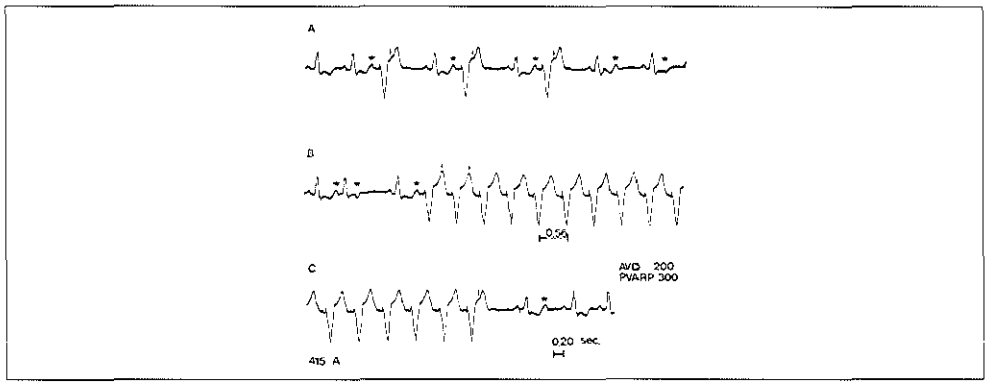

Figure 6

TABLE I Clinical and Electrophysiologic Data

	Group I RC Present	Group II RC Absent
Patients	15	35
Age (yr)		
Range	57 – 97	37 – 90
Mean	75 ± 11	74 ± 11
Male/female	1.1	1.1
Site of AV block		
AV node	6	9
Intra-Hisian	1	
Infra-Hisian	5	19
Unknown	3	7
Retrograde conduction		
Conduction times (ms)	170 – 360	
Mean	237 ± 58	
Persistence (beats/min)	100 – 200	
Mean	129 ± 35	
FU duration	27 ± 10	19 ± 9
Complications during FU		
Pocket infection	1	
Chronic atrial fibrillation		4
Atrial malsensing	1	
Deaths	2 (13%)	7 (20%)

AV block = atrioventricular block; FU = follow-up; RC = retrograde conduction.

TABLE II Retrograde Conduction and Antiarrhythmic Drugs During Follow-Up in Group I

Pt	FU (mo)	Drugs (mg/day)	RC Tests	RC
1	42	...	14	+
2	39*	Digoxin 0.25	13	+
3	38*	Digoxin 0.25	9	+
		Digoxin 0.25 + Amiodarone 400	3	0
4	34	—	10	0
5	33	Digoxin 0.25	5	+
		Digoxin 0.25 + Amiodarone 200	5	0
6	32	...	10	+
7	31	...	9	+
8	28	...	8	+
9	23	...	7	+
10	22	...	5	+
		Diltiazem 180	3	+
11	22	Digoxin 0.125	7	+
12	21	Digoxin 0.125	6	+
13	19	Digoxin 0.0625	5	+
14	14	Digoxin 0.125	4	+
15	8	...	3	+
Mean ± SD	27 ± 10		8 ± 3	

* Patient died

FU = follow-up; RC = retrograde conduction.

TABLE III Retrograde Conduction and Antiarrhythmic Drugs During Follow-Up in Group II

Pt	FU (mo)	Drugs (mg/day)	RC Tests	RC
16	42	Digoxin 0.125	13	0
17	37	...	12	0
18	35	Digoxin 0.25	2 (AF)	0
19	13*	Digoxin 0.25	6	0
		Amiodarone 200		
20	34	Digoxin 0.125	11	0
		Disopyramide 500		
21	32	...	10	0
22	7*	...	2	0
23	26*	Digoxin 0.0625	10	0
		Metoprolol 200		
24	29	Digoxin 0.25	2 (AF)	0
25	22	...	9	0
26	21	Digoxin 0.25	2 (AF)	0
27	21*	...	4	0
28	26	Atenolol 100	8	0
29	24	...	8	0
30	13*	Digoxin 0.25	4	0
31	17*	Digoxin 0.125	5	0
32	23	Digoxin 0.25	7	0
33	22	...	5	0
			2	+
34	19	...	6	0
35	18	...	6	0
36	16	Digoxin 0.125	1	+
			4	0
37	16	...	5	0
38	16	...	5	0
39	14	...	4	0
40	14	Digoxin 0.25	4	0
41	13	Digoxin 0.25	4	0
42	13	Metoprolol 200	4	0
43	12	Digoxin 0.25	1 (AF)	0
44	12	...	3	0
45	11	...	3	0
46	11	Metoprolol 200	3	0
47	6*	Digoxin 0.0625 +	2	0
		Amiodarone 200		0
48	9	...	3	0
49	9	Digoxin 0.25	3	0
50	9	Sotalol 80	3	0
Mean ± SD	19 ± 9		5 ± 3	

* Patient died.
AF = atrial fibrillation; FU = follow-up; RC = retrograde conduction.

Results

Table I lists the clinical and electrophysiologic date of group I and II patients. Table II and III list the antiarrhythmic drugs prescribed during follow–up.

Group I: After hospital discharge, a pacemaker pocket infection in 1 patient necessitated the removal of the endocardial DDD system, and an epicardial VVI unit was replaced 6 months after the first implantation. In this patient, the prevalence of retrograde conduction could still be assessed during follow–up. However, the inducibility of pacemaker–mediated tachycardia could no longer be studied. In patients in group I, the mean number of noninvasive tests performed after hospital discharge was 8 ± 3 per patient. In 12 patients, retrograde conduction remained intact ($p < 0.01$) throughout the complete follow–up period. In 2 of 3 patients in whom retrograde block occurred, the incidence was related to the initiation of amiodarone therapy to control supraventricular arrhythmias. During serial electrophysiologic studies, pacemaker–mediated tachycardias could not be induced in any of these patients. However, in 1 patient, it was necessary to reprogram the postventricular atrial refractory period, because telemetry recording after pacemaker implantation demonstrated pacemaker–mediated tachycardia during the night (Fig. 5 and 6).

Holter tracings did not show pacemaker–mediated tachycardia in any patients in group I. During follow–up, 2 patients (13%) died: 1 in the hospital because of a cerebrovascular accident and 1 suddenly outside the hospital.

Group II: In 1 patient, atrial malsensing occurred within 3 months after pacemaker implantation, and despite repositioning of the atrial lead, malsensing remained present. In this patient, it was also impossible to study the inducibility of pacemaker–mediated tachycardia, although the prevalence of retrograde conduction could be studied by programming the VVI pacing mode. In 4 patients, chronic atrial fibrillation occurred despite the administration of antiarrhythmic drugs or elective cardioversion. These 4 patients were excluded from further study. In the remaining 31 patients, the mean number of noninvasive tests performed after hospital discharge was 5 ± 3 per patient. In 29 patients, retrograde conduction remained absent throughout the complete follow–up period ($p < 0.01$). In 2 patients, retrograde conduction was intermittently present, but pacemaker–mediated tachycardias could not be induced.

Pacemaker–mediated tachycardias were not observed during either moni-

toring by telemetry or holter recording. Seven patients (20%) died during follow–up. In the hospital, 3 of them died from heart failure, 2 patients from carcinoma and 1 patient from renal failure. Out of the hospital, 1 patient died from unknown cause.

Discussion

Serial electrophysiologic testing in humans has been limited by the invasive character of the procedure. However, several pacemakers are currently available that enable us to perform noninvasively serial electrophysiologic studies.

In our series, the prevalence of retrograde conduction was assessed by ventricular pacing. Recently, Mahmud et al[6] suggested that the introduction of ventricular extrastimuli, coupled to AV sequential pacing, may elicit a higher prevalence of retrograde conduction than would be observed with ventricular pacing alone. We therefore may have underestimated the prevalence of retrograde conduction. However, Mahmud et al studied 13 patients with intact AV conduction, and the site of retrograde block in all patients was at the level of the AV node. It is unknown if extrapolation of these results to patients with heart block is warranted. Schuilenburg[7] demonstrated in patients with AV block that retrograde infranodal block is not uncommon, which may eliminate the facilitative effect of the AV sequential method on retrograde conduction to the atrium.

Taking this limitation into account, our results suggest that retrograde conduction remains stable in most patients with heart block during long–term follow–up after DDD pacemaker implantation. Pacemaker–mediated tachycardias could not be induced in any of our patients during serial electrophysiologic testing, suggesting adequate protection against these tachycardias. Unfortunately, these observations do not absolutely guarantee protection against pacemaker–mediated tachycardia, as was shown by 1 of our patients (Fig.5 and 6).

In addition, for safety precautions, we routinely programmed a postventricular atrial refractory period of 300 ms in patients with retrograde block during preoperative studies, thereby precluding the consequences of retrograde conduction with retrograde conduction times less than 300 ms (which might have occurred intermittently during follow–up).

Our approach of lengthening postventricular atrial refractory periods

proved to be a safe strategy during long–term follow–up. However, we had to accept that maximal tracking rates of the pulse generators were limited. In this regard, several suggestions were made by Den Dulk et al[8]: Bipolar atrial sensing will prevent myopotentials from initiating a pacemaker–mediated tachycardia; reset of a prolonged postventricular atrial refractory period after a sensed atrial or ventricular premature beat will prevent sensing of retrograde P waves; and DDD escape, instead of DVI escape, after a premature beat will block subsequent retrograde conduction. In future DDD systems the problem of retrograde conduction must be solved without compromising the upper rate limit of the pulse generator.

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Chapter V

CONSIDERATIONS IN THE SELECTION AND USE OF A CARDIAC PACING SYSTEM

5.1. Introduction

The primary clinical objectives of cardiac pacing are to prolong life, to restore cardiac function as optimally as possible and prevent symptoms of the pacemaker recipients. Until the late 1970s, choosing a pacing system for a specific patient was simple; the pacemaker needed only to pace the ventricle and prevent the slow heart rate. Since the development and clinical application of dual–chamber and rate–modulated pacing, the primary objectives should also include the restoration and maintenance of optimal cardiac function to enable the patient to be as active as possible.

Choosing a pacing system for a specific patient demands the ability to implant a ventricular as well as an atrial lead and a comprehensive knowledge of physiologic pacing. Unfortunately, in the last 10 years, many pacemaker implanting physicians were not able to keep pace with the rapid evolving therapeutic options in cardiac stimulation[1]. An inappropriate overuse of ventricular pacing systems is directly related to this[1–3]. In the selection of a cardiac pacing system for a specific patient, several things need to be considered:

- Hemodynamics
- Significance of rate control
- Electrophysiologic factors
- Other cardiac and noncardiac factors
- Pacemaker mode selection

5.2. Hemodynamics

5.2.1. Significance of A–V synchrony

In sinus rhythm in a normal heart, atrial contraction at the end of diastole acts as a boosterpump to enhance ventricular filling, to produce an adequate degree of ventricular myocardial fiber stretch and to optimize the function of the A–V valves[4,11]. The effect of atrial contraction of the paced heart has been extensively studied in man[4–10].

It could be shown that in normal persons at rest, atrial systole accounts for 20–25% of total ventricular filling and output [4–6]. In patients with noncompliant or hypertrophic heart disease, as seen in chronic coronary disease, hypertensive heart disease, aortic stenosis and hypertrophic cardiomyopathy, the atrial contribution to ventricular filling is even greater [12,13,15–20].

For most patients, superior cardiac performance and an improved subjective sense of well–being result if A–V synchrony is maintained or restored[14–26]. Although only rough estimates are available, it would appear that a significant percentage of patients cannot tolerate ventricular pacing [26–28]. Frequently intact retrograde conduction can be demonstrated in these patients[26,29,30]. Retrograde conduction can stimulate reflex peripheral vasodilatation and systemic hypotension with signs or symptoms suggesting low cardiac output, congestive heart failure and/or cerebral hypoperfusion.

This collection of signs and symptoms has been named the pacemaker syndrome (Table 1 and 2).

Table 1

Signs Of Pacemaker Syndrome
Hypotension
Tachypnoea
Fluctuating blood pressure
Cannon waves in the neck
Neck vein distention
Variability of heart sounds or murmurs
Tachycardia
Overt signs of heart failure

Table 2

Symptoms of the pacemaker syndrome	
Hypotension	– changes in mentation – diaphoresis – shock – orthostatic changes
Low cardiac output	– lethargy – easy fatigability – light headedness
Congestive heart failure	– dyspnoea – orthopnoea – edema
Neurologic symptoms	– dizziness – confusion – syncope
Hemodynamic symptoms	– chest pain – uncomfortable pulsations in neck or abdomen – cough
Arrhytmias	– palpitations

The major cause of pacemaker syndrome relates primarly to constant or intermittent V–A conduction, inappropriate or inadequate circulatory reflexes and less of A–V synchrony (see Table 3.)

Table 3.

Hemodynamic determinants in the pacemaker syndrome		
Loss of A–V synchrony		Effect
	– atrial filling	—
	– ventricular wall motion	–
	– catecholamines	+
	– stroke volume	–
Retrograde V–A conduction		Effect
	– atrial filling	—
	– atrial venous regurgitation	+
	– atrial arrhythmias	+
	– natriuretic factor	+
+ = *increase* , – = *decrease* , — *significant decrease*		

No single patient characteristic or preimplantation test identifies all patients at risk of developing the pacemaker syndrome[28]. However, patients with consistent V–A conduction and a VVI pacing–induced drop of systemic blood pressure of more than 25 mmHg at implant are at high risk[29,30]. More than 75% of the patients with the sick sinus syndrome and over 10% of the patients with fixed complete A–V block demonstrate retrograde A–V conduction [31–33]. Moreover, retrograde conduction is affected by sympathetic tone and drugs and can show up for the first time after implantation. As tested by ventricular pacing at implant, the incidence of retrograde conduction in all pacemaker recipients is as high as 45–50%[26,33,34]. Historically[29], the incidence of pacemaker syndrome has been estimated at approximately 7%, rather low with respect to the much higher incidence of retrograde conduction[35,36]. However, any syndrome represents a wide spectrum of symptoms, there is a great difference between a full–blown syncope and complaints of easy fatigability. This latter complaint is often overlooked, particularly in the elderly patient, because the Stokes–Adams attacks have been solved by the pacemaker, not realising that the fatigability could be a result of the pacemaker syndrome. Recent studies have evaluated patients who served as their own control with respect to VVI and physiological pacing [26,28,37,38]. In these patients, the incidence of pacemaker syndrome was much higher than previously reported;

65% of patients experienced moderate to severe symptoms.

In a double blind crossover comparison of DDD pacing and VVIR pacing in patients with complete bidirectional A–V block [39], no significant difference was identified between pacing modes in symptom scores for dyspnoea, fatigue, mood disturbance and exercise time. However, resting plasma concentrations of atrial natriuretic peptide was raised during VVIR pacing and were restored to normal with DDD pacing. The long–term hemodynamic consequense of this finding is as yet unknown.

Even in patients with intermittent retrograde conduction, symptoms of dizziness, dyspnoea and weakness were reported[37]. Several authors[28,41] found that the absence of V–A conduction, percentage of time paced and heart rate response to exercise was not conclusively predictive of the patient experiencing increased symptoms with VVI or VVIR compared to DDD pacing.

Probably, in some of these patients intermittent retrograde conduction played a role.

5.2.2. Significance of the appropriate A–V interval

Atrioventricular nodal conduction is mediated by the autonomic nervous system. During physiological stress, the native P–R interval shortens as the sinus rate increases, to compensate for the shorter diastolic filling period, while maintaining optimal ventricular filling thus maximizing the cardiac output[42,43].

Noninvasive studies of dual–chamber pacing by pulsed Doppler showed the hemodynamic advantages of dual–chamber pacing compared with VVI pacing[10,13,16,19]. The increase in cardiac output yielded by dual–chamber pacing is generally reported to be between 15–30%[10,13,16], and is variable from patient to patient. However, when the A–V delay is optimized during DDD pacing at rest and during exercise, the increase in cardiac output is in a smaller range and varied between 20–30%[44–47,49,50]. Measuring stroke volume beat–by–beat by means of impedance cardiography, Krapp et al[48] observed a maximal stroke volume at a P wave to pacemaker–induced R wave of 130 ms in patients paced for complete A–V block. However, marked interindividual variations were observed. Furthermore, it was shown that an optimal A–V interval was even more critical with increasing heart rates[8,48,52]; however, these studies were performed at rest with the heart rate being artificially increased just by pacing. Further studies are needed during exercise testing to

evaluate the hemodynamic effects of a rate–dependent A–V delay.

A second problem arises when one has to choose one A–V interval for both atrial tracking and atrial pacing in dual–chamber pacing. Rarely does sensing coincide with the onset of the complex as seen on the surface ECG. There is always a certain latency period before the pacemaker sensing circuitry recognizes the intrinsic atrial signal. Without a correction for this latency period, the interval between atrial sensing and a ventricular event will be longer than the interval between a paced atrial complex and a ventricular event[51].

Recently developed DDD generators are able to adapt to this difference.

5.2.3. A–V synchrony and myocardial function

Intrinsic myocardial performance is an important variable for determining the significance of A–V synchrony in an individual patient, A–V synchronization was once thought to play a more important role in maintaining cardiac output in the failing heart than in the normal heart[53,60,61]. Today it is evident that the reverse is true[54,55,56,57]. Greenberg et al[7] showed that patients with impaired left ventricular function and a pulmonary wedge pressure over 30 mmHg failed to derive any significant benefit from A–V synchrony. Atrial pacing in patients with normal hearts or hypertrophic hearts resulted in a 20–50% greater stroke volume as compared to ventricular pacing. The reason why atrial contribution to ventricular stroke volume becomes less significant in the failing heart is that, due to the elevation of overall left atrial pressure, the ventricle will maximally fill early in diastole and not require an atrial kick. Besides, in patients with left ventricle dysfunction, the Starling curve is flat and there would be hardly any augmentation in stroke volume with further rises in filling pressure (Figure 1). Finally, abnormal left ventricle function causes atrial dilatation and an observed reduction in atrial efficiency[10,13,15,16,62].

It is very important to realize that, in the failing heart, the presence or absence of a properly–timed atrial contribution can make the difference between compensated or decompensated heart function. Moreover,these patients spend most of the day at a heart rate where they can benefit from the A–V synchrony. Any experienced cardiologist knows the importance of AV synchrony when complete A–V block complicates valvular surgery. In this respect we can regard the promissing studies of Hochleitner et al[119], who reported beneficial effects of DDD pacing in the treatment of end–stage dilated cardiomyopathy. Using an A–V delay of 100 msec, left ventricular ejection fraction was im-

proved, as were major clinical symptoms.

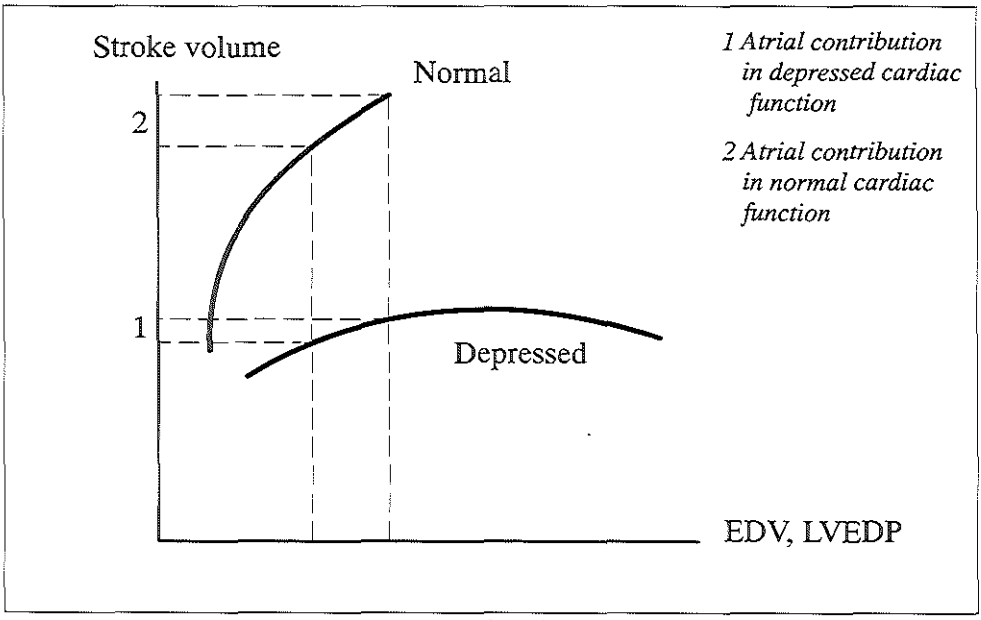

Figure 1 Starling curve

In these patients were no rhythm or conduction disturbances which otherwise warranted pacemaker implantation.

Summarizing the A–V synchrony for the paced heart:

1. Atrial contribution to cardiac output diminishes with rising left ventricle filling pressures and increasing degree of myocardial dysfunction.
2. The absence of atrial contraction merely impairs the end diastolic phase of ventricular filling.
3. Consistent V–A conduction leads to considerable venous regurgitation and impairment of the rapid diastolic filling phase.
4. A marked fall in ventricular stroke volume and pulmonary and venous congestion can cause the pacemaker syndrome.

5.3. Significance of Rate Control[6,8,61,65–67]

Discussed in Chapter IV, section 4.4.2.

5.4. Electrophysiologic Factors

Recurrent supraventricular tachyarrhythmias, particularly in paroxysmal

atrial fibrillation, have always been regarded as a limitation for dual–chamber pacing, as normal tracking function of these devices carry the possibility of fast ventricular rates[68,69,70,71,73,74]. However the maintenance of A–V synchrony and prevention of V–A conduction have been reported to reduce the recurrence of intermittent atrial tachyarrhythmias and may prolong survival in patients with sick sinus syndrome, with and without congestive heart failure[74,75,76,77]. (Table 4)

Table 4

Complications in the sick sinus syndrome for different pacing modes		
Incidence	**VVI**	**DDD(R)/AAI(R)**
Chronic atrial fibrillation	22.3 – 47%	3.4 – 6.7%
Thrombo–embolism	13 – 20%	1.6 – 7.2%
Congestive heart failure	23 – 37%	7 – 15%
Pooled data from several retrospective[75,76,77,78,82] and 1 prospective study[79]. Follow periods between 3 – 10 years.		

DDDR pacing adjusts the atrial pacing rate based upon sensor output, and competition between intrinsic sinus rhythm and sensor–driven atrial rate can induce atrial arrhythmias[84]. However, Spencer et al[86,87] concluded that DDDR pacing provides heart rate augmentation and does not result in a significant increase in atrial arrhythmias. Atrial or dual–chamber pacing can be very helpful in the treatment of these arrhythmias especially in the group of sick sinus patients with bradycardia induced atrial tachyarrhythmias[83,85,88].

Echo studies showed that permanent ventricular pacing with retrograde conduction may lead to a significant enlargement of the left atrium and decrease in atrial wall motion[77,89,90]. This predisposes to arrhythmias and embolic complications[78,79,81,82]. Gross et al[80] followed 489 DDD patients over an 8–year period with a mean follow–up of 33 months; 9.8% the DDD group developed atrial fibrillation. A prior history of atrial fibrillation and the presence of dominant sinoatrial disease predicted a substantially higher risk for atrial fibrillation in this patient group. Most patients remained in sinus rhythm and were manageable in the DDD mode. They concluded that atrial fibrillation is a limited problem in the DDD patient population and possible occurrence of atrial fibrillation should not preclude DDD use in the vast majority of patients in sinus rhythm at the time of implant. Sutton[83] summarizes

some factors toward successful atrial arrhythmia control in sinoatrial disease:
1. Presenting sinus bradycardia < 60 ppm.
2. Presenting atrial arrhythmias all shown to be bradycardia dependent.
3. Left atrial size on M–mode echocardiography < 5.0 cm.
4. Low incidence of presenting atrial arrhythmias.

5.4.1. Chronotropic incompetence

Chronotropic incompetence is the inability to increase heart rate in response to increases in metabolic demand. Moreover, in these patients a blunted heart rate response to sympathomimetic (isoproterenol) and vagolytic (atropine) drugs has been demonstrated. After producing parasympathetic blockade with 1–2 mg i.v., the normal response for the sinus rate would be an increase to either greater than 100 beats per minute or by 30% to 50 % over the resting sinus rate[120]. Unfortunately, no standardized or systematic protocols have been described to define chronotropic incompetence[82,95,121].

Chronotropic incompetence was first recognized as a feature of sinoatrial disease by Holden et al in 1978[91]. Other authors have shown, in a limited number of patients, that this feature is uncommon in sinoatrial disease[92,93,94]. They conclude that exercise testing before implant can detect the patients who show chronotropic incompetence.

In our pacemaker clinic we have defined chronotropic incompetence as the inability to raise heart above 100 beats per minute, irrespective of the patient's age, during a maximal bicycle exercise test. In some patients an atropine test is performed.

With the advent of rate–modulated pacing, the possibility exists to handle this problem. Follow–up studies of sinoatrial disease, demonstrate that patients who do not demonstrate it prior to implant do not seem to develop it later on[93,94]. In a recent study, Jutzy et al[99] showed that DDDR pacing was superior to VVIR pacing and superior to DDD pacing in patients with sinoatrial disease or binodal disease when chronotropic incompetence was present.

Although the differences in exercise time and oxygen uptake were not statistically significant, these differences were accompanied by an enhanced feeling of well–being. In other small studies, the level of significance was reached when the exercise time in DDDR mode was compared to VVIR mode[96,97,98]. Using standard Doppler measurements, obtained in a blinded fashion, Procter et al[122] showed that the addition of rate responsiveness to dual–chamber pac-

ing results in a significant improvement in cardiac output for patients with chronotropic incompetence.

5.4.2. Development of atrioventricular block in sino–atrial disease

Retrospective studies suggested that the frequency of progression to significant A–V block in patients with sino–atrial disease is between 1.1–8.4%[100–106]. This had led some authors[101–104] to suggest that all patients with sinoatrial disease requiring pacing should receive dual–chamber systems, particularly the patients requiring antiarrhythmic medication.

Others have emphasized the safety and efficacy of long term AAI pacing in selected patients with sinoatrial disease[95,105–110].

In most centers, such selection involves determination of the A–V Wenckebach point[107–111]. Wenckebach point above 130 bpm is regarded sufficient proof of A–V node integrity to implant an AAI system[107,109,110].

In a small prospective study of 24 patients with sinoatrial disease, Haywood et al[111] demonstrated that an A–V Wenckebach point above 120 bpm does not confer immunity from progression to symptomatic A–V block . Only one of the 4 patients (17%) who progressed to A–V block and required the system revision was a sequential fall in A–V Wenckebach point recorded at successive follow–up visits within 6 months after implant. They suggest that measurement of H–V interval in response to incremental atrial pacing would be a more sensitive predictor of progression to A–V block. To perform such an electrophysical assessment in all patients being paced for sinoatrial disease, would impose a considerable burden on pacing centers. Without any doubt, this study demonstrates that, next to the Wenckebach test, other variables such as ambulatory 24–hour ECG, exercise test and medication, should be carefully evaluated before an atrial device is implanted in patients with sino–atrial disease.

In our clinic, atrial devices are excluded in sick sinus patients to the following criteria

Exclusion criteria for atrial pacing in sino–atrial disease

1. Wenckebach point < 130 bpm

2. Signs of A–V conduction disease on ECG or 24–hour ambulatory ECG or exercise ECG (including asymptomatic first–degree or second–degree Wenckebach block)

3. Signs of intraventricular conduction disease (including left hemiblock or incomplete right bundle branch block)

4. Associated atrial arrhythmias requiring high doses of betablocking agents or amiodarone

Using these exclusion criteria in our atrial–paced population of 43 patients with sinoatrial disease, with a mean follow–up of 23 months, only 2 patients (2.3%) required the pacing system to be upgraded to a DDDR unit.

5.5. Other Factors (cardiac and noncardiac)

The selection of the best pacing mode for a given patient involves a variety of factors next to hemodynamic and electrophysical considerations.

When one of these factors is the reason to deviate from the selection of an optimal pacing system, the potential limitations of that pacing system should be weighed against the advantage of that choice for the patient.

For example it would be, unjustified to implant a VVI unit in a patient with symptomatic sick sinus syndrome with V–A conduction and creating a pacemaker syndrome, because of a limited life expectancy of that patient.

In Table 4, some factors are summarized. In some clinical conditions, we have to accept that the best solution is surgical not always achievable.

Table 4

Noncardiac factors	Cardiac factors
Age	
Overall physical and mental state	Associated cardiac disease (angina pectoris)
Concomittant diseases	
Limited exercise tolerance	Congestive heart failure
Limited life expectancy	
Patient occupation	Dilated valvular heart disease
Inability to visit pacemaker clinic	Severe atrial enlargement
Economic constraints	Atrial standstill

5.6. Pacemaker mode selection

5.6.1. Sino–atrial disease or Sick Sinus Syndrome (SSS)

S.S.S. with normal A–V conduction and normal chronotropic response: AAI mode.

S.S.S. and chronotropic incompetence: AAIR mode.

S.S.S. with abnormal A–V conduction or/and with intraventricular conduction disturbance with severe atrial arrhythmias, not bradycardia–dependent, necessitating high doses of anti–arrhythmic medication: DDD mode.

S.S.S. as above and chronotropic incompetence: DDDR mode.

5.6.2. Atrioventricular nodal disease (A.V.N.)

A.V.N. disease with normal sinus node function: DDD mode.

A.V.N. disease with normal sinus node function and frequent atrial tachyarrhythmias: DVIR mode.

A.V.N. disease with abnormal sinus node function (chronotropic incompetence): DDDR mode.

A.V.N. disease with abnormal sinus node function and frequent atrial tachyarrhythmias: DDIR mode.

A.V.N. disease with chronic atrial fibrillation: VVIR

5.6.3. Chronic atrial fibrillation

Chronic atrial fibrillation with intermittent slow ventricular response: VVI or VVIR mode.

Chronic atrial fibrillation with permanent slow ventricular response: VVIR mode.

Chronic atrial fibrillation should only be accepted as an endstage when the trigger for the rhythm disturbance can not be treated, for example, in valvular heart disease with severe atrial enlargement. Otherwise, after a period of anti-coagulant therapy, electrocardioversion should be undertaken; and when the sinus rhythm has been regained, pacemaker therapy or pacemaker mode has to be reconsidered.

5.6.4. Hypersensitive carotid sinus syndrome (C.S.S.)

Cardioinhibitory type, abnormal sinus and abnormal A–V node response: VVI mode or DDD mode.

Cardioinhibitory type, with normal A–V response: DDD mode.

Cardioinhibitory type, with concomittant sinus node disease and normal A–V node response: DDD,DDR mode or DDI mode + hysteresis.

Cardioinhibitory type, as above with abnormal A–V node response: DDD,DDDR mode or DDI mode + hysteresis.

Mixed type (cardioinhibitory and vasodepressive): none or DDD, DDR mode or DDI + hysteresis.

C.S.S. and S.S.S. are frequently associated. In a study of Brignole et al[112,113], S.S.S. was present in 40% of patients with C.S.S. and C.S.S. observed in 42% of the patients with S.S.S. He reported successful VVI pacing in C.S.S. patients without S.S.S, but advised dual–chamber for those with retrograde conduction and for those with orthostatic hypotension.

Until now, opinion about pacemaker mode selection in the C.S.S. is divided in the literature[114,115].

5.6.5.. Extraordinary indications

Asymmetric septal hypertrophy (A.S.H.): D.D.D. mode.

McDonald et al (1988) reported using permanent dual–chamber pacing as the primary treatment for hypertrophic cardiomyopathy[117]. Starting the ventricular activation from the apex of the right ventricular instead of normally from the subvalvular hypertrophic septum resulted in a marked decrease of outflow obstruction. In a recent abstract[118], Kappenberger et al concluded that atrial synchronized ventricular pacing, together with an optimized short A–V interval (between 50–100 ms), reduces significantly and definitively the outflow gradient and improves symptoms in patients with HOCM.

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Chapter V

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Chapter VI

SENSORS IN RATE–MODULATED CARDIAC PACING

6.1. Introduction

Rate–modulated pacing consists of detecting a physiologic signal that reflects metabolic demand which can be used to adjust the rate of cardiac stimulation to meet that demand.

The ideal physiologic signal or sensor mimics closely the chronotropic response of a normal sinus node. The requirements for an ideal sensor for adaptive–rate pacing are:

- direct correlation with metabolic need
- proportional response to workload
- quick response
- long–term reliability
- not requiring sophisticated lead technology
- easy to implant

In Chapter IV, several authors (1,2) presented different sensor classifications. Rossi et al (1) considers the oxygen need for every energy consuming process to be the optimal parameter for measuring metabolic demand. In this view, only minute ventilation and central venous oxygen saturation are directly related to the oxygen uptake of the body. In clinical practice, however, a simpler sensor classification is desirable; sensors can be regarded as physiologic or non–physiologic indicators. A physiologic indicator is tied to the autonomic regulatory process and will react to exercise and emotion. A non–physiologic indicator is based on a signal outside the autonomic regulatory process. There are primary or secondary physiologic sensors dependent on the existence of a direct or indirect relation to the autonomic drive (Table 1).

Table 1

Sensors in cardiac pacing		
Non–physiologic	**Physiologic**	
	Primary	**Secondary**
activity	A–R interval	pH
accelerometer	pre–ejection interval	minute ventillation
respiratory rate	Q–T interval	temperature
	QRS gradient	oxygen saturation
	dP/dt	stroke volume

In our pacemaker clinic, we have experience with rate–modulated pacing systems controlled by the non–physiologic indicator activity and the secondary physiologic indicators stroke volume, central venous temperature and right ventricle dP/dT. These sensors will be discussed in more detail in this chapter. The primary sensors will be attended in Chapter VII.

6.2. Non–physiologic sensors

1. Activity – piezo–electric crystal accelerometer

6.2.1. Piezo–electric crystal

The activity–sensing pacemaker consists of a piezo–electric crystal bonded to the inside of the pacemaker can. The crystal converts pressure and low freqency vibrations into an electrical signal that controls the pacemaker circuitry (Figure 1). For the detection of low frequency mechanical vibrations typical for body motion, no special lead is required. The first "activity" pacemaker was implanted in 1983[3,4]; there are now more than 250,000 implants worldwide. The simplicity of the concept, the rapid and appropriate response during walking, the easy implantation, follow–up and programmability were probably the basis for this unequalled success. Lindemans[5] reported on a group of 122 patients paced with an activity device and found a 55% improvement in exercise tolerance using a Naughton treadmill protocol. Faerestrand and Ohm (6) followed patients with activity pacemakers and showed a significant 29% increase in exercise duration with rate–modulated pacing, six months after im-

plantation, compared to the ventricular pacing mode. Treadmill testing is the preferred method for assessing the activity rate–modulated pacing system. The pacing system is more sensitive for walking in place or static arm exercise than for bicycle stress testing or swimming[7, 8].

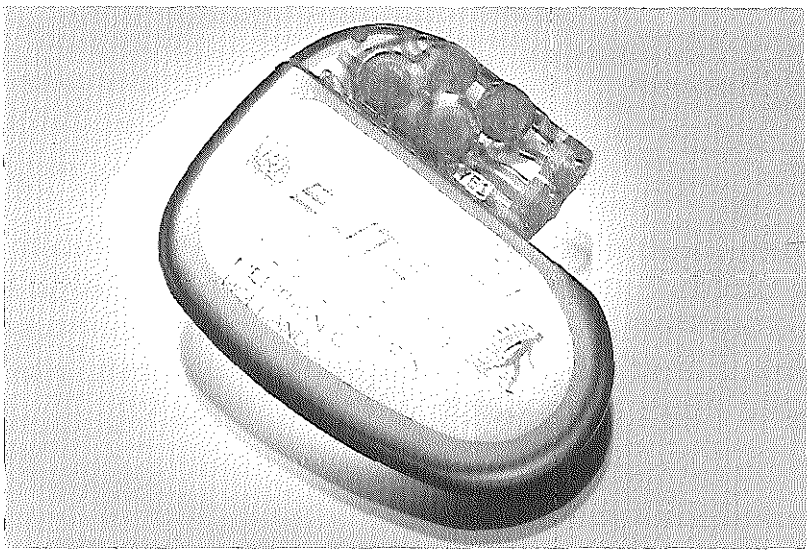

Figure 1. acitivity–sensing pacemaker.

Potentially, the activity sensor can give rise to false pacing rate increase. Vibration from sources other than the skeletal muscles may result in stimulation of the sensor with consequent pacing rate changes. This may occur in a bumpy automobile or public transport (airplane, helicopter) or by applied pressure on the implant site[10–13]. In practice however, this seldom leads to symptomatic rate increase. The activity pacemaker has good exercise–onset response characteristics[5,7,8,10] as manifested by the prompt rise in rate with treadmill exercise, climbing stairs and jogging. However, since vibration ceases at once after an exercise is finished, a pacing rate decay curve determines the recovery time. Lau et al[7] indicated that the decay is too rapid for heavy or prolonged exertion. He recommended ways of improving the algorithm[7,12].

In summary, activity sensor (piezo–electric crystal):

Advantages	– Fast response
	– Regular pacing lead
	– Simple, reliable design
Limitations	– Inferior specificity
	– Inferior proportionality
	– Not reflective of metabolic need

6.2.2. Accelerometer

The accelerometer has been in use for more than 10 years in the aerospace and automobile industries in applications that demand reliable and precise movement detection[14,15]. In pacemaker technology, an accelerometer measures the change in velocity of the motion of a small mass built in a miniaturized integrated circuit chip mounted inside the pulse generator. The accelerometer measures the frequency and the energy content of the motion. On the basis of this precise motion information the pacemaker algorithm can employ selective filtering to minimize inappropriate rate response.

Several studies[16,17] demonstrate that an accelerometer–based pacing rate correlates more closely with normal sinus rhythm than does the rate response from a piezo–electric device.

However, in contrast to the piezo–electric activity sensor, the accelerometer sensor still has to prove his value and reliability.

6.3. Secondary physiologic sensors

6.3.1. pH

The pH (the acidity) of the central venous blood measured in the right ventricle is one of the earliest clinically used metabolic sensors in cardiac pacing[18]. The pacing rate was increased with a decrease in blood pH. Camilli reported a reasonably fast and proportional rate control but discovered problems with the chronic stability of the chemical sensor[19]. As yet, there are no implantable pH rate–mediated models available today.

In summary, pH sensor:

Advantages	– Simple control mechanism
Limitations	– Special lead

– Poor chronic stability
– pH changes are slight
– Slow reponse
– Body attemps to buffer pH changes
– pH variations due to pharmacological, renal and pulmonary influences

6.3.2. Mixed venous oxygen saturation

The input for this type of pacing device is the measurement of the oxygen saturation of hemoglobin (SO2). The optical sensor, located on the catheter in the right ventricle, detects the fall of SO2 during exercise. The extent of the fall is proportional to the exercise load. The first clinical experience with this type of sensor was reported in 1980 by Wirtzfield and Stangl[20,21]. In summary , SO2 sensor:

Advantage
– Reasonable fast response
– Proportional to workload
– Linear relation to oxygen consumption

Limitations
– Special lead and pacemaker header
– Placement of the sensor is critical
– Fibrotic sheath can interfere with sensor function
– Non–linear relation to exercise

6.3.3. Respiration (minute ventilation)

The respiratory rate increases during exercise. It can be detected by monitoring the change in tidal volume and the respiratory rate (tidal volume x respiratory rate = minute ventilation). The idea of a pacemaker controlled by respiratory rate was first proposed by Krasner in 1966[22].

It has been long recognized that, during increasing exercise, the minute ventilation increases linearly with oxygen consumption up to the anaerobic threshold. At the onset of exercise, the major determinant of minute ventilation is an elevation of respiratory rate followed by the increase of tidal volume[23,24]. Most of the pioneer work with this indicator of metabolic demand was performed by Rossi et al[24,25], who initially only used the respiratory rate

to control the pacing rate. At present, two methods of detection are used[25,26]:

A. Measuring transthoracic impedance between the pacing lead and a remote prepectoral electrode, placed subcutaneously, by passing a low–level AC current between the two. As air fills the lungs during inspiration, the impedance increases since air has higher resistivity than does body tissue. Impedance (and therefore voltage) changes during the respiratory cycle are used to count the respiratory rate. A voltage to frequency converter can translate respiratory rate to pacing rate.
B. In a more recently developed method, the transthoracic impedance is measured between the tip of the pacing lead and the pacemaker can. The impedance varies with the volume of air in the lungs and thus both the rate and the tidal volume can be measured.

Compared with exercise in the VVI mode, symptom–limited treadmill tests in the minute ventilation rate–mediated mode showed a 33% improvement in exercise capacity and a 44% improvement in cardiac output (Doppler measurements) in patients with bradycardias[27,28].

In summary, respiration sensor:

Advantages	– Reasonably fast response
	– Ability to react to other respiratory conditions (lung disease etc.)
	– Some systems use standard bipolar pacing leads
Limitations	– Increased battery consumption
	– Some systems use a special lead
	– Specificity limited (hyperventilation, coughing)

6.3.4. Right ventricular blood temperature

Due to the inefficiency of the skeletal muscles, heat is generated during muscular activity. In fact, human muscle is able to convert only about 20 to 25% of its energy input into work, the rest becomes heat that increases central venous temperature by as much as 1–2 degrees Celsius. The more work performed, the more heat is generated and when physical activity declines so does temperature[29,30]. Temperature is therefore specific and proportional as an indicator of physical activity. A recent study[33] found a correlation coefficient

of 0.97 between the rise in central venous temperature and the pacing rate of pacemaker recipients on the bicycle ergometer[23]. Changes in blood temperature can be readily monitored by various sensors that change their signal in proportion to temperature. The most commonly applied temperature sensor, the thermistor, varies its resistance in proportion to the temperature of the surrounding blood. In aerospace and undersea exploration, thermistors have proven their chronic stability and reliability. For a pacing system to successfully use temperature to control the pacing rate, it must effectively address several potential limitations[31,32,33,34]. First, a well–designed system has to discriminate between exercise–related temperature changes and febrile or diurnal temperature variations. Secondly, at the onset of exercise or even at emotional stress, cooler skeletal muscle blood briefly decreases the mixed blood temperature of returned venous blood. This intial decline in right ventricular blood temperature can delay the increase in pacing rate. In clinical studies, several different temperature–dip patterns were observed at the onset of exercise complicating the pacemaker algorithm[32,33].

Clinical reports suggest that, in the more recent temperature–controlled pacers, a response time of 20 to 30 seconds is achievable[31,33]. Improvements in oxygen consumption, exercise performance and subjective well–being in the temperature controlled adaptive–rate compared with the VVI mode have all been demonstrated[32,34,35]

In summary, temperture sensor:

Advantages	– Simple concept
	– Thermistor is a reliable sensor
	– Proportional to workload
Limitations	– Temperature decrease at start of exercise
	– Complex algorithm (temperature dip)
	– Special lead and special pacemaker header
	– Slow response
	– Specifity limited (fever, hot and cold drinks, hot tub)
	– No clinical information about atrial application

6.3.5. Right ventricular stroke volume

Increased metabolic need, induced through physical or emotional stress, produces an increase in right and left ventricular stroke volume[41]. Salo[43,44] measured resistance of blood in the right ventricle with a multi–electrode lead by introducing a low–level AC current between two electrodes of that lead. Measured resistance is directly proportional to stroke volume[42]. In the end–diastolic phase, when the right ventricle is filled with blood, resistance is low; in the end–systolic phase, a low blood volume creates a higher resistance. From this measurement three physiologic parameters can be derived:

1. Right ventricular stroke volume.
2. The rate of change of the stroke volume signal (dV/dt) is the measure of relative contractility.
3. The time period of the onset of the ventricular signal (paced or sensed) to the point at which ejection of the right ventricle begins indicates the pre–ejection interval (P.E.I.).

A number of factors, such as blood temperature, hematocrit and blood velocity, are known to alter the resistivity of the blood and, therefore, may interfere with the algorithm of a rate–mediated pacing system based on stroke volume measurement. Further, next to sympathetic tone, several other factors affect stroke volume such as preload, heart rate, A–V synchrony, heart rhythm, posture and the inotrope state of the ventricle.

The P.E.I. measurement will also be influenced when sensed or paced ventricular events alternate or intermittent bundle branch block occurs. The application of right ventricular stroke volume and P.E.I. will be discussed in more detail in respectively the next paragraph and next chapter.

6.4. Primary Physiologic sensors

6.4.1. Right ventricular pressure change (dP/dt)

As autonomic activity increases with physiologic stresses of exercise or emotion, the vigor of cardiac contractions increase and the maximum rate of pressure development, dP/dt max, increases. Thus, changes in dP/dt max are used to identify increases in autonomic activity, and proportional increases in pacing rate are provided. Measurement of right ventricular dP/dt involves the use of a piezo–electric crystal welded into a hermetically sealed envelope a few centimeters behind the unipolar pacing electrode[36,37,38]. The pressure

waveform is differentiated and the maximum positive derivative (dP/dt max) is averaged and used as the input in the pacing rate control algorithm[39]. There is a rapid acceleration of the pacing rate with exercise and the fall in pacing rate following cessation of exercise also shows a physiologic pattern[39,40].

A theoretical disadvantage of dP/dt sensor–driven pacing is the possibility of a positive feedback mechanism. The increased pacing rate may heighten the inotropic state of the myocardium by itself, giving rise to a further increase in pacing rate[40]. Moreover, the effect of other physiologic and pathologic conditions common in the elderly pacemaker population, as atrial fibrillation, right ventricular disease and the effect of cardiotonic drugs, require further evaluation.

In summary, dP/dt sensor:

Advantages	– Fast response
	– Specific to metabolic demand
	– Proportional to workload
Limitations	– Special lead
	– Unknown chronic stability
	– Compromised myocardial function may limit utility

Magnet Induced Upper–rate Pacing In An Activity Responsive DDDR Pacemaker

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PACE: Accepted for publication

Summary

We report a case of magnet head induced inappropriate upper–rate pacing during programming of a DDDR Activity pacemaker.Test data from manufacturing showed that the device had an activity threshold within the specified limits. By means of the sensor markers it was demonstrated that the pacemaker in the sensor mode detected the cardiac mechanical activity. As a consequence a positive feedback loop occurred with a pacing rate increase ending at or close to the programmed upper–rate. This hypersensitive sensor reaction only occurred during pacemaker programming with the patient in the supine position. During a follow up period of more than six months, the pacemaker functioned well without any sign of inappropriate pacemaker behaviour.

Introduction

Rate Adaptive Pacemakers using piezo–electric activity sensors have been very successfully employed since 1983 in more than 200.000 patients worldwide[2,3].Particularly the relative simplicity of the implant and replacement procedure (no special lead is required) and the easy follow up and patient management were the basis for the succes. In randomized cross–over trials pacemakers dependent patients showed a significant improvement in exercise capacity when their pacemaker was programmed to the rate responsive mode [3–6].The speed of onset of rate response is a significant advantage of vibration dependent rate modulation, however the magnitude and direction of rate response have their limitations[7]. These limitations are inherent to the mechanical proporties of the applied piezo–electrical transducer, the crystal will respond to exercise as well as non exercise related vibrations[10–12]. In the Activitrax pacemaker the sensor is affixed to the interior backside surface of the generator housing and can react next to vibration to pressure stimuli[10,11]. Application of a weight such as the programmer on the prepectoral pocket has been demonstrated to increase the pacing rate[11]. In our report we describe a patient in whom the DDDR pacemaker showed an unexpected upper–rate response during application of the programmer head on the pacemaker site. This response was not purely pressure related.

Case Report

An 35 year old man was admitted to the coronary care unit, with palpitations and mild dyspnoea. On physical examination, there was a striking thin build, no signs of heart failure were found.

As a three year old boy, he underwent a closure of an atrial septal defect and he was uneventful until persistent paroxysmal atrial tachycardias appeared. During the past three years, medication of digoxin, verapamil, disopyramide and flecainide were unsuccessful. In between the arrhythmia attacks, he had no complaints what so ever and lived an active life, even running half a marathon on several occasions. On admission, the ECG revealed a narrow QRS complex and tachycardia at 192 bpm. Sotalol 20 mg intravenously slowed down the ventricle rate to almost 100 bpm because of 2 : 1 block. The diagnosis of atrial tachycardia was obvious.

Conversion to sinus rhythm was preceded by a symptomatic sinus pause of 4 seconds. Under telemetric control, Sotalol orally t.d. 80 mg was given. However, a first degree A–V block developed and periods of symptomatic slow nodal rhythm occurred.The support of a permanent pacemaker was advised and the patient gave informed consent for the implantation of a dual chamberpacemaker, at that time still under clinical evaluation.

A Medtronic Elite™ pulse generator (Model 7074) was implanted left prepectoral and connected to a C.P.I. screw–in atrial lead (Model 4266) and a Medtronic ventricular lead with passive fixation (Model 4004). The atrial and ventricular stimulation thresholds (at 0.42 ms) were 1.3 V and 0.5 V respectively, P– and R–wave 4.0 mV and 7.9 mV respectively.

The pacemaker was programmed DDD, however atrial tachyarrhythmias reoccurred and the Sotalol medication 80 mg t.d. was restarted.Drug induced chronotropic incompetence of the sinus node was anticipated and the pacemaker was programmed to the DDDR mode before the patient left the hospital. Five weeks after implantation, the patient returned for the 1–month follow–up in accordance with the study protocol. After a test for cross–talk, performed in the DDD mode, the device was reprogrammed to the DDDR mode. After the device had been reprogrammed (with the magnet head resting on the pacemaker pocket), the pacing rate rapidly increased up to the programmed upper rate of 150 ppm. (fig 1).

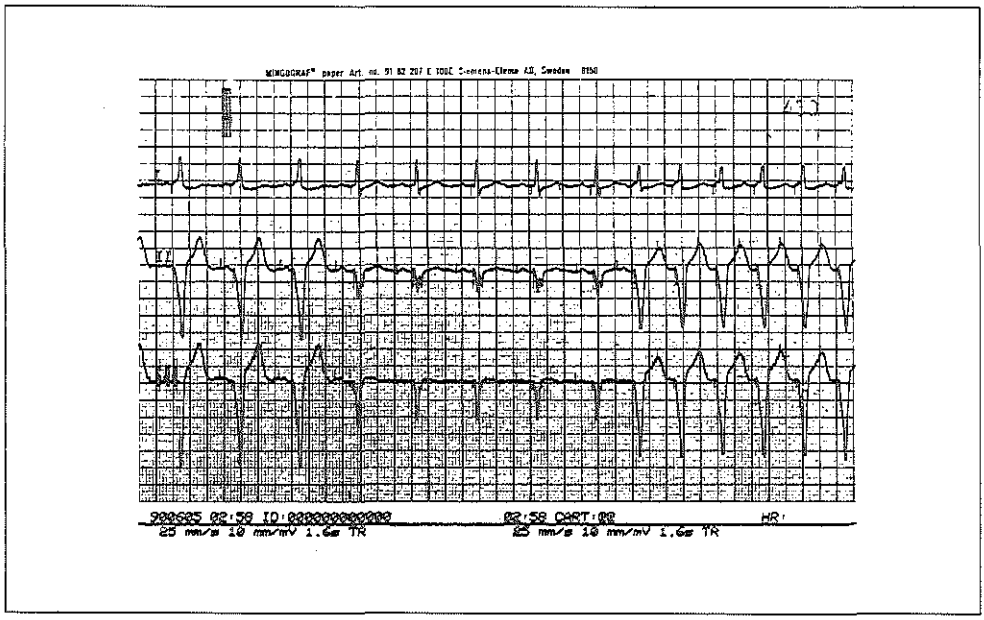

Figure 1. Three channel E.C.G. recording. The programmer head has been placed on the pacemaker. The patient in the supine position. As shown the DDD pacing rate increases rapidly.

The mechanism of this pacemaker tachycardia was not understood initially and it was decided to reprogram the device to the DDD mode and to perform a Holter recording. During the Holter recording period, the patient was feeling well and analysis of the Holter tape demonstrated proper operation of the pulse generator in the DDD mode.

Two weeks after this event, a special test, proposed by the manufacturer of the device under clinical investigation, was performed for determination of the cause of the high rate pacing.

For this purpose, the diagnostic Event Counter of the Elite pulse generator was used. The Event Counter can be programmed to monitor the rate indicated by the activity sensor, while the device is functioning in a non–activity mode, e.g. DDD. The results did not reveal any suspicious pacemaker behaviour; the pacing rate at which the device would have paced (provided it had been programmed to the DDDR mode), was as expected, taking into account the activities of the young and active patient during the 6 hours of recording.

For safety reasons, the patient was sent home with the device programmed

to DDD. The 3–month follow–up was used to further investigate the case. Reprogramming the device to the DDDR mode reproduced pacing at a rate close to the upper rate. The Marker Channel feature was programmed to telemeter the signal of the activity sensor, while the patient was in the supine position and the device in DDD mode (figure 2).

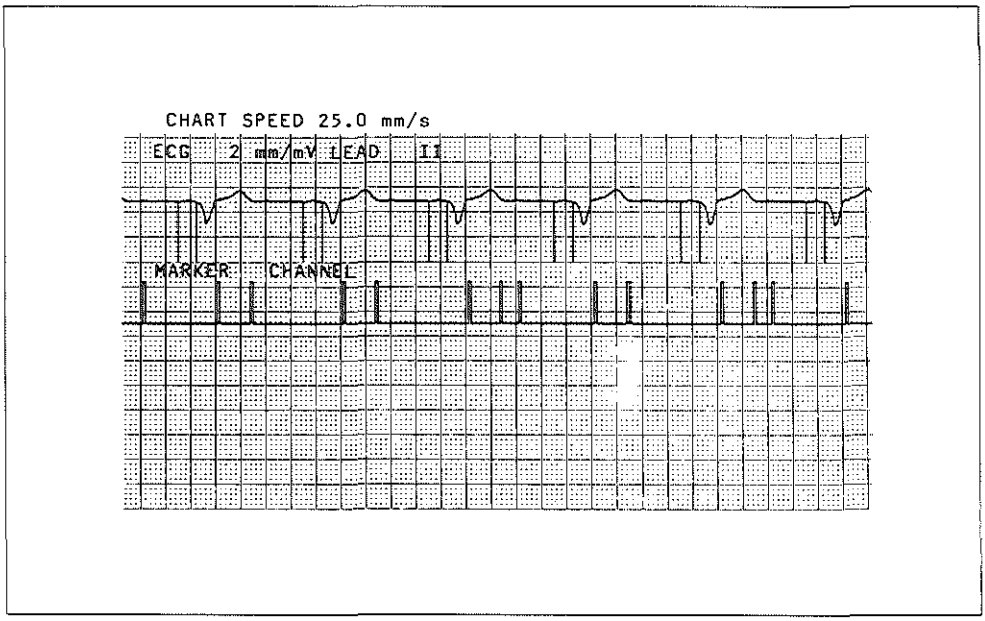

Figure 2. Programmer printout, recorded while the patient was in the supine position, with the programmer head lying on the pacemaker pocket (DDD mode, magnet canceled, lower–rate 60 ppm, upper–rate 150 ppm, Activity Rate Response: 7, Activity Threshold: Medium, Activity Acceleration: 0.5 min.). Upper tracing: surface E.C.G., showing AV–sequential pacing at the programmed lower–rate. Lower tracing: Marker channel, programmed to Sensor Detect Markers. The markers following each Q.R.S. complex indicate that the heart's mechanical activity is detected by the pulse generator's activity sensor.

It was obvious that the sensor was detecting the heart's mechanical activities : each QRS complex was followed by sensor output signals. In the DDDR mode, this induced a positive feedback loop, ending at at or close to the programmed upper rate. Figure 3 shows the result of the same test, with the magnet approximately 1 cm lifted above the pocket.

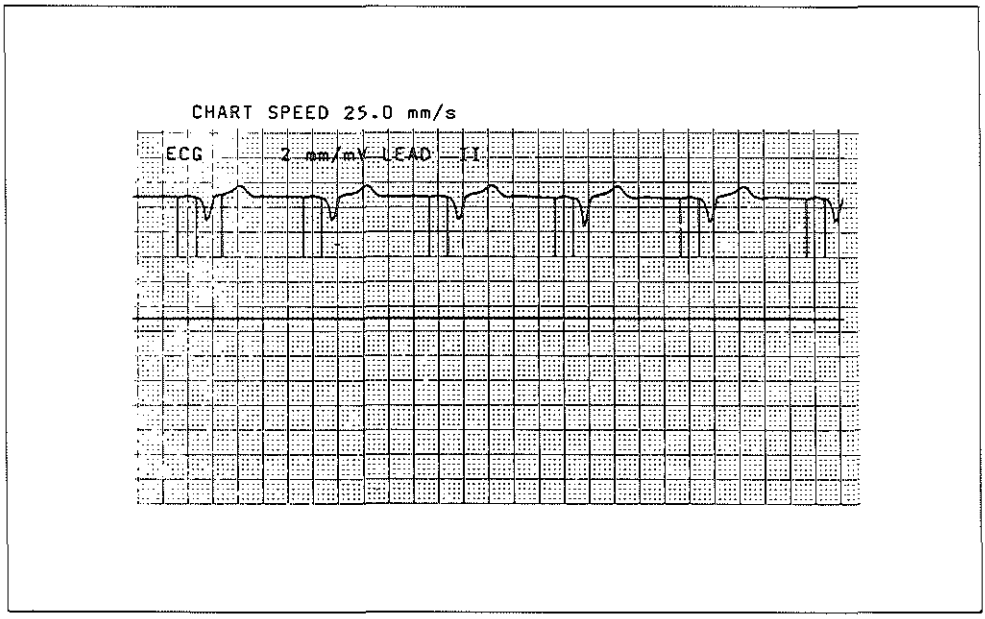

Figure 3. Same as figure 2, with the programmer head lifted approximately 1 cm above the pocket. The absence of Sensor Detect markers indicates that the sensor does not detect any activity.

Now the sensor was not detecting any activity. It neither occurred with the patient in sitting or upright position. These observations are in accordance with the Holter recording results. The detection of activity in the supine position was eliminated by reprogramming the Activity Threshold.

Discussion

For more than 7 years activity triggered rate modulated pacing has given many pacemaker patients impressive improvements in their exercise capabilities. When during implantation special care is taken to position the generator in direct contact with underlying body tissue, in most cases the patient can be assured for long term appropriate rate response with little need for reprogram-

ming. However, as several studies demonstrated rate modulated devices using piezo–electric sensors have their limitations[6,7]. These limitations are directly related to physical characteristics of the piezo–electric crystal. The typically used crystal is most sensitive to vibrations between 10 and 50 Hz. Body motions as walking, climbing stairs and bycicle riding result however in vibrations generally less than 10 Hz. Even careful filtering of the incoming sensor signals can not prevent sensing of unphysiological vibrations. These vibrations can result from loud music, power tools, aircraft engine noise and bumpy automobiles[1,4,8,9]. Pressure related symptomatic pacing rate increases were reported during pacemaker programming[10].

Some patients suffered from palpitations when lying on the implant site or using an automobile seat belt. A pressure related phenomenon was innitialy presumed when in our patient during programming the pacemaker in the DDDR mode an increasing pacing rate occurred.

Our patient was slender in statute and it seemed possible that high sensor signals were caused by direct contact of the patients ribs with the backside of the can. However the marker channel feature of the activity pacemaker revealed the unexpected answer. Each Q.R.S.complex was followed by several sensor output signals, clearly the mechanical cardiac activity was picked up by the piezo–electric sensor. When the pacemaker was programmed in the DDDR mode this resulted in a possitive feedback loop ending up to upper rate pacing. When the programmer head was lifted 1 cm above the pacemaker pocket no sensor output signals were seen. Also programming while the patient was in a sitting position did not result in a pacing rate increase. Obviously the weight of the programmer head was necessary to push the device to the apex of the heart. Probably the slender statute played an imported role, under the pacemaker there was little muscle or fat to act as padding. In daily life no inadequate pacemaker function was reported and during a follow up after more than 6 months there was safe and effective rate modulated pacing. During programming the over sensitive sensor response could be avoided by changing the activity threshold from medium to high.

In Conclusion

An unexpected and unnecessary pacing rate increase was induced by programming an activity pacemaker to the rate–responsive mode. The origin of this eccentricity was elucidated by evaluation of the sensor detect option of the marker channel.

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Impedance Measurements In The Human Right Ventricle Using A New Pacing System

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PACE 1991;14:1336 – 1342

Summary

Wortel H. et al : Impedance Measurements in the Human Right Ventricle Using a New Pacing System. A promising new pacemaker that provides on–line measurements of right ventricular (RV) impedance was evaluated in ten patients with symptomatic second– or third–degree atrioventricular (AV) block. We tested the assumption that if changes in RV impedance represented changes in RV stroke volume (SV), conditions known significantly to affect RV SV should be accompanied by significant changes in RV impedance. One week after pacemaker implantation, RV impedance was measured noninvasively during normal respirationin the supine (baseline), left laterial, right lateral, sitting and standing positions. In addition, all patients performed a Valsalva maneuver test. The amplitude of the impedance signal was different during in– and expiration in every body position studied. At baseline, the amplitude of the impedance signal was 18.80 $\pm$ 2.24 mm; in the right lateral position 16.75 $\pm$ 3.24 mm (P=0.04) and 17.80 $\pm$ 2.35 mm in the left lateral position (P=0.04). The amplitude of the signal in sitting position was 16.65 $\pm$ 2.89 mm (P=0.07) and in the standing position 16.95 $\pm$ 3.44 mm (p=0.11). The most impressive change in amplitude was noted during performance of the Valsalva maneuver. During this test the amplitude decreased to 13 $\pm$ 2.81 mm and rose to 20 $\pm$ 2.66 mm (P=0.002) afterwards. These results strongly support the assumption that changes of RV impedance as measured by this catheter represent changes in RV SV. This new pacing system is the first pacemaker that reports on the hemodynamic response of every heartbeat by measuring RV impedance. (Pace, Vol 14, september 1991)

keywords: Impedance catheter, stroke volume, right ventricle

Introduction

In 1978 Corten and Koops[1] introduced an eight–electrode catheter to measure left ventricular (LV) volume on a beat–to–beat basis. The catheter was applied in the canine as well as the human left ventricle by Baan and co–workers[2,3]. In their reports[2–4] the investigators stated this catheter may be a useful tool not only to monitor LV volume changes, but also to provide accurate absolute–volume measurements.

Recently, a tripolar impedance catheter was developed for use as a pacing catheter in an adaptive rate pacemaker[5]. The purpose of our study was to determine wheter impedance catheter measurements in the right ventricle (RV) would relate to RV stroke volume (SV) like LV impedance catheter measurements relate to LV SV. All measurements were performed noninvasively in the outpatient clinic after pacemaker implantation. The amplitude of the RV impedance signal was measured during respiration , during different postures, and during the performance of a Valsalva maneuver.

Methods

Patients and Procedures

In ten physically active patients with symptomatic second– or third–degree atrioventricular (AV) block, a dual chamber pacemaker (Precept DR [DDDR] Cardiac Pacemakers Inc., St. Paul, MN, USA) was implanted. All implantation procedures were performed by puncture of the left subclavian vein. First, through a 11 French Cordis (Cordis Corp.,Miami,Fl,USA) ,or Daig (Daig Corp., Minnetonka, MN, USA) introducer, the ventricular catheter was positioned with its distal electrode in the RV apex.

The movement pattern of the catheter over the tricuspid valve and the position of the proximal ring electrodes in the right ventricle were verified by fluoroscopy (Fig. 1). Subsequently, the introducer was peeled off and the guidewire was left in the superior vena cava.

The atrial lead was then positioned in the right atrial appendage through a ten French Cordis introducer. All pacemakers were initially programmed in the conventional DDD mode (lower rate limit = 50 ppm, AV–delay = 175 msec, upper rate limit = 125 ppm). Patients were discharged from the hospital 2–3 days after pacemaker implantation. RV impedance measurements were performed 7 – 10 days after hospital discharge, as patients visited the outpatient clinic for removing of the stitches from the wound.

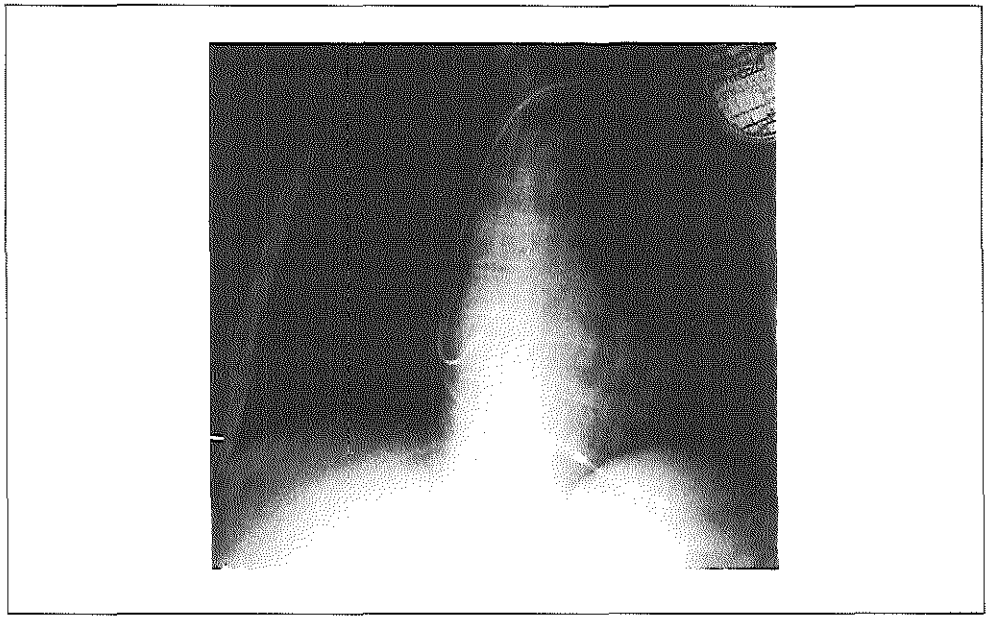

Figure 1. Chest X ray of PRECEPT pacemaker system. The tripolar pacemaker lead is in the right ventricular cavity. The tip electrode is for pacing and for injecting a constant current, whereas the other two ring electrodes are both voltage measuring electrodes.

Impedance Catheter and Pulse Generator

PRECEPT DR is a single or dual chamber adaptive rate pacemaker offering a choice between relative RV SV and preejection interval as indicators for metabolic demand. The volume related signal used to derive both parameters is obtained by RV impedance measurements. For this purpose a constant amplitude, alternating current of 6 microA is emitted from the tip of a tripolar electrode catheter to the housing of the pulse generator (Fig 1).

The alternating current generates a voltage between the two ring electrodes both contained in the RV cavity. This voltage is inversely proportional to the blood volume enclosed by the ventricular wall and the two parallel planes running through the proximal ring electrodes and perpendicular to the direction of the current. Based on studies done in the animal laboratory, Salo et al.[6,7] suggested that volume dynamics of this cross–sectional area may represent those of the entire right ventricle.

PRECEPT DR provides telemetry of a signal directly proportional to volt-

age measured in the right ventricle. This signal (Sensorgram™ can be recorded simultaneously with the ECG (Fig 2).

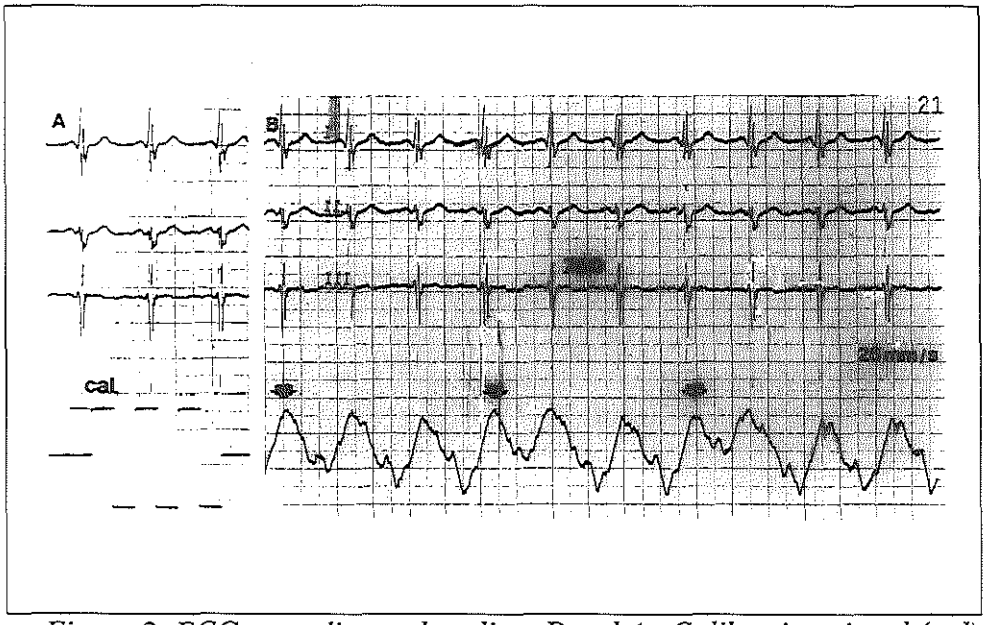

Figure 2. ECG recording at baseline. Panel A: Calibration signal (cal), Panel B: Note the variations in amplitude of the impedance signal Sensorgram with respiration. Arrows mark the respiration cycle. The Sensorgram is directly proportional to voltage measured in the right ventricle

Study Protocol

Patients were at rest in supine postion on the examination table. A three channel ECG recorder was used to record the calibration and impendance signal simultaneously with the ECG. Fig. 2 shows a recording at baseline conditions. The next step was performance of a Valsalva maneuver with the patient still in the supine position (Fig. 3). For this purpose, patients were asked to perform a forced experiation against the back of the right hand. Patients then rolled over to their left lateral side and recordings were made 2–3 minutes after the change to this new body position. Patients returned to the supine position and then rolled over to the right lateral side where, after 2–3 minutes, recordings were made. The last step of the protocol was changing from a supine position to sitting on the examination table and from sitting to standing next to the examination table. All recordings were made after 2–3 minutes for adjustment.

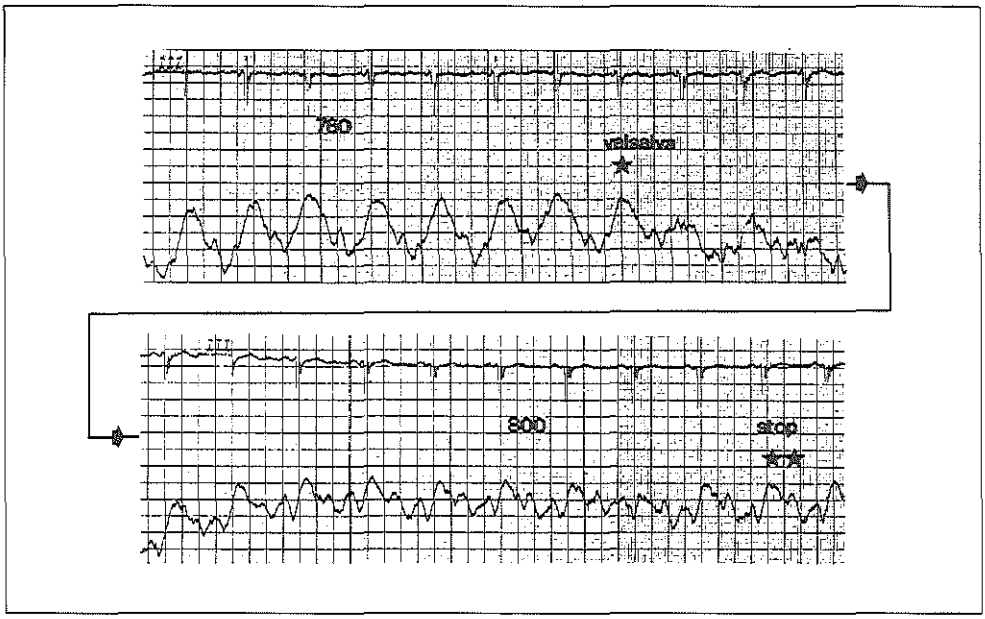

Figure 3. Continuous tracing of ECG and Sensorgram during a Valsalva maneuver test. An extreme reduction of the amplitude of the right ventricular impedance signal is observed during increase of the intrathoracic pressure.

Statistical Analysis

Sensorgram™ were measured using a ruler with millimeter scale. Intervals are given in mm based on an average of 5–10 beats. Each patient served as his of her own control. All data were presented as means ± SD. Differences between values were compared by means of the two–tailed sign test.

RESULTS

Ten patients were studied with a mean age of 74 ± 6 years. The youngest patient was 62 years, the eldest patient was 82. All patients were physically active and all patients received a permanent pacemaker because of symptomatic second– or third–degree AV block.

The data represents the amplitudes of the measured impedance signals. Figure 4A shows the amplitude of the RV impedance at baseline during normal respiration. We observed that the amplitude of the impedance signal was smaller at the onset of inspiration than at the end of inspiration. This was true in all body positions tested. The amplitude of the RV impedance signal during

Valsalva maneuver is shown in Figure 4B. In Figure 4B, 11 tests are shown performed by ten patients. In one of our patients, spontaneous heart rhythm was present during the Valsalva maneuver. The amplitude of the impedance signal was 6 mm during the test and 15 mm afterwards. This patient was asked to repeat the test when AV synchronous pacing rhythm was present. During the latter, the amplitude of the impedance signal increased from 13 mm during the test to 21 mm thereafter. Table I and table II summarize impedance measurements at different positions of the human body.

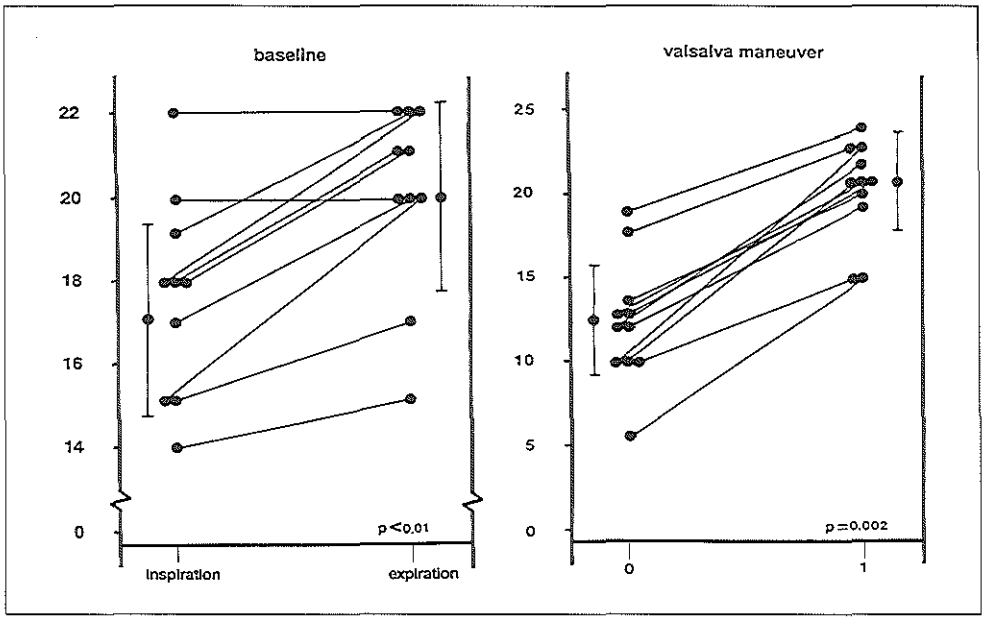

Figure 4(A). Amplitude variations of the measured impedance signal at baseline due to respiration.(B) Amplitude of the measured impedance signal during Valsalva maneuver (0) and after the Valsalva test (1).

Table 1

Amplitude of the Impedance Signal During Inspiration and Expiration (Measurements in mm)			
	Inspiration (mean ± SD)	**Expiration (mean ± SD)**	**P value (sign test)**
baseline	17.60 ± 2.46	20.00 ± 2.31	0.01
right	16.00 ± 2.94	17.50 ± 3.72	0.06
left	17.20 ± 2.35	18.40 ± 2.55	0.06
sitting	15.80 ± 2.82	17.50 ± 3.14	0.02
standing	16.20 ± 3.29	17.70 ± 3.77	0.06
Baseline = supine position; right = right lateral side; left = left lateral side			

Table 2

Amplitude of the Impedance Signal During at Different Body Positions (Measurements in mm)		
	Amplitude*	**P value****
baseline	18.80 ± 2.24	
right	16.75 ± 3.24	0.04
left	17.80 ± 2.35	0.04
sitting	16.65 ± 2.89	0.07
standing	16.95 ± 3.44	0.11
** Mean of the sum of all patient's mean amplitudes ([inspiration + expiration/2])*		
*** Two–sided paired sign test was performed comparing basiline with four different positions of the body. Changing from the left lateral side to the right lateral side (17.80 ± 2.35 vs 16.75 ± 3.24) was associated with a P value of 0.29 (NS). Right = right lateral side; left = left lateral side*		

Discussion

Considerations

In our experiments we implanted all pulse generators in the upper left thoracic region. Thus, the direction of the electrical current was not parallel to the catheter as opposed to experiments by Baan et al.[2,3] in the left ventricle, Woodward et al.[8] and McKay et al.[9] in the right ventricle, which complicates a simple comparison of our results.

In addition, the three–electrode impedance catheter presented in this article measures with one pair of sensing electrodes (proximal ring electrodes) and not with five pairs of electrodes like Baan et al.[2], which means that we only measured a voltage difference over one cross–sectional RV area determined by one plane through the proximal ring electrode perpendicular to the direction of the current and by a second plane parallel to the first plane through the other ring electrode.

With regards to parallel conductance (coductance=impedance–1), we assumed that the portion of the total conductance 10 that is due to electrical current passing outside the RV blood pool was constant. We ignored this portion in our study of relative changes of RV impedance. However, Boltwood et al. [10] suggested that over a wide hemodynamic range this portion may not always be constant.

Measurements

The only tools needed to measure impedance changes in the RV cavity were a ruler, an ECG recorder and a pacemaker programmer. It is well to remember that sophisticated techniques like electromagnetic flow probe SV, thermodilution SV and volume changes assessed by radionuclide or contrast angiography are techniques that cannot compete in elegance with impedance volume measurements of this pacemaker.

Respiration.

We observed a variation in amplitude of the impedance signal, which was clearly related to respiration (Fig. 2). The amplitude of the impedance signal was smaller at the end of expiration and onset of inspiration than at the end of inspiration and onset of expiration, which supports the classic assumption that RS SV increases during inspiration and decreases during expiration.

Valsalva maneuver.

The pacing system measures voltage and Sensorgram (tm) shows changes of RV impedance on a beat–to–beat basis. During the Valsalva maneuver, the

amplitude of the impedance signal decreased significantly, which indicates a significant reduction of the change of RV impedance and consequently a significant reduction of RV SV.

Postural Changes.

Rushmer[11] described the effects of posture on SV in intact dogs and human subjects. For this purpose, aortic blood flow in dogs was measured by means of an indwelling ultrasonic flowmeter. In man SV was not assessed directly, but derived from cardiac output measurements either using the Fick principle or the thermodilution technique.

According to Rushmer[11] and Weissler et al.[12], a reduction of SV on standing was observed consistently in all normal human subjects and Valsalva maneuver tests also resulted in a reduction of SV. Our observations on on–line impedance measurements in the right human ventricle agree with these observations.

Future Implications

Since the catheter used in this series was shown to be very sensitive, it would be interesting to find out what the effect is of different pacing modes on RV impedance curves. So far, only Salo et al.[6,13] studied the effects of VVI and VDD pacing on voltage changes in the RV and LV cavity in dogs. This kind of study in man will definitely generate information previously difficult or impossible to obtain, allowing a much more thorough analysis of the hemodynamic effects of various pacing modes.

Another unexplored area would be the field of RV and LV function in patients with heart failure. In contrast to its LV counterpart, the right ventricle has been allocated to relative obscurity. This comparitive neglect is due to a number of factors. The most important one probably is the fact that the left ventricle has a fairly simple geometrical shape and can be modeled with rather straightforward mathematical manipulations, whereas the right ventricle is a structure that defies simple geometric analysis[14]. In this series we only implanted the device in physically active patients without any sign or symptom of heart failure. It would be interesting to compare these results with those obtained in patients with heart failure.

Recently, Khoury et al.[15] reported on the application of a RV impedance catheter to assess the occurrence of tachycardia–induced ventricular failure as an antitachycardia system control and suggested an algorithm based on impedance catheter measurements for future antitachycardia systems.

At present, we do not know whether it will be possible to guide therapy in patients with severely diseased hearts by measuring RV impedance, however we do assume that in the near future sensor driven pacemakers will be applied not only for adaptive rate pacing, but also for monitoring of cardiac output [16].

Conclusion

The effects of respirationand postural changes on RV impedance were studied in ten physically active patients who underwent implantation of a PRECEPT pacemaker. In addition, the effect of Valsalva maneuver on RV impedance was assessed. The results of this study strongly support the assumption that changes of RV impedance represent changes in RV SV. On–line measurement of RV impedance is a promising new technique, which may generate information previously difficult or impossible to obtain in patients. The Precept pacing system is the first pacemaker that reports on the hemodynamic response of every heartbeat by measuring the RV impedance.

Acknowledgement: The authors would like to thank Prof.Dr. Jan Baan for his critical review of the manuscript and Paul G.H. Mulder M.S. for the statistical analysis.

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Chapter VII

TIME INTERVALS IN RATE–MODULATED CARDIAC PACING

7.1. Primary physiologic sensors

The heart rate is under the influence of the sympathetic and parasympathetic nervous system, with predominance of the former under cardiocirculatory stress as physical exercise or emotion. Sympathetic nerve stimulation increases sinus rate and the speed of atrioventricular conduction; the ventricular depolarization and repolarization shortens. The cardiac response to sympathetic nerve stimulation is fast, the response is maintained by the release of catecholamines by the adrenals. Several intervals of impulse propagation in the heart can accurately be measured. The duration of these intervals are a direct manifestation of sympathetic tone and catecholamine influence on the heart varying in parallel with sinus rate[1,2]. This close parallelism makes these intervals attractive as physiologic indicators of cardiac demand. The following cardiac interval derivatives are proposed or used as a physiologic signal to drive rate–mediated pacing systems: the A–R interval, the pre–ejection interval, the Q–T interval and the ventricular depolarization gradient.

7.2. The A–R Interval

The A–R interval is the interval from an atrial stimulus to the following ventricular R wave. Ruiter et al[5] showed the existence of a linear correlation between the A–R interval and the sympathetic tone during different kinds of exercise.

We demonstrated the feasibility of using this measurement for a rate–modulated system. Others[1,3] had already shown that the P–R interval shorthens linearly during exercise.

A program using this linear relationship was developed and temporarily down–loaded to a DDD generator. Preliminary studies are promising and demonstrate the suitability of the A–R interval as an indicator of sympathetic drive. In a dual–chamber, dual–lead unit, the measurement of the A–R interval is simple. The feasibility of adaptive–rate pacing with a single lead AAI pacemaker, using the A–R interval, depends upon the morphology, amplitude and

slew rate of the far–field ventricular deflection in the right atrial electrogram. Far–field ventricular sensing via the atrial electrode is very commonly seen in uni and bipolar atrial ECGs[6].

Far–field ventricular complexes were present in all unipolar atrial recordings in a retrospective study of Den Heyer et al[7]. The characteristics of these atrial sensed far–field ventricular signals render the possibility of A–R interval–based single lead AAIR pacing. In this chapter our study with the A–R interval will discussed.

In summary, A–R interval sensor

Advantages	– Specific
	– Proportional to workload
	– Fast response
	– Rate independent
	– No special lead
Limitations	– Normal A–V conduction is essential
	– Can be influenced by drugs
	– Long–term reliability of far–field QRS sensing is unknown
	– Intermittent intraventricular conduction disturbance

7.3. The Pre–Ejection Interval (P.E.I.)

The pre–ejection interval is composed of two intervals: the electro–mechanical latency period and the isovolumetric contraction time[4,9]. The electro mechanical latency period relates primarily with intraventricular conduction; for example a right bundle branch block will produce a delay of this first part of P.E.I. The isovolumetric contraction time comprises the time between the onset of mechanical activation of the ventricle and the onset of ejection. This interval is a direct reflection of contractility and, hence, of sympathetic tone[8]. In studies performed by Chirife et al, the P.E.I. was determined using a standard bipolar pacing lead[10]. Measurements were taken from the onset of the intracardiac ECG or pacemaker spike to the onset of right ventricular ejection determined from a right ventricular volume curve. Right ventricular volume curves were obtained by the impedance method as has been described in Chapter VI. In a clinical trial, Higgens et al[11, 12] used a multipolar pacing lead and showed that P.E.I. derived from intracardiac impedance signals could be

reliably used in most of the patients as a signal to mediate pacing rate. In the last section of this chapter we will discuss our experience with the P.E.I. sensor.

In summary, P.E.I.sensor:

Advantages	– Specific
	– Proportional to workload
	– Fast response
	– Rate independent
	– Good chronic reliability
Limitations	– Special multipolar electrode (in the future a normal bipolar lead can be used)
	– Posture related changes
	– Battery consumption

7.4. The Q–T Interval

The exercise–induced decrease in the interval between the pacing stimulus and the T–wave has been investigated by Rickards et al[13,14] as a parameter for controlling pacing rate. Because about half of the exercise–induced decrease in the natural Q–T interval results from increased catecholamine levels rather than increased heart rate, the Q–T interval can serve as an indicator for optimizing heart rate. The commonly used term Q–T interval is, in fact, the measured interval from the unipolar ventricular stimulus and the downslope of the endocardial T–wave evoked by the stimulus and is a reflection of the sympathetic drive[13]. In practice, it is necessary to pace the ventricle periodically even during normal sinus rhythm to produce a stimulus T–interval (stim–T) that can be measured. The rate algorithm of the pacemaker translates variations in the measured stim–T interval into pacing rate changes[15,18].

The history of adaptive–rate pacing using the Q–T interval spans over 9 years in which time, more than 6,000 of these pacemakers have been implanted throughout the world[17]. A commercially–available Q–T interval sensing pacemaker is able to automatically adjust the adaptive–rate parameters to suite individual patient requirements, avoiding repetitive testing to apposite the device parameters during different situations in daily life[16,23]. Res et al reported[17] that these automatic functions were effective and time saving during follow–up visits. Many studies showed that the Q–T pacemaker produces an adequate rate response to standardized exercise stress tests and to nor-

mal daily activities[15,18,19,20]. Earlier problems seen with the Q–T method were related to setting the correct pacing parameters, a relatively slow response to the onset of exercise and a slow decay after exercise[20,21]. These difficulties are largely overcome due to adjustments in the pacing algorithm and now the device is able to function automatically to a large extent[17]. However, anything that affects the Q–T interval can affect the rate–mediating behavior of the pacemaker including myocardial infarction, ischemia, cardiomyopathy, electrolyte imbalance and cardioactive drugs.

Slow variations in the Stim–T interval as induced by antiarrhytmic agents, will not have a marked influence on the rate–adaptive function of the Q–T pacemaker. The algorithm of the device contains a numeric filter that disregards slow variations in the Stim–T interval.

Robbens et al[29] studied a patient with a Q–T pacemaker during an acute inferior myocardial infarction. The pacemaker behaved "physiologically" and no unexpected rate changes were observed.

Recently, the Q–T principle has been combined with the piezo–electric activity sensor in a dual–sensor, dual–demand pacemaker[24].

In summary, Q–T sensor:

Advantages	– Proportional to workload
	– Chronic reliability
	– Regular lead
Limitations	– Only ventricular applications
	– Evoked response required
	– Slow initial response to exercise
	– Moderate specificity

7.5. Ventricular Depolarization Gradient (QRS gradient, Paced Depolarization Integral)

The ventricular depolarization gradient is an electrocardiographic variable derived from the electronic integration of a pace–evoked QRS complex. The time integrate of the paced ventricular deflection increases with increasing pacing rate and decreasing workload and decreases with decreasing pacing rate and increasing workload thereby providing a true reference signal for rate–mediated pacing[25,26].

Special electronic circuits have been developed to remove the post–stimu-

lus electrode polarization at the electrode tissue interface[28].

Like the Q–T pacemaker, the QRS gradient measurement is dependent on the pace–evoked ventricular response. Since the pacemaker must measure the evoked QRS response, its absence can be readily recognized by the sensing circuitry of the pacemaker when pacing is below stimulation threshold. This renders the possibility of an automatic threshold adjustment. The first clinical experience with this rate–responsive system is very promising (27,28).

Advantages	– Specific (both exertional and emotional stress)
	– Fast response
	– Chronic stability
	– Rate independent
	– No special lead
Limitations	– Needs evoked response
	– Questions on specificity and proportionality

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The A–R interval as exercise indicator A New Option for Rate Adaptation in Single and Dual Chamber Pacing

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PACE 1990;13:1656 – 1665

Summary

We investigated the possibility to use the interval from an atrial stimulus to the ventricular R–wave (A–R interval) as an indicator of physical stress. In 16 patients with pacemakers implanted for severe atrial bradycardia but with intact A–V conduction the A–R interval was studied during incremental atrial pacing at rest and during exercise with a constant workload.

In addition the protocol the atrial pacing rate was kept constant just above spontaneous sinus rate and the dynamics of the A–R interval were studied during exercise with a low constant workload and during a maximal exercise test with increasing workload.

Incremental atrial pacing prolonged the A–R interval, and this response was blunted during exercise ($P < 0.003$), atrial pacing at a constant rate and during a constant workload resulted in an almost direct shortening of the A–R interval.

When the workload was increased but the atrial rate kept constant a pronounced shortening of the A–R interval was noted ($P < 0.0001$).

It is concluded that changes of the A–R interval during different kinds of exercise were prompt and predictable. In patients with sinus node dysfunction but intact A–V conduction the shortning of the A–R interval during exercise may be a suitable indicator for rate adaptive atrial pacing.

A–R interval, rate adaptive pacing, A–V nodal Wenckebach block, exercise stress test

Introduction

With exercise the chronotropic response of the heart is the major determinant of the increase in cardiac performance[1]. For this reason rate modulated pacing in restoring heart rate response to daily activity improved the quality of life of many pacemaker patients[2,5].

The most reliable sensor of the metabolic demand during exercise or emotion is a normally functioning sinus node. In patients with a high degree atrio-

ventricular (A–V) block and a normal functioning atrium, dual chamber pacing can provide optimal rate control over a wide range of atrial rates with preservation of the benificial effects of A–V synchrony.

Unfortunately, it has been suggested that the atrial rate functions as a reliable indication of emotional or physical stress in only 20% of the patients undergoing permanent pacemaker insertion[2,3].

In the remaining patients, pacing systems that respond to other indices of increased metabolic demand have been applied[2–4,6].

A variety of indicators have been investigated over the past few years: clinical experience has been obtained with single chamber units incorporating a sensor for activity, respiration, Q–T interval, or temperature.

We investigated whether a continuous measurement of the interval from an atrial stimulus to the ventricular R wave as a reliable indicator of physical stress in patients with sinus node dysfunction and normal anterograde A–V conduction.

Patients And Methods

Patients

The study included 16 patients, 6 males and 10 females with an average age of 69.9 (age range: 51 – 81). Suitable candidates for this study were patients with chronotropic incompetence but with intact A–V conduction. Table I summarizes the patient population.

Table 1

Clinical Patient Pre– and Postpacing Data								
	Clinical Data Prepacing					Clinical Data Postpacing		
Pat NR.	Age [years]	Sex [M/F]	C.D.	Heartrate	Symptoms	Pacing mode	Pacemaker type	Drug
1	66	F	SB	80–120	Syncope	AAI	Medtronic 8423	Metoprolol 200
2	68	M	PAF	60–110	Dizziness	AAI	Medtronic 8423	
3	51	M	SA, SB	40–50	Dizziness	AAI	Medtronic 8423	
4	72	F	SB	20–60	Syncope	AAI	Medtronic 8420	
5	72	M	SB, PAF	48–120	Dizziness	AAI	Medtronic 8400	Metoprolol 200
6	73	M	SA, SB	45–72	Dizziness	AAI	Medtronic 8423	
7	81	F	SB, PAT	30–60	Dizziness	AAI	Medtronic 8423	
8	70	F	SA, SB	15–145	Syncope	AAI	Medtronic 8423	Verapamil 80, Digoxin 0.25
9	75	F	SA, SB	20–48	Dizziness	AAI	Medtronic 8400	Metoprolol 200
10	50	F	SB, PAF	40–160	Dizziness	AAI	CPI 635	Dysopyramide 250 Metoprolol 200
11	76	M	SA, SB, AVN	34–70	Syncope	DDD	Medtronic 7006	
12	78	F	SA, SB, PAF, PAT	28–54	Syncope	AAI	CPI 645	Atenolol 100
13	79	M	SA, SB, PAT	42–84	Dizziness	AAI	Medtronic 8420	
14	71	F	SA, SB, PAF	32–110	Dizziness	AAI	Medtronic 8420	Digitaline 0.1 Diltiazem 60
15	79	F	SA, SB	30–68	Syncope	AAI	Medtronic 8400	
16	57	F	SA, SB, AVN	34–102	Dizziness	DDD	CPI 935	

Clinical Patient Pre– and Postpacing Data Abbreviations :C.D. = conduction disorder SA = sinusarrest SB = sinusbradycardia SAB = sino–atrial block PAF = paroxysmal atrial fibrillation PAT = paroxysmal atrial tachycardia AVN = A–V nodal disease AAI = atrial demand DDD = A–V universal

Fourteen patients had atrial demand pacemakers (AAI) and two patients had programmable A–V universal mode (DDD) pacemakers implanted at least three months before the study.

All patients underwent an electrophysiological study to assess AV nodal and infranodal conduction properties.Assessment was performed either pre-pacemaker implantation or during pacemaker implantation. Only patients with intact A–V nodal and infranodal conduction were included. The criterion for intact A–V nodal conduction was 1:1 conduction up to a rate of least 120 beats/min. The criterion for normal infranodal conduction was an H–V interval of < 60 msec. The clinical picture of all patients was symptomatic sinus-node dysfunction, eight patients suffered from the brady–tachy variant, and seven patients of this subset were treated with antiarrhytmic drugs.

Only patients in whom overdrive suppression of the spontaneous heart rhythm during exercise was possible, either due to chronotropic incompetence or the usage of beta–blocking agents were included in the study, since in these patients interference between spontaneous rate and artifical pacing does not occur.

Methods

All patients performed bicycle exercise stress test < 3–6 months after pacemaker implantation.The patients were placed in an upright position on the bicycle ergometer, three surface ECG leads (I, II or III, AVF) were recorded continuously with a TEAC HR 10 casetterecorder with a recording speed of 4,76 cm/sec using a frequency modulated signal. The frequency response at these settings was DC to 1.250 Hz. The three ECG leads were also recorded on paper with a Siemens Mingograph (Siemens–Elema, Solna, Sweden) at a recording speed of 25 mm/sec and 100 mm/s every last 10 seconds of each minute. The taped signal was reproduced on a TEAC R 71. The signal was amplified and led through an 8 bit AD converter with a sampling frequency of 2.000 Hz. The data were real–time analyzed with an Apple IIe computer (Apple, Cupertino, CA, USA), which detected the atrial stimulus artifact and the peak of the R wave, and stored the R wave amplitude, and the interval from the atrial stimulus to the R wave (A–R interval) in a data file. The data file was transfered to an Apple Macintosh computer for the statistical analysis.

Figure 1 demonstrates the data recording and analysis set up.

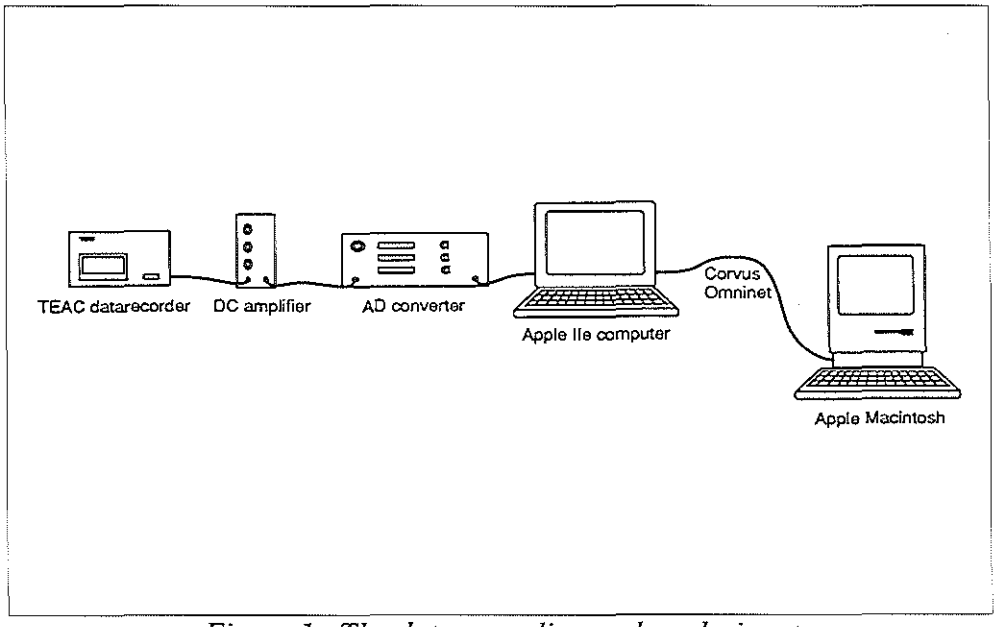

Figure 1. The data recording and analysis setup.

The pacing rates were changed with the programmer positioned over the pulse generator. During the study, the paced atrial rate was kept above the spontaneous sinus rate.

The protocol consisted of four parts:

1 Incremental atrial pacing at rest (Fig. 2, left panel) The A–R interval was measured at rest and at atrial paced rates of 60, 70, 80, etc., until the Wenckebach point was reached. The changes between the various rates were stepwise and each frequency was kept constant for 1 minute. For analysis, the computer program averaged the last 20 A–R intervals prior to a rate change.

2 Exercise with increasing workload (Fig. 2, left panel). The A–R interval was measured during exercise with increasing workload. The workload steps were 20, 40, 50, 60 Watt etc. until maximal workload was reached; the workload was increased every minute. The pacing rate was kept constant above sinus rate to produce overdrive suppression even at the highest workload. The A–R intervals were averaged over 20–second periods. If spontaneous sinus rate became faster than the atrial pacing rate, the measurement was repeated at a higher pacing rate after the patient had recovered and the steady state was reached again.

3 Exercise with a constant low workload and a constant atrial pacing rate (Fig. 2, right panel).

The A–R interval was measured during exercise with a low constant workload of 40 Watt for a period of 5 minutes. The paced atrial rate was kept just above the sinus rate, producing 100% pacing. The A–R intervals were averaged over 20–second periods.

4 Exercise with a constant workload and incremental atrial pacing (Fig. 2, right panel). The A–R interval was measured during exercise with a constant workload at 50% of the maximum workload and incremental pacing.

The pacing rate was increased in steps of 10 beats/min until Wenckebach point was reached. At each frequency level the pacing rate was kept constant for 1 minute.

The date analysis contained: the quantitive analysis of A–R interval during exercise; and the response of the A–R interval to pacing rate changes during exercise.

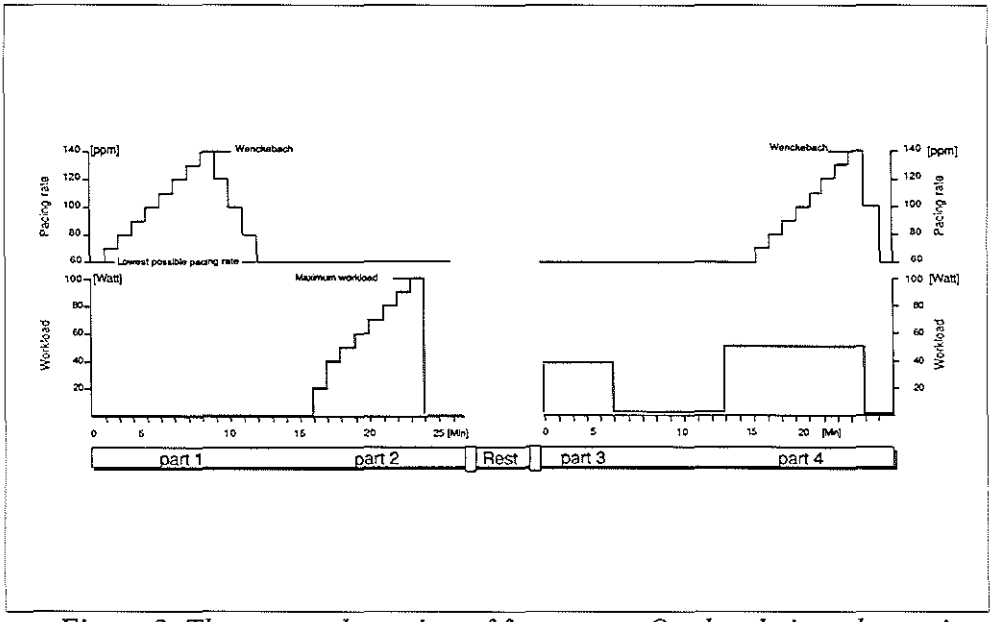

Figure 2. The protocol consists of four parts: On the abcissa the pacing rate in beats/min. (bpm) and the workload in watts. On the ordinate the time scale in minutes (min). ***Part I:*** *the Wenckebach test at rest (left panel);* ***Part II:*** *the maximal exercise test (right panel);* ***Part III:*** *the exercise test at constant low workload (right panel);* ***Part IV:*** *the Wenckebach test at constant workload (right panel).*

Statistics

Results are presented as mean $\pm$ standard error. Student's paired t–test was used for comparison of means. A P of 0.05 or less was considered the limit of significance.

Results

Incremental atrial pacing at rest with the patients sitting in an upright position on a bicycle ergometer resulted in an increasing A–R interval in all patients until Wenckebach block developed, or the maximal programmable atrial rate was reached (patient 10 and 12). Atrial pacing was started just above spontaneous sinus rate, the lowest pacing rate which produced 100% pacing in all patients was 80 beats/min. In two patients, the quality of the ECG recordings was insufficient, in the remaining 14 patients the atrial pacing range 80 – 130 beats/min could be analyzed. Table II demonstrates the results of the incre-

mental atrial pacing studies in patients with and without antiarrhythmic drug therapy. In all patients, the A–R interval increased significantly from a mean of 230.38 ms ± 26.1 at 80 beats/min to a mean of 265.53 ms ± 33.1 at 120 beats/min ($P < 0.01$). In five patients (patients 1, 2, 4, 10, and 12) the Wenckebach point was reached at pacing rates faster than 160 beats/min and the A–R interval increased from a mean of 228. 81 ms ± 12.1 at 60 beats/min to a mean of 281.53 ms ± 18.1 at 160 beats/min ($P < 0.001$).

Incremental atrial pacing during exercise with a constant workload of 50% of the maximal workload showed a more gradual increase of the A–R interval from a mean of 218.91 ms ± 11.8 at 80 beats/min to a mean of 230.94 ms ± 19.1 at 120 beats/min (P=NS) (Table II). In patients on or off antiarrhytmic drugs, these measurements were not significantly different (Table II). At lower pacing rates the A–R data set was not complete because in several patients the spontaneous heart rates exceeded the atrial paced rate of the pacemaker.

To obtain overdrive atrial pacing at exercise, the pacing rate had been set above 80 beats/min in eight patients and even above 100 beats/min in two patients. In four patients, the ECG tracings could not be analyzed.

Incremental atrial pacing during exercise with a constant workload resulted in less prolongation of the A–R interval compared to the A–R interval at atrial pacing at rest. In the total patient group, the P values at 80, 100, and 120 beats/min were $P < 0.08$, $P < 0.03$, and $P < 0.003$, respectively. The P values for the A–R interval at 100 en 120 beats/min were statistically significant (Table II). The P values were not significant probably due to the small sample size in both subgroups. The different response of the A–R interval during both Wenckebach tests are graphically compared in Figure 3 for all patients as well as the two subgroups. The mean A–R intervals are given for different pacing rates at rest and during exercise at constant workload (Fig. 3). Atrial pacing prolongs the A–R interval progressively at higher pacing rates, however this reponse was blunted by exercise.

Exercise with a low constant workload of 40 watts at a fixed pacing rate just above spontaneous sinus rate resulted in a decrease of the A–R interval in the total patient population from a mean of 239.43 msec ± 38.2 to a mean of 226.90 ± 18.4 at the fifth minute of exercise ($P < 0.06$ NS) (Table III). Again the same response was observed in both subgroups.

In 11 patients, the ECG recordings could be analyzed completely. In patient 16, there was competition between sinus rhythm and atrial pacing during the

last minute of exercise resulting in a relatively short A–R interval at the end of exercise.

Table 2

Wenckenbach Test at Rest and Wenckenbach Test at Exercise With a Constant Workload							
	Rest			Constant Workload			
Pat. nr.	80 ppm	100 ppm	120 ppm	Workload	80 ppm	100 ppm	120 ppm
Without drugs							
1	224.20	240.53	263.31	90		199.74	216.24
2	275.54	276.89	293.97	100		244.00	247.80
3	222.79	231.92	253.97	60	227.43	237.95	251.34
4	201.00	213.08	225.31	80	206.07	212.09	215.99
5							
6	286.51	299.49	327.14				
7	247.83	265.21	305.88		207.51	243.27	
8	206.89	217.00	231.33	60			218.10
9	200.80	210.00	216.91	70		199.78	211.69
Mean	233.19	244.27	264.73	77	213.67	222.81	226.88
S.D.	33.4	33.0	40.6	16	11.9	21.3	17.8
	*	———	P <0.6	———	*		
		**	———	P <0.08	———	**	
			***	———	P <0.06	———	***
With drugs							
10	235.81	245.20	263.08	40	227.81	246.23	260.57
11	212.88	235.53	297.29	80	208.41	225.00	246.44
12	217.02	236.28	270.08	60			205.36
13	225.50	241.70	242.34	60		221.57	213.72
14	220.00	223.00	240.00	70	215.00	230.00	240.00
15	248.56	267.51	286.84	60	220.27	231.24	243.94
16					238.80	296.60	
Mean	226.63	241.54	266.61	62	222.06	241.77	235.01
S.D	13.4	14.8	23.1	13	11.8	28.2	21.1
	*	———	P <0.14	———	*		
		**	———	P <0.2	———	**	
			***	———	P <0.04	———	****
Total							
Mean	230.38	243.10	265.53	69	218.91	232.29	230.94
S.D.	26.1	25.9	33.1	16	11.8	25.8	19.1
	*	———	P <0.08	———	*		
		**	———	P <0.03	———	**	
			***	———	P <0.003	———	***

The total patient group was divided in two subgroups, patients with and without antiarrhythmic drugs. For each pacing rate in rest and during a constant workload the A–R intervals given as the mean value ± S.D. are statistically compared.

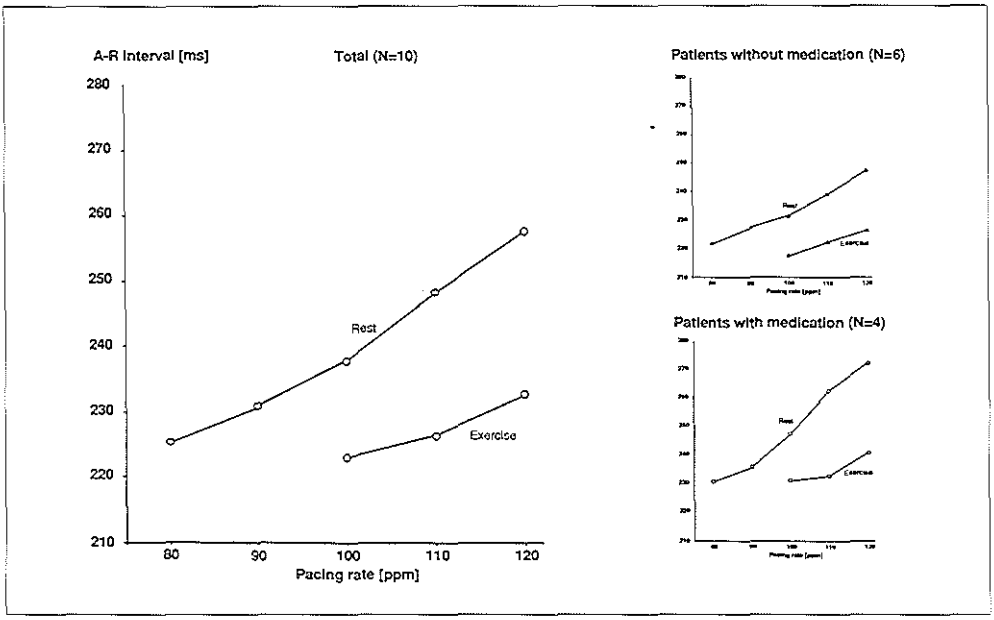

Figure 3. Wenckebach test at rest and during exercise with a constant workload. The mean A–R interval for ten patients is given in relation to pacing rate.

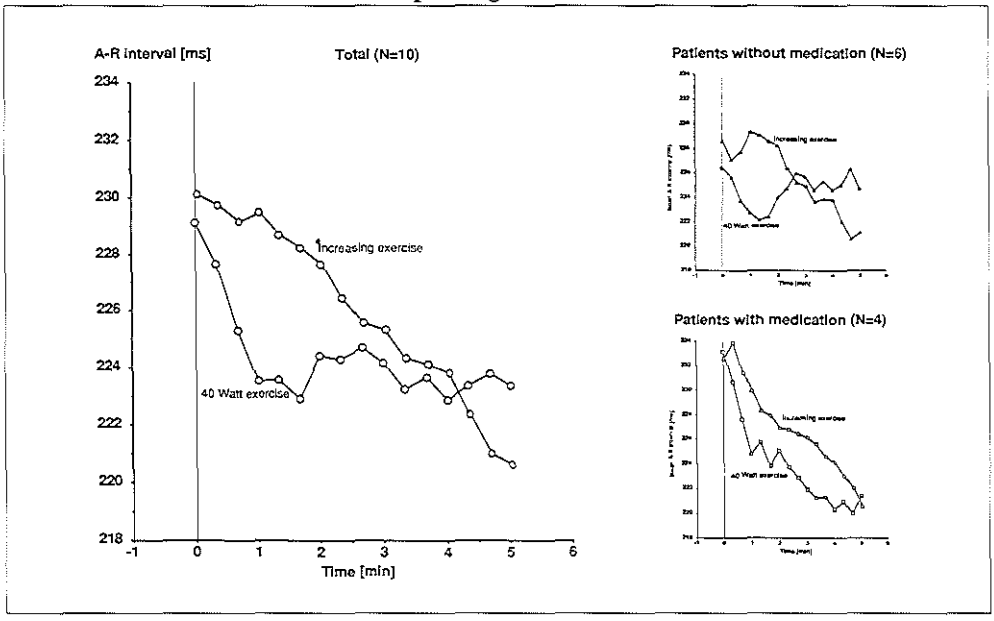

Figure 4. In ten patients (N = 10) the relation between the mean A–R interval and exercise time is shown. At the left panel the total patient group, and at the right panel both subgroups. Maximal exercise test with increasing workload; exercise test at a constant low workload of 40 Watts

Table 3

Exercise Test at Low Constant Workload and Exercise Test at Increasing Maximal Workload							
	40 Watt			Increasing Workload			
Pat. nr.	Pacing Rate	Start	End	Pacing Rate	Start	End	Maximum Workload
Without drugs							
1	100	208.33	218.16	100	235.59	183.46	140
2	80	260.89	259.32	110	266.86	232.64	170
3	80	229.79	226.71	80	226.19	222.33	80
4	100	215.73	210.97	100	216.28	208.38	120
5							
6				100	298.61	266.32	90
7				80	251.20	239.21	90
8	100	225.19	218.75	100	219.69	204.67	80
9	100	218.74	214.44	100	207.42	188.55	100
Mean	93	226.45	224.73	96	240.23	218.20	109
S.D.	10	18.4	17.7	11	30.5	27.6	32
		* P < 0.5 *			** P < 0.007 **		
With drugs							
10	80	240.29	227.56	80	233.72	224.71	80
11	80	211.50	211.08	80	214.81	200.72	160
12				100	233.03	199.43	60
13	100	225.06	211.14	100	230.73	205.70	80
14				100	235.22	214.57	130
15	80	255.68	235.94	80	251.04	234.79	80
16	80	342.57	261.80	80	245.83	213.28	100
Mean	84	255.02	229.50	89	234.91	213.31	99
S.D.	9	51.7	21.0	11	11.6	12.9	35
		* P < 0.15 *			** P < 0.001 **		
Total							
Mean	89	239.43	226.90	93	237.75	215.92	104
S.D.	10	38.2	18.4	11	23.1	21.4	33
		* P < 0.06 *			** P < 0.0001 **		

Exercise Test at Low Constant Workload and Exercise Test at increasing Maximal Workload. The pacing rate was kept constant just above spontaneous sinus rate. The total patient group was dividend in two subgroups, patients with and without antiarrhythmic drugs.

In each group the A–R intervals given as the mean value ± S.D. for both exercise tests were statistically compared.

Maximal exercise with increasing workload showed the most pronounced A–R interval shortening in all patients. A shortening of the mean A–R interval of 237.75 msec ± 23.1 at rest to 215.92 msec ± 21.4 at maximum workload ($P < 0.0001$) (Table III). The ECG tracings could be analyzed in 15 patients.

During a maximal exercise test the A–R interval decreased continuously, there was a lineair relationship between the A–R interval and exercise time (R=0.98). Ten Patients were able to exercise at least 5 minutes. In these patients, both exercise tests at constant pacing rate were compared in Figure 4.

The first minute of exercise at constant low workload the A–R interval showed an almost direct shortening. After 1 minute, a plateau phase was reached resulting in an almost constant A–R interval in the patients group without antiarrhythmic medication. The shortening of the A–R interval was more linear in the patient group on antiarrhythmic medication.

Discussion

In the normal heart, incremental atrial stimulation will result in a progressive increase in the atrial spike to ventricular R wave interval (A–R interval) until AV nodal Wenckebach block develops. As expected, in our patients with sick sinus syndrome and normal or slightly impaired AV conduction, incremental atrial pacing showed an identical effect on the A–R interval.

In contrast, during physical exercise the AV or A–R interval shortens under the influence of sympathetic stimulation and a decrease in vagal tone. The same effect can be achieved during incremental atrial pacing by a continuous infusion of isoprenaline or atropine while the shortening of the A–R interval during exercise can be influenced with beta blocker medication[7,8].

In our study, some patients showed a short initial increase in the A–R interval during the first minute of exercise. A likely explanation for this phenomenom is that in these patients, the stress of waiting on the sign to start exercise offers more sympathetic drive than the first minute of exercise.

This adaption of the AV interval is subtle and fast. The neurohumoral stimuli that increase heart rate during physical or emotional stress also enhance AV nodal conduction, creating a subtle balance between sinus rate and AV nodal conduction[7,9]. When during a constant moderate level of exercise incremental atrial pacing interferes with the physiological balance between heart rate and AV nodal conduction, the A–R interval is not shortened but prolonged.

However, this prolongation of the A–R interval is more gradual over the

whole rate range compared to A–R interval during incremental atrial pacing at rest. During constant low exercise workload with the atrial pacing rate just above the spontaneous sinus rate, the A–R interval decreased initially rapidly, followed by a constant steady–state level, suggesting a linear relationship between sympathetic drive and A–R interval. Daubert et al.[9] showed in subjects with healthy hearts during exercise the same linearity between heart rate, workload, and AV interval. The adaptation of the AV interval took place instantaneously and even minimal variation in heart rate was accompanied by an immediate, inversely proportional change in the AV interval. Although it was not possible to study all patients in a drugfree state, we observed no differential responses either during low exercise or maximum exercise levels, between patients on beta–blocking agents and patients who were not these medications (Fig.4, right panel).

It has been suggested that the ideal metabolic demand sensor would measure sympathetic tone or circulating catecholamine levels[2,3]. At present, such sensors do not exist and measurements of the metabolic demand must be made indirectely. The linear correlation between the A–R interval and the sympathetic tone during exercise makes it feasible to use the A–R interval as a metabolic sensor.

A program using this linear relationship was developed and temporarily downloaded to a DDD generator. A linear response curve may not be optimal for physiological rate control, but it can serve the purpose of studying the feasibility of such a system.

The algorithm measures accurately the A–R interval, and adapts the atrial escape interval on a beat–to–beat basis to changes in the A–R interval.

In order to maintain an optimal rate response under changing circumstances, for example due to dromotropic drugs affecting AV conduction or intermittent intraventricular conduction defects, the rate response algorithm is able to change the slope of pacing working line automatically. However, this adaption will be stepwise and depend on the magnitude and rapidity of the alteration in the A–R interval behavior. Further studies will be carried out to improve the algorithm.

In dual chamber, dual lead units, the measurement of the A–R interval is simple. In an atrial single chamber unit using the sensed atrial depolarization and the far–field signal of the ventricular depolarization, the A–R interval can be measured. This far–field QRS signal can be picked up by almost all unipo-

lar atrial leads.[10] However, in bipolar atrial single chamber systems, far–field ventricular sensing cannot always be accomplished.

In conclusion, the response of the A–R interval during different kinds of exercise was prompt and predictable in patients with sinus node dysfunction but normal anterograde AV conduction. In these patients, the shortening of the A–R interval during exercise may be an indicator for an adequate atrial pacing rate, even in patients on beta–blocking agents.

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Adaptive–Rate Pacing Controlled by the Right Ventricular Pre–Ejection Interval: Clinical Experience with a Physiologic Pacing System

PACE: Accepted for publication

RUITER, J.H., ET AL.: Adaptive–Rate Pacing Controlled by the Right Ventricular Pre–Ejection Interval. In the Precept™ pacing system, the right ventricular intracardiac impedance waveform is used to evaluate either of two indicators of metabolic demand—relative right ventricular stroke volume and pre–ejection interval (PEI). PEI is known to reliably parallel contractility changes, which reflective of physical and emotional stress. The stability and dynamic behavior of PEI were tested in 10 patients with a Precept pacing system under various forms of exercise and during postural changes. Although significant patient–to–patient variability of the sensor values was observed, reflecting individual physiologic differences, the chronic stability of PEI was excellent in the total device experience of 147 months. In all patients, PEI shortened significantly during bicycle ergometry from a mean value of 137.7 ± 17.8 (range 96–162) to a mean value of 103.0 ± 21.6 (range 92–109) ($p < 0.05$). Low–level bicycle exercise of short duration resulted in a prompt decrease in PEI and increase in pacing rate in all patients. There were no uniform postural responses overall, although some posture–related rate changes were observed in two patients. We conclude that the first generation of a PEI based pacing system holds promise for adaptive–rate pacing.

adaptive–rate pacing, right ventricle, pre–ejection interval, exercise

Introduction

Many candidates for permanent pacing therapy have chronotropic incompetence, an inadequate sinus node response to exercise or other physiologic stimuli.[1,2] To compensate for this, a variety of indicators or sensors other than the sinus node have been used or proposed for use in modulating the patient's pacing rate to his metabolic demand under cardiovascular challenges.

One of these indicators is the right ventricular pre–ejection interval (PEI), the systolic time interval from the onset of electrical ventricular depolarization to the onset of right ventricular ejection. This interval correlates well with hemodynamics. PEI comprises two distinct cardiac phases—an initial electromechanical lag time between the onset of ventricular depolarization (electrical activity) and the onset of ventricular contraction (mechanical activity), fol-

lowed by an isovolumetric contraction period. This latter phase can be regarded as a direct reflection of the speed of ventricular contractility. It is sensitive to sympathetic tone, including the influence of circulating catecholamines.[10,14]

Rushmer found that right ventricular ejection can be derived from intracardiac measurement of right ventricular volume.[3] Rushmer and Geddes then established the relation between intracardiac impedance and stroke volume.[3,4]

Later, Baan, McKay and Salo refined this relationship.[5,6,7] In 1984 Salo et al. also described the use of stroke volume as a control sensor for rate modulated pacing.[8]

In several publications, Chirife et al. have shown that PEI is a reliable physiologic indicator of metabolic demand.[10–13] Under various cardiovascular challenges, PEI was shown to be 1) influenced by physical and emotional stimuli; 2) relatively unaffected by changes in pacing rate; 3) inversely proportional to sinus rate (beats per minute); 4) quick to respond to physical and emotional stimuli; and 5) not susceptible to voluntary influence.

In 1989 McGoon et al. demonstrated a prototype pacing system using an algorithm to modulate pacing rate based on changes in PEI.[9]

This work ultimately led to development of a new adaptive–rate pacing system (Precept™, Cardiac Pacemakers, Inc., St. Paul, Minnesota, USA) that uses the PEI as a rate control sensor. Present study was performed to assess the following attributes of the system: the response of the PEI sensor to exercise; the physiologic nature of the pacemaker's algorithm; the chronic stability of PEI sensor values; the effect of postural changes on PEI values; and the chronic functionality of the pacemaker system.

Device Description

The Precept DR Model 1200 pulse generator is a multiprogrammable dual–chamber adaptive–rate pacemaker offering rate modulation based on either of two sensors that indicate metabolic demand–pre–ejection interval (PEI) and relative right ventricular stroke volume (RSV). The Precept DR also offers all the conventional dual chamber pacing and sensing functions. The Precept VR Model 1100 pulse generator is a complementary single–chamber adaptive–rate device. The units also incorporate a model 4400 tripolar endocardial lead (Figure 1).

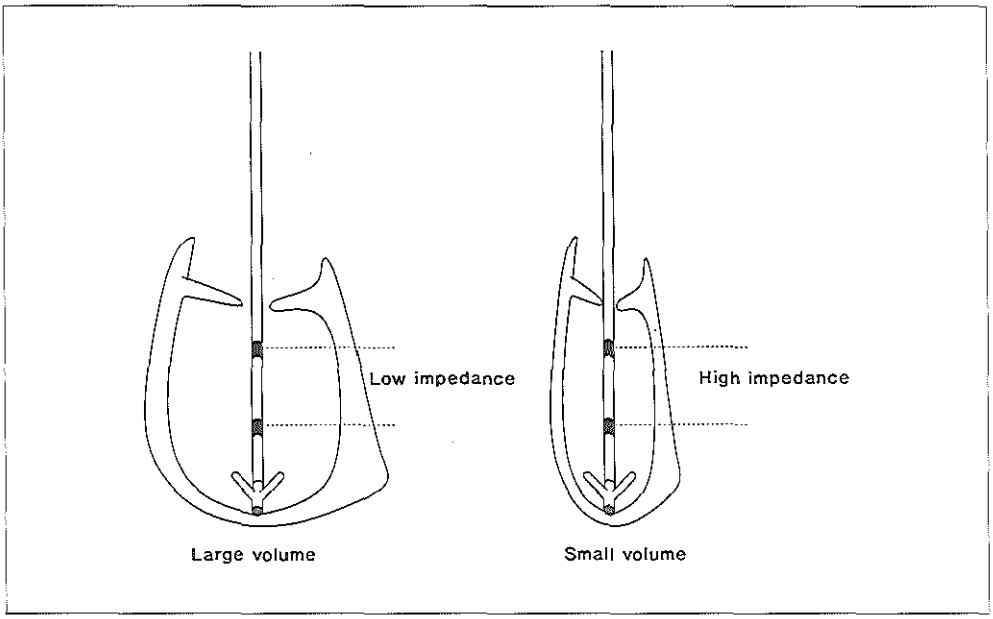

Figure 1. The Precept Model 4400 tripolar lead measures relative right ventricular volume via a current passed between two electrodes in the ventricle. Impedance is inversely proportional to the volume of blood in the ventricle.

The volume–related signal is determined by continuous right ventricular impedance measurements. A continuous low–level (6 microampere) alternating current is passed from the distal electrode to the pacemaker can. This same lead is also used for conventional pacing and sensing functions.

A volume–dependent voltage, the intracardiac sensor signal (Sensorgram-TM), is measured between the two proximal ring electrodes situated in the right ventricle. This voltage is inversely proportional to the blood volume in the right ventricle. In the end–diastolic phase, when the right ventricle is filled with blood, impedance is low, and the current will travel relatively easily. In the end–systolic phase, low blood volume results in a higher impedance. The technology for measuring intraventricular impedance has been described by Salo et al.[8]

PEI is measured from the pacing spike or the sensed intrinsic R–wave, as detected by the pacemaker's sensing circuitry, to the onset of right ventricular ejection determined by detection of the rapid volume change (Figure 2). The

pacemaker's algorithm translates the sensor signal into a corresponding sensor value, or index, of 0 – 255 counts. The algorithm minimizes excessive cycle–to–cycle variations by calculating a continuous moving average over the previous 16 cardiac cycles.

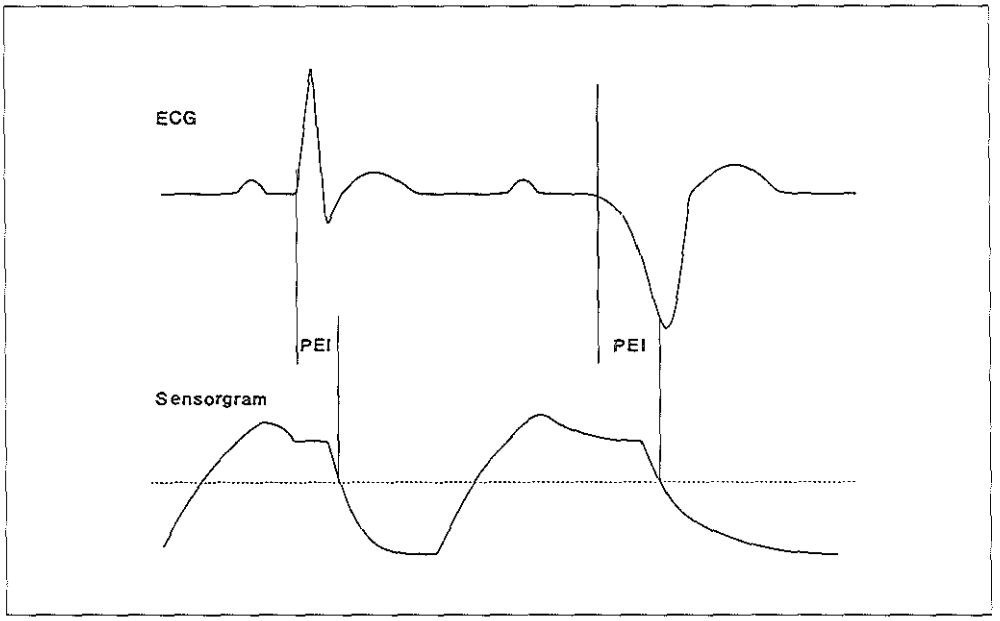

Figure 2. PEI is measured from the onset of paced or sensed electrical activity to the onset of mechanical activity –the ejection of blood from the right ventricle.

In addition RSV can also be derived by the pulse generator's circuitry that continuously monitors relative right ventricular volume. Volume measurements are considered "relative" rather than absolute because they represent an estimate of the volume of a cross section of the ventricle rather than the total ventricle. Since the pacing algorithm is based on detecting relative changes in the sensor index, calibration of the sensor signal against an independent standard is not required.

Programming the pulse generator to an adaptive–rate mode determines a baseline sensor value that is specific to the patient. Determining this reference value takes only 30–60 seconds. The ongoing rate control sensor value—i.e., the 16–cycle moving average—is compared to this baseline value. A PEI value that represents a decrease from the baseline indicates metabolic stress and

results in a pacing rate increase.

The system is designed to allow periodic updating of the baseline value to account for changes in the patient's sensor characteristic caused by diurnal cycles, medications, short–term illness and long–term disease progression.

Following are brief explanations of programmable parameters for adaptive–rate response:

Adaptive–Rate Parameters

Sensor Select:	Allows the selection of either PEI or RSV for rate control.
Maximum Sensor Rate:	The maximum pacing rate allowed under sensor control. This parameter is programmed independently from the upper rate limit (maximum atrial tracking rate) to provide flexibility of therapy.
Response Slope:	Eight different response slopes are programmable to adapt the intensity of the response to patients' needs. A higher setting will produce a greater increase in pacing rate.
Pace/Sense Offset:	In some patients, sensor values may differ between paced and intrinsic rhythms due to differences in conduction pathways or sensing characteristics associated with QRS detection. Pace/Sense Offset may be programmed to automatically compensate for such a difference.
Baseline Tracking:	Specifies how often the baseline will be evaluated to account for changes in sensor values caused by diurnal cycles, medications, long–term disease progression, etc.

Diagnostic Features

Programming, interrogation and diagnostic signal transmission can be performed with the CPI Model 2035 Handheld Programmer equipped with an appropriate software module (Model 2060 or 2065).

Special diagnostic features associated with the sensor include:

Sensor Evaluation:	Real–time interrogation of sensor data telemetered from the pulse generator.
Sensorgram:	Real–time telemetered recording of the relative

right ventricular volume signal. Continous output may be recorded using a conventional ECG recorder (Figure 3).

Event Markers: Real–time event markers identify key intrinsic and pacemaker–related events available via an ECG recorder. Markers identify paced and sensed beats, refractory periods and beat–to–beat sensor values.

Sensor Diagnostics: Allows use of diagnostic functions such as Sensorgram and Sensor Evaluation even when the pulse generator is programmed to a conventional pacing mode.

Patients and Methods

Patients

From April 1989 to November 1990, Precept DR Model 1200 (DDDR) and Precept VR Model 1100 (VVIR) pacemakers were implanted in 10 physically active patients. The study group ranged in age from 52 to 84 years (mean 70 ± 5) and included nine males and one female.

Table 1

Patients	Follow–up (months)	Age	Preimplant ECG	Medication
1	16	84	SSS+AVN	
2	16	74	SSS+AVN	Sotalol
3	18	76	SSS+AVN+PAF	Flecaïnide
4	18	69	SSS+AVN+PAF	
5	16	52	SSS+AVN+PAF	Sotalol
6	15	57	AVN+LBBB	
7	12	65	SSS+AVN	
8	12	70	SSS+AVN	
9	11	71	SSS+RBBB+LAH+PAF	Disopyramide
10	16	74	SSS+RBBB+LAH+PAF	Sotalol

SSS = Sick Sinus Syndrome AVN = Atrio–ventricular Nodal Disease
PAF = Paroxysmal Atrial Fibrillation LAH = Left Anterior Hemi block
RBBB = Right Bundle Branch Block LBBB = Left Bundle Branch Block

Individual clinical data are presented in Table I. Nine patients received the DDDR device; one patient received the VVIR system. Indications for permanent pacing included sick sinus syndrome, atrioventricular conduction disease, right and bifascicular heart block and refractory paroxysmal atrial fibrillation.

Methodology

The study protocol was designed to evaluate PEI sensor behavior and the associated pacing rate modulations at frequent intervals from implant through the 12–month follow–up examination. At implant, acute pacing and sensing thresholds were determined, PEI sensor values were telemetered from the device and a representative Sensorgram was recorded. Patients were discharged with the pacemaker programmed to the DDD or VVI mode.

At one month postdischarge, patients performed a two–minute step test. During this test, response slope was titrated until an adequate pacing rate increase was achieved. Patients then performed two symptom–limited maximal bicycle exercise tests consisting of one–minute stages. Workload was increased by 25 watts at the end of each stage. The first test was performed with the pacemaker programmed to the DDD or VVI mode. The second test was performed in the DDDR or VVIR mode, with a slope setting determined earlier during the step test. In addition, postural effects were evaluated. The patient was paced in the DDD or VVI mode, 10 beats above the intrinsic sinus rate. Sensor values were obtained in supine, sitting and standing positions.

After these tests, the generator was programmed to the adaptive–rate mode and the patients returned home.

Between the one month follow–up and the three month follow–up, an ambulatory 24–hour Holter was recorded to evaluate proper pacemaker functioning and appropriateness of rate modulation. At three, six and 12 months postdischarge, the ECG, Sensorgram and event markers were recorded. Pacing and sensing thresholds were determined and optimized.

Statistics

Sensor data are expressed as mean $\pm$ standard deviation. Paired "t"–tests were used to determine significance. A p–value of 0.05 or less was considered significant. Averages of two sensor values were used during data analysis.

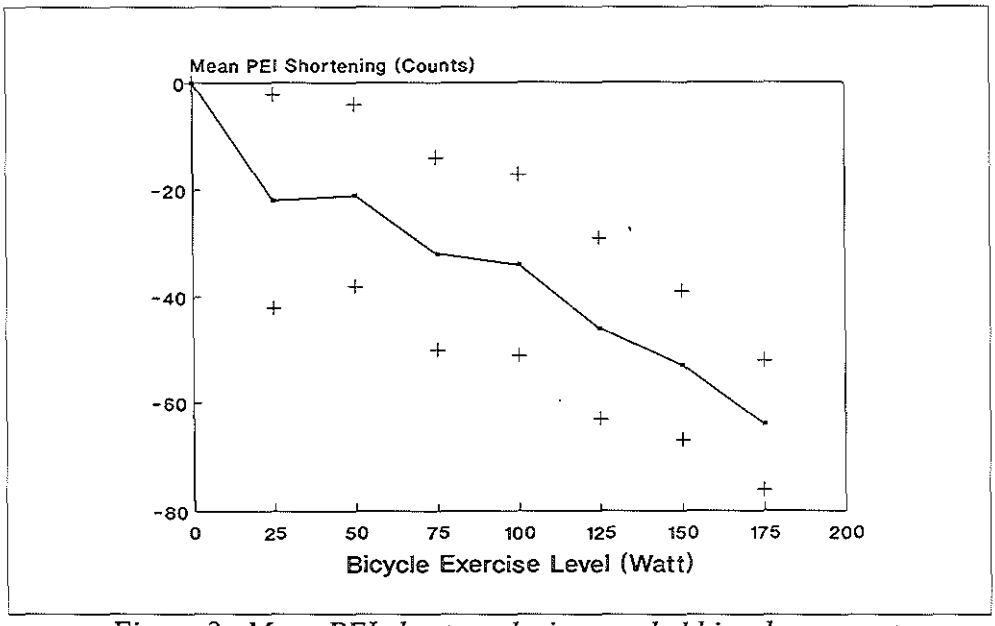

Figure 3. Mean PEI shortens during graded bicycle ergometry.

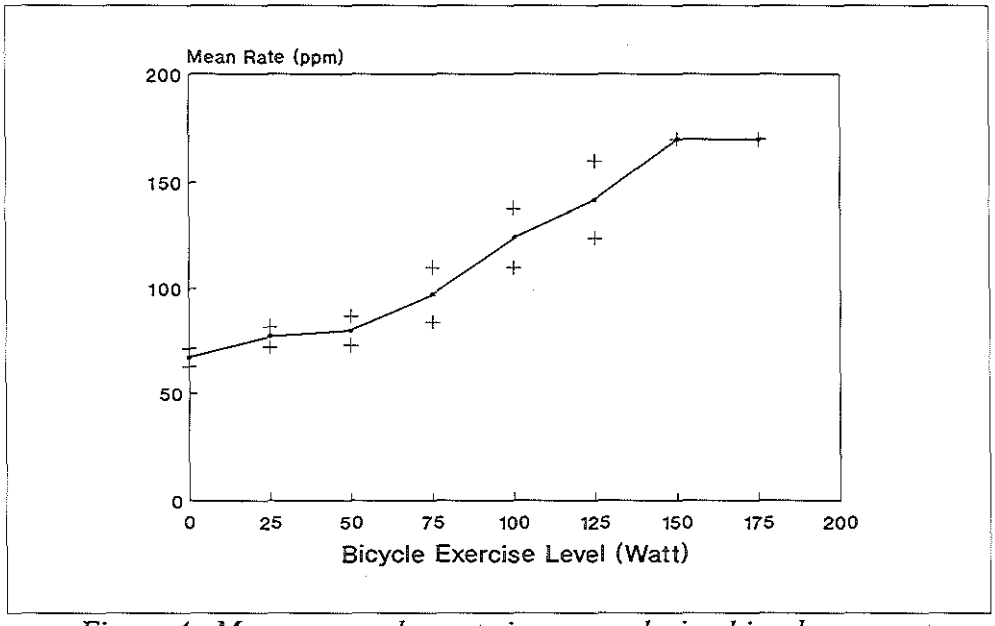

Figure 4. Mean pacemaker rate increases during bicycle ergometry.

Results

During the study period, data was collected for 10 patients. The total device experience was 147 months.

The two–minute step test resulted in a significant decrease in PEI from 136.9 ± 29.1 (range 103–151) to 116.2 ± 21.2 (range 91–126) ($p<0.05$).

Also in all patients, PEI shortened significantly during a symptom–limited bicycle stress test performed in DDD mode (figure 3). Mean PEI values decreased from 137.7 ± 17.8 (range 96–162) to 103.0 ± 21.6 (range 92–109) ($p<0.05$).

Bicycle ergometry was repeated in DDDR mode using PEI as the sensor for rate modulation. Figure 4 shows a mean pacing rate increase from 67 ppm ± 4.3 (N=8) at rest to 97 ppm ± 13 (N=7) at the 100 Watt stage, to 170 ppm at 175 Watts (achieved by one patient).

In patient 10 who had the VVIR pulse generator, the follow–up data were obtained during atrial fibrillation. PEI values were small and shortening of PEI was limited. Since the chronotropic response in this patient was sufficient, the pacemaker could be left in the VVI mode.

Table 2

Pt	At Implant.	1Mth	6Mths	12Mths	Mean	SD
1	166	172	162	174	168.5	4.8
2	120	126	129	118	123.3	4.4
3	147	149	142	152	147.5	3.6
4	150	132	138	134	138.5	7.0
5	132	150	148	144	143.5	7.0
6	119	123	103	112	114.3	7.6
7	128	129	131	134	130.5	2.3
8	142	147	135	149	143.5	5.4
9	166	162	164	158	162.5	3.0
10	96	102	104	112	103.5	5.7

Table II. The PEI sensor values at implant and during follow–up visits. The values are expressed as the mean of two measurements.
Pt = patient Mth = Month SD = standard deviation

In Table II the PEI sensor values at implant and during follow–up visits are presented. The values are expressed as the mean of two measurements. These measurements were taken with the patients in the supine position during atrial pacing at a constant rate of 70 ppm. In two patients (3 and 8), the atrial pacing rate had to be increased to 80 ppm in order to overdrive the intrinsic sinus rate. Under these conditions the variability between the PEI measurements in each patient was small. Also, during the subsequent follow–ups, no significant fluctuations were noticed, demonstrating an excellent chronic sensor stability.

In all patients except patient 8, PEI was shorter during sinus rhythm (PEI = 136.4 ± 21.3) than during atrial pacing (PEI = 121.0 ± 20.3) measured at a rate 10 bpm above intrinsic sinus rhythm.

The PEI sensor values in supine, sitting and standing positions are given in Table III.

Table 3

Patients nr	Supine	Sitting	Stand-ing	On bike	Mean	SD
1	166	154	140	158	154.5	9.4
2	124	130	148	144	136.5	9.8
3	125	142	135	147	137.3	8.3
4	150	104	103	132	122.3	19.8
5	150	127	151	133	140.3	10.5
6	102	102	103	129	109.0	11.6
7	131	168	142	129	142.5	15.5
8	135	185	158	147	156.3	18.5
9	162	162	144	162	157.5	7.8
10	109	95	119	96	104.8	9.9
Mean	135.4	136.9	134.3	137.7		
S.D.	20.4	29.0	18.5	17.8		

Table III. The PEI sensor values in four different postures are given with their mean values and standard deviation.

Again the values were obtained during atrial pacing. Although the mean value of PEI does not seem to be affected by posture, considerable PEI changes were noted in the individual patients. In patients 4 and 5 this resulted in symp-

tomatic pacing rate increases, documented during 24–hour Holter recordings. Programming from PEI to RSV resulted in similar behavior; therefore these patients were left in the DDD mode. In patient 9, undesirable posture–related pacing rate increases could be supressed by the selection of a relatively insensitive PEI sensor slope setting; this resulted however, in less optimal rate modulation during exercise.

In the remaining patients, the pacemaker was programmed chronically to the adaptive–rate mode and functioned well during the 12–month follow–up period. Ambulatory 24–hour Holter recordings showed proper pacemaker functioning and adequate rate adaptation.

Discussion

Chronic pacing and sensing performance of the Precept pacing system in patient population was excellent. The long term stability of the right ventricular volume signal and PEI values was adequate for reliable application in a rate–modulated pacing system. PEI demonstrated a rapid and significant decrease proportional to workload at all levels of exercise. Even during brief exercise at relatively low levels, the PEI decrease was prompt and resulted in adequate rate modulation. The results showed that PEI provides an accurate physiologic indicator for exercise.

PEI measurement dependends on the sensing of the QRS complex and the detection of the moment when the right ventricular volume changes. Several factors, other than sympathetic tone affect right ventricular stroke volume. These include preload, heart rate, heart rhythm and inotropic state of the right ventricle. Right ventricular function was not normal in our patients, several of whom had a history of myocardial infarction and left ventricular failure or chronic lung disease.

The preload of the right ventricle will partially depend on the timing of the atrial contraction. A better–timed atrial contraction will result in a better filling of the right ventricle and, according to Starling's law, in a larger stroke volume.

Furthermore, changes in preload, thus in stroke volume, can be expected during transitions from atrial sensing to atrial pacing and from atrio–ventricular synchrony to atrio–ventricular dyssynchrony.[15] Since SV detection and PEI measurement are closely related, PEI is likely to change when SV changes. Our data, comparing PEI during atrial pacing and atrial sensing, sup-

ported this assumption.

As mentioned, PEI determination depends also on the moment of R–wave sensing. As acknowledged in the description of Pace/Sense Offset, PEI will differ in cardiac cycles when sensed or paced QRS events alternate or intermittent bundle branch block occurs. The algorithm of the Pace/Sense Offset feature will correct for the timing differences involved in paced or sensed R–waves. However, the pacemaker's algorithm will follow physiological stroke volume fluctuations.

Rushmer[16] has shown that important posture–related SV changes do exist. As shown by Wortel et al.[17], these physiological changes are recognized reliably by the tripolar conduction catheter. In some patients, these changes are large enough to give rise to relatively large RSV and PEI fluctuations.

Excessive cycle–to–cycle variations are avoided by sensor averaging over 16 beats; however, this algorithm will not prevent pacing rate increases due to change of posture. Programming the pacemaker to a lower response slope will smooth the rate increase; however, rate response during exercise will be reduced.

In conclusion, PEI is a reliable indicator of metabolic need. Its response is fast and proportional to workload. Experience with the first generation of the Precept pacing system using PEI as an indicator of metabolic need shows promising results. Although postural effects of PEI were noted in some patients, appropriate rate modulation could be achieved in the majority of patients. Furthermore, the choice between the multiple sensors proved beneficial for optimising rate modulation.

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Chapter VIII

COMPLICATIONS OF CARDIAC PACING

Complications of pacing include a variety of pacemaker and pacemaker lead problems. This chapter will be confirmed to complications related to pacemaker implantation and component failure in the pacemaker system.

8.1. Complications associated with the surgical procedure

8.1.1. Introduction

The skill and knowledge of the operating physician are essential in limiting implantation related complications. Patient risk factors, such as age, concomitant disease, the presence of artificial heart valves, tricuspid regurgitation, and anticoagulant or antiplatelet therapy, must always be taken into consideration.

8.1.2. Subclavian introducer technique

More than 75% of the implants today are done with the subclavian stick technique using an introduction system (2–4,7). Many complications can occur with this procedure (table 1) (5,6). These complications led Furman (1) to advise to use more frequently the venous cutdown technique of cephalic, external, or internal jugular vein, even in dual–lead procedures.

Tabel I

Complications associated with the subclavian introducer technique
Hemothorax
Pneumothorax
Brachial plexus trauma
Thoracic duct injury
Venous thrombosis
Arterial trauma
Septic arthritis
Air embolization
Tracheal perforation
Phrenic nerve injury

In our experience the cephalic vein is seldom suitable for the insertion of

two leads. The jugular approach requires that the lead(s) be tunneled down to the infraclavicular generator pocket. The superficial route over the clavicle is associated with an increased potential risk for erosion or fracture of the lead . The infraclavicular route requires the skill of a surgeon.

When the subclavian puncture procedure is done correctly the risks are few; the benefits are many as it saves time and two leads can be used .

In our institution, the pacemaker implants are performed by cardiologists, the subclavian puncture approach is used in over 85 % of the cases. From January 1985 to July 1991, 599 pacing systems were implanted. During the implantation procedure, in these series, two patients experienced pneumothorax requiring chest drainage.

Other severe complications associated with the subclavian introducer approach were not present.

The best insurance against any of the risks associated with the subclavian stick technique is a thorough understanding of the entire procedure.

8.1.3. Pocket hematoma

Wound hematomas at the time of the pacemaker implant are notorious in patients on antiplatelet drugs, particularly aspirine and nonsteroid anti–inflammatory drugs are disreputable.

A second high–risk group are patients with severe renal or liver failure with disturbances in the hemostasis. Frequently, hematomas can be avoided by making the pacemaker pocket directly after a successful puncture of the subclavian vein and placing a sponge in the pocket to create pressure hemostatis.

8.1.4. Pacemaker pocket infection

The single greatest problem associated with pulse generators and the most difficult to deal with, involves infected pacemaker systems. Prevention is clearly the best approach. We have to realize that mechanical factors and surgical technique affect wound infection importantly. The incision for the pacer pocket can at best be made parallel to and just beneath the clavicle. The pocket has to be positioned below this incision point, there should be no incision line over the generator to avoid pressure on the stiches[8]. It is advisable to close the wound by suturing from both ends towards the middle to achieve appropriate closure[8] leaving a drain in place is asking for contamination of the pacemaker pocket.

In acute wound infection, within 48 hours from surgery, Staphylococcus Aureus is most commonly encountered[9,10,13,14]. Infections can occur as long as six months to several years after the surgical procedure, in these cases mostly Staphylococcus Epidermidis can be cultured[10,11,13,14]. Prophylactic antibiotics may be helpful, especially if a temporary lead is used[24]; the duration of antibiotic prophylaxis should be short[24–26].

Pacemaker infection and the clinical value of antibiotic prophylaxis for pacemaker implantation are discussed in more detail in the following sections of this chapter.

8.1.4.1. Treatment of infected pacemaker systems

In cases where there is an established infection, reported in the literature as 1–6%, the pacemaker leads should be regarded as contaminated[9,10,13]. The infection can spread down the lead system to the heart; a complicating endocarditis or sepsis can be deadly. Removal of the entire pacemaker system, generator and leads, from the infection location is recommended[9,10,12,13], coupled with a course of antibiotics appropriate for the organism cultured. After removal of the infected hardware, a new pacemaker system may be implanted immediately at the opposite site. Others[14] advocated a later new implant date using temporary pacing with antimicrobial therapy at implantation. Subsequently, close follow–up of both the old and new pacemaker sites is mandatory. However, the removal of chronically implanted leads can be very difficult, requiring in some patients thoracotomy with cardiopulmonary bypass. The intention to avoid major surgery in the mostly elderly pacemaker patient brought new interest in"in situ" management of pacemaker infections and in intravascular lead extraction procedures.

Some reports mention successful local irrigation and wound revision with relocation of the generator[15–17]. Recently there are several devices developed to extract an abandoned lead[18–21] with success rates reported up to 80%. However the clinical experience with these extractions is still limited[22,23].

Potentially, percutaneous lead extractions are lower risk procedures and less invasive. Traction procedures with external weight applied to the partially exteriorized lead can have disastrous consequences and should be avoided[9,22,23]. In the cases of pacemaker infection in our institution, the removal of the endocardial leads required thoracotomy. All patients cured un-

eventful. These cases and four cases of late purulent pacemaker pocket infections are described in one of the following paragraphs.

8.1.5. Pocket erosion

Fibrotic tissue holds the pulse generator and lead(s) in stable position for prolonged periods. On occasion, the lead(s) or the generator migrates toward the skin surface, perhaps even breaking it.

Erosion has almost disappeared during the last several years due to the markedly reduced size and mass of the pulse generator. Although pocket erosion should always be suspected, often a low grade pacemaker pocket infection is the real underlying problem.

8.2. Lead associated problems

8.2.1. Dislodgement

With the new pacing leads which are available today, dislodgement should occur in less than 5% for atrial implants and less than 2% for ventricular implants[5,6,27,28]. To guarantee a stable position, screw–in leads have been developed, these leads can be implanted at the best location in the atrium and ventricle, and can be removed easily in case of complications[27]. Screw–in leads have proven long–term reliability with satisfying results of pacing and sensing[27,28]. Particularly in pediatric pacing, easy lead revision or explantation is a major advantage, trauma of the lead or a growth spurt of the patient may require a new lead.

8.2.2. Lead penetration

Lead penetration has become rare problem since the advent of highly flexible leads. It can be avoided by withdrawing the guidewire a small distance while positioning the electrode in the atrium or ventricle.

8.2.3. Diaphragmatic stimulation

Diaphragmatic stimulation occurs primarly in thin–walled dilated hearts[5]. It can usually be handled by using a screw–in lead in a different position. In the post–implant period, programming the pacemaker to a lower output voltage, if possible, will be effective.

8.2.4. Vein thrombosis

Some degree of phlebitis, thrombosis and embolism is associated with implantation of leads[6,29,30]. Probably 25–50% of the subclavian veins used as access for pacing leads thrombose completely overtime[29–31]. Symptomatic vein thrombosis is, however very uncommon.

Goudevenos et al[29] reviewed the literature on cases of pacemaker induced superior vena cava (SVC) syndrome; they found the incidence to be less than 0.1%. The presence of a dual–lead system does not significantly increase the risk. However retained leads and evidence of an earlier pacemaker infection were predisposing factors for SVC obstruction. Those authors describe four cases of successful balloon angioplasty in the treatment of pacemaker induced superior vena cava syndrome.

8.2.5. Malpositioning

Malpositioning the lead in the coronary sinus can be avoided by using a curved stylet as it passes through the tricuspid valve to the direction of the pulmonary outflow tract. In several reports[32,35], congenital malformation complicating pacemaker lead insertion are mentioned. When the abberation is recognized during implantation, often a transvenous screw–in lead can be placed in a stable ventricular or atrial position[33,34].

8.2.6. Insulation defect

Fracture or damage to the lead conductor or insulation can occur within the heart, the blood stream, the venous entry site between clavicula and the first rib, and at the ligature site in the pocket[36,38]. How to limit insulation defects? Before implant the physician's lead manual should be read carefully. The lead conductor, its insulation, and the fixation mechanism may be damaged at implantation if stretched, crimped or crushed. The lead should thus be handled with care. When the lead is secured in the pocket always use the suture sleeve.

Polyurethane lead insulation failures have been reported. They are manufacturer and model specific, and not generic to polyurethane[36,39]. The expected failure rates for polyurethane and siliconen leads are reported to be less than 2% with a follow–up of 10 years[37]. It can be anticipated that a lead which survives to the seventh year will have prolonged longevity, as thereafter, additional failure is uncommon[37].

8.3. Pulse generator malfunction

Hauser et al reported in 1986 the longevity and reliability of 9651 lithium pulse generators as given in the Chicago cardiac pacemaker registry (40). A pulse generator was considered failed if it was operating outside the manufacturer's specifications or if it did not function as intended. In 142 (1.4%) cases, pacemaker failure was detected and constituted a reason for early generator replacement. The causes of failure are given in table 2.

Causes of pulse generator failure	**n = 142**	
	no	%
Component defect	86	60.6
Malfunction	26	18.3
Loss of hermeticity	24	16.9
Electrical overstress	4	2.8
Unexpected battery depletion	1	0.7
Radiation damage	1	0.7

Table 2 Longevity and reliability of 9651 lithium pulse generators. (Adapted from Hauser et al ref.40)

The 26 generators listed as malfunctioning were reported by their manufacturers as being within their specification after the unit was explanted. In other words, the cause of failure was not elucidated on the manufacturer's engineering analysis. Four units were damaged by routine electrocardioversion and one unit that failed following a course of palliative radiation in a patient with lung cancer. The signs of lithium pulse generator failure are listed in table 3.

Signs of pulse generator failure n = 142		
	no	%
No or reduced output	63	44.5
Undersensing	26	18.7
Rate increase	25	18.3
Programming failure	12	8.3
Rate decrease	10	7.0
Pulse width increase	5	3.5
Pulse width decrease	1	0.7

Table 3 Longevity and reliability of 9651 pulse generators. (Adapted from Hauser et al ref. 40)

During the period of 12 years, 136 units have to be replaced because of early battery depletion, particularly, the first generation of DDD models had high current drain.

From January 1985 until July 1991 in Alkmaar, 599 pacemakers were implanted. Only four cases (0.7%) of pacemaker component failure were detected. In two cases there was a capacitor–related malfunction. The other two generators showed no output at implantation because of an internal isolation defect; damage during transport was suggested by the manufacturer.

Electronic component failure has emerged as the most common cause of pulse generator malfunction. The lithium battery shows an excellent clinical performance and hermetic seal defects of the generator can are now infrequent[40].

Survival data of large populations of paced patients show that a single pulse generator is capable of functioning well for the lifetime of the average pacemaker patient.

In the next paragraph, pacemaker implantation related complications in our pacemaker population are given for the period of January 1986 until January 1991, with emphasize on different pacing modes.

In addition, pacemaker infection and a case of a persistent left–sided superior vena cava is discussed in more detail.

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Chapter VIII

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Complications in Physiologic versus Ventricular pacing. A five year experience.

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The Neth. J. of Card. Accepted for publication

Summary.

Physiologic pacing {AAI(R)/DDD(R)} can be regarded as thepacing mode of choise in patients with the Sick Sinus Syndrome and in many patients with A–V nodal or combined nodal disease.During a period of 5 years we implanted 285 ventricular and 178physiologic pacemakers, 71 generators were replaced (implants +replacements N=463). Complications requiring a reoperation wereobserved in 10 (3.5%) ventricular and in 17 (9.5%) physiologicpaced patients (Relative risk 2.7 ; 95% confidence interval 1.3 – 5.6). Non routine pacemaker reprogramming was only necessary in the physiologic pacemaker group. However, the hemodynamic benefits of physiologic pacing favourably counterbalance the small rise in acute and chronic complications in comparison to ventricular pacing.

Keywords: Pacemaker – Complications – Physiologic – Ventricular.

Introduction.

In 1628 Sir William Harvey recognised the importance of the atrium in cardiac function[1]. The hemodynamic benefits of atrial contribution was demonstrated in pacemaker patients in 1968 in a study by Benchimol[2]. In 1973 Furman described the clinical therapeutic use of atrial pacing itself in a large group of patients[3]. Microtechnology and increasingly stable atrial leads made the developement of the dual demand (DDD) pacemaker possible in 1976. However, initial enthusiasm was soon tempered by the recognition of serious limitations in the first generation of DDD devices. Pacemaker mediated tachycardias, complexities of pacemaker follow up, and atrial lead dislodgements served to discourage many cardiologists. Whereas reliable atrial leads and chip technology solved many of the initial DDD generator related problems[4,5], most of the implanting physicians continued to ignore the role of the atrium again as a number of single chamber rate modulated pacemakers (R= rate modulated) were released. The benefit of A–V synchrony was continually rediscussed and the improvement of cardiac function appreciated, but its clinical importance was unclear. Recently, for patients with Sick Sinus Syndrome (S.S.S.) reports have provided convincing evidence that the occurrence of life

threatening conditions as atrial fibrillation, congestive heart failure and thromboembolism can partially be avoided by implanting atrial (AAI/AAIR) or dual demand pacing systems (DDD/DDDR) instead of ventricular pacemakers (VVI/VVIR)[6]. However, the implantation rate of physiologic pacemakers (AAI/AAIR and DDD/DDDR) in the Netherlands continues to be low[9]. In an editorial of november 1990 van Hemel stressed the importance of atrial pacing particularly in patients with S.S.S. and he advocated the dissemination of knowledge of and experience in atrial pacing in the Dutch Cardiology profession [9]. In an attempt to provide additional information on this subject, our own 5 year clinical experience with physiologic pacing is reported. As expected, a higher complication rate with physiologic pacing is the most important drawback in implanting atrial leads. This report will present a comparison of the physiologic and the ventricular paced patients groups, regarding the complications and need of reoperations.

Patients and Methods.

Between January 1986 and January 1991, 463 patients underwent implantation of a permanent pacemaker in our hospital. 316 were single chamber systems, 31 atrial demand (AAI) or atrial demand rate responsive (AAIR) systems, 285 ventricular demand (VVI) or ventricular demand rate responsive (VVIR) systems, and 147 dual chamber systems (DDD or DDDR). For 384 (83%) patients, the implant was their first device. Nine (1.9%) patients were upgraded from a VVI system to a DDD system and 71 (15.1%) patients had their existing pulse generator replaced with a similar system.

The average age of the patients was 67.5 $\pm$11.9 years (range 28–87) with a dual chamber pacemaker, 77.2 $\pm$ 9.7 years (range 35–98) with VVI(R) units and 67.3 $\pm$ 13.5 years (range 26–82)with AAI(R) units.

The patients population consisted of 266 (57%) males and 197 (43%) females. The sex and age distribution for the several pacemaker classifications is given in figure 1. Pacemaker indication and selection of stimulation mode andpacemaker parameters were determined by the referring cardiologist, implanting cardiologist and the pacemaker technician. Presenting symptoms and indications for implantation in both VVI(R) and DDD(R) /AAI(R) patient groups are given in figures 2 and 3. In all cases pacemaker implantation was performed in the catherization room by an experienced cardiologist.

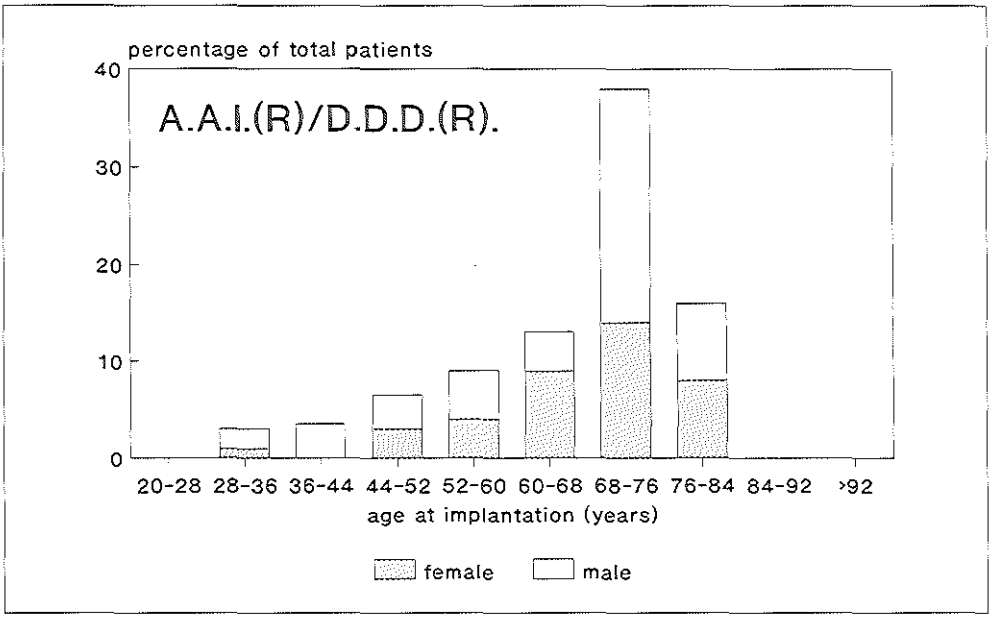

Figure 1. Age and sex distribution of ventricular and physiologic paced patient groups.

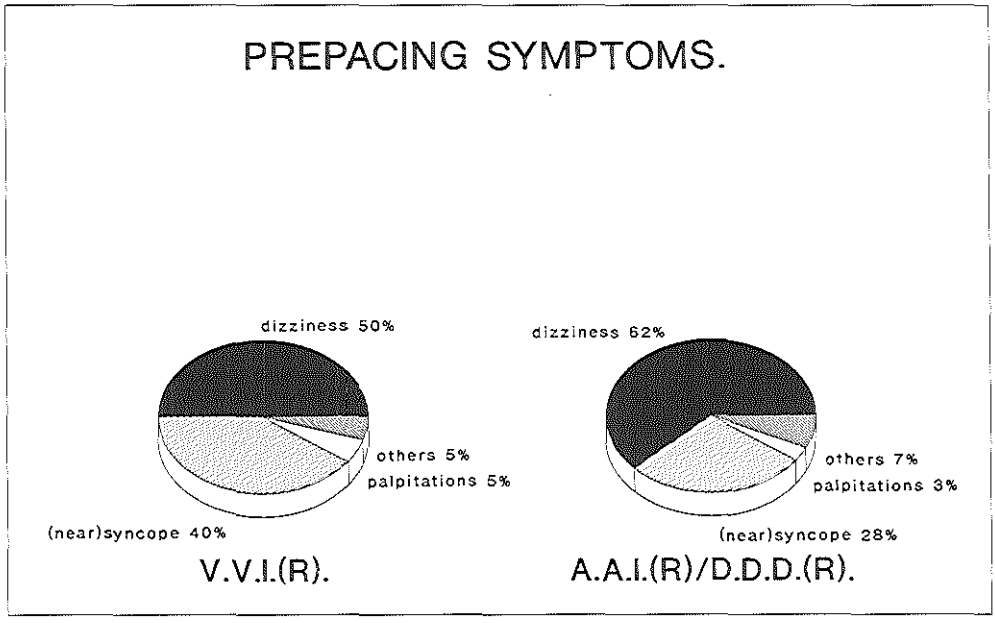

Figure 2. A distribution of prepacing symptoms in the ventricular and physiologic paced patient groups. Pacemaker replacements excluded (N=71).

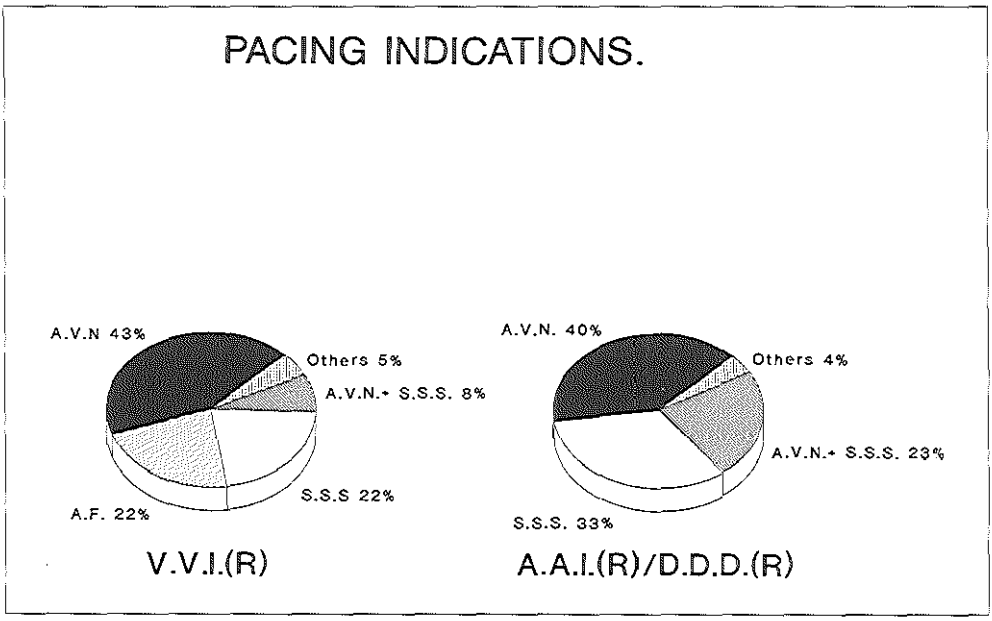

Figure 3. A distribution of pacing indications in the ventricular and physiologic paced patient groups. Pacemaker replacements excluded (N=71).

One hour before the implant, and 6 and 12 hours after the procedure, 1 gram flucloxacilline was given intravenously. When penicillin allergy was suspected, erythromycin was administrated instead.

The implantation procedure was performed using standard techniques . The left prepectoral site was chosen for right–handed patients and the opposite side for left–handers.

The leads were inserted either through the subclavian or the cephalic vein. Atrial screw–in leads were preferred for patients with a history of cardiac surgery, all other atrial implants used J.shaped bipolar tined leads. For ventricular implants tinedbipolar leads were used often. Pacing leads were positioned using fluoroscopy. Electrical measurements and pacing protocols were performed with a pacing system analyzer. Intracardiac electrograms were recorded on paper at a recording speed of 100 mm/sec. In atrial or dual demand implants, Wenckebach block was routinely induced and retrograde A–V conduction was studied. Patients generally left hospital the third day after a single chamber implantation and the fourth day after the implant of a dual chamber

unit. Pacemaker follow–ups were conducted 1,3,6 and 12 months after the implantation. In every patient with a Rate mediated or Dual chamber unit ambulatory 24 hours E.C.G.monitoring and when possible, an exercise test was performed. After the first year of implant the patients were followed at regulary intervals of 6 or 12 months.

The following complications or dysfunctions were anticipated : the occurrence of atrial fibrillation in the atrial or dual demand paced population, the loss of atrial or ventricular sensing, atrial or ventricular lead dislodgement, atrial or ventricular lead fracture, a rising threshold, pacemaker pocket infection, pacemaker pocket haematoma, pectoral muscle stimulation, diafragma or phrenic nerve stimulation, pacemaker mediated tachycardia, inhibition due to electromagnetic interference and electronic pacemaker failure.

Statistical analysis

The relative risk or risk ratio was calculated as a complication rate in the AAI/DDD group divided by the complication rate in the VVI group. A risk ratio of 1 indicates an equal statistical risk in each group. The 95 % confidence interval for the risk ratio's was calculated according to Katz et al[22].

Results.

Single chamber ventricular (VVI/VVIR) pacemakers were implanted in 61.6 % of the cases,and in 6.7 % single chamber atrial (AAI/AAIR) devices were used. The remainder 31.7 % were dual chamber units (DDD/DDDR). The subclavian puncture technique was performed in 410 (88.5%) patients,the cephalic access in 53 (11.5 %). During implantation 2 (0.4%) complications were seen, two DDD implants experienced pneumothorax requiring chest drainage. There were no thrombotic complications noted. During the 5 year follow–up, 65 (14 %) patients died, the mean age was 79.8 $\pm$ 7.3 years (range 69 – 99) after a mean implantation period of 20.2 $\pm$ 14.2 months (range 1 – 57).The cumulative survival by pacing modality is given in table 1. Patients with AAI(R)/DDD(R) units had a cumulative survival after 5 years of 92.0 % versus 82.0 % for the VVI(R) group. None of the deaths was known to be pacemaker related. 27 (5.8%) complications required a reoperation (table 2);in 9.5 % of the AAI(R)/DDD(R) and 3.5 % of the VVI(R) implants. The relative risk to encounter a complication in the AAI(R)/DDD(R) group is 2.7 higher than in the VVI(R) group. The risk ratio of 2.7 is significant (95 % confidence limits 1.3 – 5.6).12 (2.6 %) patients were lost to follow–up.

Table 1

Cumulative Survival Statistics. Cumulative survival by pacing modality(%)				
Time (years)	**V.V.I(R)**		**D.D.D.(R) / A.A.I.(R)**	
Years	**N**	**%**	**N**	**%**
0	285	100	178	100
1	264	93	172	97
2	249	87	166	93
3	240	84	165	93
4	236	83	163	92
5	235	82	163	92

Table 2

Complications Requiring Reoperation		
Number of devices	285	178
Complication	**V.V.I(R)**	**D.D.D.(R)/A.A.I.(R)**
Lead dispacement A		6
Lead displacement V	3	2
Lead fracture	1	2
High threshold	1	1
Muscular stimulation	1	
Infection	2	2
Pocket haematoma	2	2
Electronic failure		1
Total	10 (3.5%)	17 (9.5%)

Lead displacements were more frequent in the DDD(R), and AAI(R) patients. In these groups, 8 (4.5 %) of the leads had to be repositioned. In the VVI(R) group, 3 (1.1 %) dislodgements appeared. The other lead–related interventions were not strikingly different for the patients groups. Nine pulse

generators had to be removed. Four units experienced electronic failure. In one unipolar VVI patient an old generator was replaced with a much smaller unit which resulted in pocket stimulation and made reintervention necessary. Four cases had pocket infection. The pocket infections occurred between 1–14 months after insertion. Staphylococcus epidermidis was cultured in 2 cases. In all pacemaker pocket infections, the entire pacing system was removed including both generator and leads.

In table 3, lists complications requiring non routine pacemaker reprogramming.In the DDD(R)/ AAI(R) population, paroxysmal atrial tachyarrythmias and loss of atrial sensing were the most frequent reasons. In the VVI(R) group only routine programming procedures were mandatory. In 144 (98 %) of the 147 DDD(R) units a dual chamber mode was maintained.

Table 3

Complications Requiring Reprogramming A.A.I.(R) /D.D.D.(R). N=178	
Complication	N
Atrial tachyarrhythmia	12 (6.7%)
Atrial malsensing	8 (4.5%)
Atrial malpacing	3 (1.7%)
Electro–Magnetic interference	3 (1.7%)
Pacemaker mediated tacycardia	2 (1.1%)
Phrenic stimulation	1 (0.6%)
Total	29 (16.3%)

Two units were permanently programmed to the VVI mode due to drugs resistent atrial fibrilliation in the patients. After treatment of pacemaker infection related endocarditis, onepatient had his pacemaker system removed and replaced by a VVIR pacemaker insertion. Of nine cases of earlier implanted VVI pacing systems, seven patients were upgraded because of pacemaker syndrome. In the remaining two patients after a successful cardioversion of atrial fibrillation an atrial lead was added.

Discussion.

After pacemaker implantation,physiological pacing can be regarded as the capability to restore cardiac output in rest, during exercise and emotion to bradycardia patients.[1,2]. Only dual chamber and atrial devices so far have the potential to achieve these expectations, as these systems are able to maintain A–V synchrony and rate responsiveness between the programmed lower and upper rate (DDD(R)). Unfortunately physiological pacing has the disadvantages of a more difficult and more complicated implantation procedure[4,5,17]. In dual chamber pacing a shorter pulse generator longevity, the necessity of two leads and a more frequent follow–up will induce higher costs with respect to single chamber systems[10]. Dual chamber pacemakers carry also the possibility of rapid ventricular pacing during atrial tachyarrhythmias and pacemaker mediated reentry tachycardia [4,5,11]. Therefore it is not suprising that some authors have drawn attention to the higher rate of complications with dual chamber than single chamber pacing[11,12,17].

Also there appears to have been misappreciation of the hemodynamic importance of A–V synchrony, although, an increased heart rate appeared to be the most important determinant of exercise induced rise of cardiac output.[13,14]. A number of reports demonstrates that the loss of A–V synchrony can cause a deterioration of cardiac function in conditions such as hypertrophic cardiomyopathy, hypertensive heart disease and aortic valve stenosis[1,14]. On the other hand, in over 40% of the pacemaker patients the A–V node is able to conduct the ventricular pulse back to the atrium[6–8]. Instead of A–V synchrony, V–A synchrony can develop with as a result atrial contractions against closed A–V valves. In some patients the so called pacemaker syndrome arises. Complaint of pulsations in the neck and abdomen or even–light headed spells can occur caused by a significant decrease in cardiac output and bloodpressure. In over 80 % of the S.S.S. patients, retrograde A–V conduction is reported, for these reasons, ventricular pacing can have potentially detremental haemodynamic effects and can even increase the mortality rate[6–8,16].

In non A–V nodal disease, implanting ventricular devices in patients with intact retrograde conduction or hypertrophic (non–compliant) heart disease can be regarded as medically unjustified, as in ventricular paced S.S.S. patients[6,8,16] a higher incidence of serious complications such as atrial fibrillation, congestive heart failure and thromboembolism has already been demonstrated. In order to know whether the potential complications of atrial leads

outweights this later consideration, the present 5 year experience with these systems is reported. Physiological and ventricular pacing groups were compared with regard to the encountered complications. The complications requiring reoperation or reprogramming in our physiological paced and ventricular paced patient populations were generally in agreement with the reported incidences. We found that 0.4% of the subclavian approaches presented with pneumothorax, which is lower than the rates reported in the literature (1–9%)[17,18]. None of our patients presented with clinically manifest deep venous thrombosis.In our series we recognised 2 (1.1%) infections in the DDD(R)/AAI(R) group versus 2 (0.7%) in the VVI(R) group.Reported infection rate varies from 1–7 % [12,17,19].In both dual chamber infections, the pocket and pacemaker leads were affected, in one patient, tricuspid valve endocarditis was proven.

All cases of pacemaker infections occurred late, more than one month after implant, requiring the removal of the entire pacing system. Some data show the same displacement rate for atrial as for ventricular leads[4]. We found a 3.4% incidence of atrial lead dislodgements and 1.1% for ventricular leads. Recently reported atrial displacement rates have ranged from 1.3% – 18% compared to 0.7–2% for ventricular leads[7,17,20]. It is apparently very important to have an experienced operator to prevent this complication. Probably, when atrial screw–in leads were used, lower atrial issues could be expected, Byrd et al [21] reports less than 2 % problems in patients with atrial implants of active fixation leads. The most important reason for pacemaker reprogramming in the DDD(R)/AAI(R) patient group were the occurrence of atrial tachyarrythmias, or atrial undersensing during exercise. Only two patients (1.4 %) with the DDD(R) generator, had to be permanently programmed to the VVIR mode due to drug resistent atrial fibrillation.

Our policy to implant only bipolar atrial leads can possibly explain the absence of cross–talk related malsensing and the low incidence of electromagnetic interference.In our AAI(R) group, only minor drug induced A–V conduction disturbances occurred. During the follow–up period no upgrading procedure was necessary. Our physiological paced patient population had more favourable survival statistics than the ventricular paced population. However, this difference can partially be explained by the negative selection of patients receiving a VVI(R) unit.

In conclusion : Acute and chronic pacemaker complications are only slight-

ly more frequent in the physiological paced patients compared to the ventricular paced group. As expected this difference is mainly related to the atrial lead. A careful selection of patients, the use of intracardiac electrocardiogram analysis and an accurate follow–up can keep the complication rate low. The advantages of the atrial contribution and the maintenance of A–V synchrony are so obvious, that these advantages favourably counterbalance the small rise in complications and the requisite of a more comprehensive knowledge of cardiac pacing.

Due to a reduction in morbidity and judicious pulse generator selection, in the long run physiologic pacing can become the most economic mode of pacing and will provide the pacemaker patient with the best quality of life[21].

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Late Purulent Pacemaker Pocket Infection Caused by Staphylococcus Epidermidis: Serious Complications of In Situ Management

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PACE 1985;8: 903 – 908

Summary

The pathophysiology of late pacemaker pocket infection is poorly understood. We report three cases of late infection caused by Staphylococcus epidermidis. Despite initial local conservative management ultimate removal of the entire pacing system was required. In late pacemaker pocket infection we recommend initial removal of the entire pacing system and replacement on the contralateral side. When retrieval of the lead system requires open–heart surgery epicardial wires should be placed.

Keywords: Pacemaker pocket infection, Pomplications of pacemaker therapy, Staphylococcus epidermidis

Introduction

The ability of some coagulase negative Staphylococci (particularly Staphylococcus epidermidis) to behave as pathogens has long been recognized.[1] Such pathogenicity is often associated with preexisting tissue damage or foreign body implantation. In permanent cardiac pacing S. epidermidis is often responsible for troublesome purulent pacemaker pocket infections.[2–4]

The general surgical principle of complete removal of foreign material to eradicate infection is sometimes violated if the organism cultured is S. epidermidis, because this microorganism is regarded as a less virulent organism and a frequent contaminant of blood cultures. In pacemaker pocket infections due to S. epidermidis, local treatment, including wound debridement, the use of appropriate antibiotics and continuous irrigation with an antiseptic solution has been reported to be successful;[5–7] however, this conservative management of S. epidermidis infections is questionable.

This report describes the complications of in situ management in three cases of purulent pacemaker pocket infection in which eventual extraction of the entire pacemaker system was necessary. In each case explanation of the pulse generator was easily performed, but removal of the infected leads anchored in the right ventricular apex necessitated a median thoracotomy with the aid of extracorporeal circulation. Permanent pacing was continued with an

epicardial lead system with the generator implanted in the left hypochondrium.

Patients And Methods

From January 1980 to December 1983, 485 pacemaker–related procedures were performed in the Thoraxcenter of the University Hospital of Rotterdam and the Sint Franciscus Gasthuis in Rotterdam. During this period, we observed four pacemaker pocket infections; one occurred early (within 8 weeks after implantation) and three were late infections. Minimal incisional wound infection (stitch abscess) was not considered to be a pacemaker infection until signs of pocket infection developed.

Routine permanent pacemaker implantations were performed by a cardiologist in the cardiac catheterization laboratory under local anesthesia using a standard aseptic technique. Patients received prohylactic antibiotics, 1 gm cephalothin IV 1 hour before and 6 and 12 hours after surgery. The pacemaker lead(s) were mostly inserted via a puncture technique of the left subclavian vein with the generator placed in a prepectoral pocket. The cephalic or jugular route was used less commonly. Leads with both active and passive fixation were employed. No pocket drains were used. Usually the patients were discharged from the hospital the second day after generator replacement and the fourth day after a new implantation procedure. Microorganisms were identified as Staphylococcus epidermidis by gram stain and by the inability to coagulate human plasma.

Case Reports

Case No. 1

A 66–year–old male underwent implantation of a permanent endocardial ventricular demand (VVI) pacemaker because of second degree AV heart block with symptoms of dizziness. His general health was good and there was no history of chronic lung disease, diabetes mellitus, heart failure, or recent antibiotic therapy.

The procedure of pacemaker implantation was complicated by the entrapment of a balloon–tip electrode in the leaflets of the tricuspid valve. Even with rotation and strenuous traction it was impossible to dislodge the electrode. A second active fixation lead was easily positioned in the right ventricular apex and connected to a generator placed in a right prepectoral pocket. The first lead was secured in the same pocket.

During routine follow–up examination 12 months after implantation, a slightly red, nontender, fluctuating swelling over the pacemaker pocket was seen. Pacemaker pocket infection was suspected. Surgery was scheduled for that same day and cephalothin prophylaxis was used. Nonfetid purulent material was obtained from the pocket, and debridement and irrigation with a povidone–iodine solution was performed. A new pacemaker pocket was developed and was situated higher. The leads were cut and the distal ends were removed via the contaminated pocket. The remaining part was connected to a new generator. The redundant lead was also secured in the pocket.

The patient visited the outpatient clinic every 6 months. Eighteen months after hospital discharge the pocket was swollen again. Cultures of aspirated fluid showd S. epidermidis. Removal of the whole pacemaker system was necessary. Because of retained lead in the tricuspid valve no attempts were made to dislodge the lead with traction. A median sternotomy with the aid of cardiopulmonary bypass was performed. There were no signs of endocarditis. Both leads were removed and permanent pacing was continued with an epicardial lead system with the generator implanted in the left hypochondrium. Cultures of the tips of the electrodes were sterile.

The patient's recovery was uneventful and up to 24 months after the second intervention there have been no signs of reinfection.

Case No. 2

A 72–year–old male with a history of hypertension and cerebrovascular disease underwent implantation of an AV universal (DDD) pacemaker system using nontraumatic leads in the right atrial appendage and right ventricular apex. The pacemaker was inserted because of dizziness and documented periods of total AV block. Electrophysiological study revealed sinus node dysfunction and advanced infranodal conduction disease.

The implantation was complicated by a small pocket hematoma and a left–sided pneumothorax. Suction drainage for 2 days was necessary.

Six months after initial implantation a slight redness and tenderness of the skin over the pacemaker pocket was noted.

These symptoms did not disappear even after 14 days of oral antibiotic therapy (dicloxacillin 500 mg four times daily).

Admission to the hospital followed and the infected area was treated surgically by debridement and irrigation with povidone–iodine. The wound healed per primam. Cultures of purulent pocket material showed S. epidermidis sen-

sitive to the semisynthetic penicillins.

Three months later reinfection occurred. On admission the patient had a low grade temperature. The initial sedimentation rate and leucocyte count were elevated. Removal of the total pacemaker system was regarded as necessary. Therapy consisting of dicloxacillin IV was started. The pulse generator and the atrial lead were removed, but the ventricular lead could not be extracted, even with prolonged steady traction at skin level. Staphylococci epidermidis were isolated from the atrial lead electrode tip and from the pocket material. Median sternotomy with cardiopulmonary bypass was planned. The right atrium was opened. The ventricle was inverted into the atrium and the electrode was cut out of its apical position. No vegetations were seen in the right atrium or right ventricle. Pacing was continued with an epicardial DDD pacing system with the generator placed in the left hypochondrium.

The postoperative course was uneventful. Intravenous dicloxacillin was continued for 6 weeks. Up to 12 months after the last intervention there have been no signs of reinfection.

CASE No. 3

An obese 84–year–old female with a history of diabetes mellitus, hypertension, and angina pectoris developed congestive heart failure. Since 1981 she was known to have total AV block. An AV universal (DDD) pacemaker was inserted into the right atrial appendage and right ventricular apex using nontraumatic leads.

Five months after initial implantation the patient was admitted to the hospital because of impending pacemaker decubitus. Using cephalothin prophylaxis, local surgical intervention followed. The leads and generator were left in situ. Bacterial cultures from the pocket were sterile.

Six months later, signs of a pocket infection were present, with local redness and swelling over the pacemaker site. The patient had a low grade tempature and during her stay in the hospital atrial fibrillation occurred. To control the systemic infection, total removal of the pacemaker system was planned. Under general anesthesia and cephalothin prophylaxis, the generator and atrial lead were removed. It was impossible to dislodge the ventricular lead, so it was shortened and connected with a ventricular demand (VVI) pacemaker in a new pacemaker pocket. Staphylococcus epidermidis was cultured from the pocket and the distal end of the atrial lead. Within 24 hours fever and chills occurred. Two of six blood cultures revealed S. epidermidis. One blood culture was posi-

tive for a Serratia species. Fever persisted even after intravenously administered combinations of gentamicin, cephotoxin and later dicloxacillin, rifhampicin.

The general condition of the patient deteriorated and cardiopulmonary bypass surgery was performed to remove the retained ventricular lead. The generator was already explanted. Pacing was continued with an AV universal (DDD) epicardial pacing system, with the generator situated in the left hypochondrium. Cultures of the ventricular electrode tip were sterile. There were no major postoperative complications.Intravenous cephalothin was continued for 3 weeks.

Up to 18 months after the last intervention the patient has been doing well and there have been no signs of pacemaker pocket reinfection.

Discussion

For clinical purposes, pacemaker infections can be subdivided into early and late infections. Recent reports show an incidence of pacemaker infection of between 1% and 10%.[2–4] Most infections occur within 4 weeks after initial implantation and are limited to the pacemaker pocket.

The early infections are due to perioperative bacterial contamination.[1,3,4] Infection is suspected when fever develops hours of days after implantation. If redness and swelling are manifest over the pacemaker pocket, the diagnosis of pacemaker pocket infection can be established. The causative microorganism is usually present in the blood and often in the pacemaker pocket. The cultured bacterial spectrum is diverse, but S. aureus and S. epidermidis play an important role.[3–4] The total removal of the entire pacemaker system has been widely accepted as the proper management of this early complication of pacemaker therapy. However, several reports describe successful in situ management of acute pocket infections caused by S. epidermidis. These authors practiced local wound care and continuous irrigation of the pocket with an antibiotic solution for several days, supported by appropriate systemic antibiotic therapy.[5–7] Yet, this conservative procedure is questionable as pacemaker leads, even leads with active fixation, can easily be retracted if it is soon after implantation. Recurrence of infection because of incomplete removal can necessitate thoracic surgery in the removal of the anchored leads. Open cardiotomy with cardiopulmonary bypass may be required.[8,9]

Retained leads present a risk of endocarditis; moreover, endocarditis re-

lated to transvenous pacemaker systems is relatively more common in S. epidermidis infections.[9,10]

Late pacemaker infections are conclusively brought about by S. epidermidis. These microorganisms can easily be isolated from the healthy skin of both males and females and can be considered commensal bacteria.[1] Most likely the infecting strain is introduced at or around the time of operation, originating from the skin flora of the patient or from a member of the hospital staff. The first manifestation of a pocket infection can appear months or even years after initial implantation.[2]

Other possible mechanisms can be metastatic bacterial spread from a remote mild skin infection or bacterial spread per continuitatum in the presence of a local pressure necrosis of the skin overlying the pacemaker. [3,4]

Impending pacemaker decubitus has become rare since the development of smaller generators and can only be a problem in thin patients, especially after multiple generator replacements. In other cases the impending decubitus is not a cause but a consequence of a late pocket infection as shown in our third patient.

There is no consensus in the literature about late purulent pacemaker pocket infections. The clinical aspect is benign, leading to a local aproach, leaving lead and generator in situ.[5–7] However, as in our patients, this potentially systemic infection carries the risk of recurrence of pocket infection, bacteremia, and even bacterial endocarditis[10,11] (Table I). It is extremely difficult to sterilize the pocket by local treatment when the generator and/or leads are left in situ.[12,13]

Table 1

Clinical Characteristics of 3 Patients with Staphylococci Epidermidis Pacemaker Infections

Pat. no	Age	Sex	Site of infection	Local Surgical Therapy*	Complications	Radical Surgical Therapy*	Complications
1	66	M	PP+ PL– PE–	12	Reinfection	18	–
2	72	M	PP+ PL+ PE+	6	Reinfection Febris	9	–
3	83	F	PP+ PL+ PE+	5, 11	Reinfection Febris Septicemia	12	–

PP = Pacemaker pocket; PL = pacemaker lead; PE = Pacemaker electrode
* Months After Initial Implantation

In two of our patients cultures from the transvenous portion of one of the leads were positive for Staphylococcus epidermidis, even after several weeks of systemic cloxacillin therapy. Probably in successful local management of purulent late pocket infections the leads and the generator are not affected. This condition is, of course, not recognizable at the time of surgery. Accordingly, a high recurrence rate of infection can be expected.[11]

Unsuccessful local treatment can delay total removal of the pacemaker system, making lead retraction more difficult or even impossible because of complete ingrowth of the electrode in the myocardium. If traction fails to dislodge the electrode, prolonged traction applied at skin level can be used in the older, stiffer leads, [14] but this method is uncomfortable for the patient and serious complications have been reported.[9]

For removal of retained infected leads we recommend, even in the elderly high–risk patient, open–heart surgery with the aid of cardiopulmonary bypass, if necessary. In most surgical centers open–heart surgery has a low mortality even in the elderly pacemaker patient. Septicemia and endocarditis as a consequence of conservative management of infection can be regarded as much more dangerous in the same patient group. When traction fails to dislodge leads, local therapy should be attempted only for patients who are physically or mentally incapable of undergoing thoracic surgery.

Pacemaker infection caused by S. epidermidis is a serious complication of pacemaker therapy. Only complete removal of the pacemaker system can assure successful treatment.

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Antibiotic Prophylaxis For Pacemaker Implantation

Hart Bulletin 1988; 19:91–93

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Summary

Pacemaker infection is a serious complication of permanent pacemaker implantation. Preventive measures that can limit the number of post–operative pocket infections should be appleid. Pacemaker implantation has to be performed with as much care and attention to proper aseptic technique and tissue handling as in any other type of surgery. Pacemaker infections are relatively uncommon, the reported incidence ranges from 1 to 6%. It is a common practice to employ prophylactic antibiotic treatment at the time of implantation in the expectation that the change of infection will be reduced. Antibiotic prophylaxis is defined as short–term treatment of a transient bacteremia. Retrospective analysis of uncontrolled series and two prospective randomized studies have left doubt about the degree of protection they provide. If prophylactic antibiotics are given, the antibiotic program should be aimed at the Staphyloccal organisms. Guidelines are given.

Introduction

The technology which has permitted the widespread use of cardiac pacemakers has proven to be a major advance in medical therapy. With these improvements, the pacemaker's main function is still to prevent bradycardia, but many new indications as supraventricular and even ventricular tachyarrhytmia's unresponsive to medication have been arised.

The advent of the microprocessor based pacemaker have almost eliminated component failure as the cause for pacemaker malfunction.

The pacemaker lead became the most vulnerable part of the pacemaker system. Early insulation deterioration and disruption in leads made from some polyurethane formulations startled the pacemaker community in the late 70's.

Almost 200.000 patients have or had such leads, many are already replaced, the remaining patients should be carefully observed for signs of lead failure. However, several polyurethane leads have exhibited a superior early and late cumulative survival as compared with siliconen rubber leads and have shown excellent long–term stability.

Infection is second only to lead malposition or dislodgement as a complication of cardiac pacemaker implantation[1]. The problem promises to be a

growing one in terms of the absolute number of patients at risk, because the rapid technological advances in pacing systems and new indications produce an even increasing population of patients who are candidates for pacing.

An infected pacemaker is potentially lethal and can constitute a considerable therapeutic challenge.

Pacemaker infections

Most pacemaker infections occur early, within days or weeks after implantation. Diagnosis is based upon the presence of one or more of the following: local inflammation, abcess, erosion through the skin of any part of the system and fever associated usually with positive blood cultures.

Positive cultures from the wound, the pacemaker pocket or the blood usually contain staphylococcus species however a variety of micro– organisms can be involved (table 1).

Table 1

Microbiology of pacemaker infections (adapted from reference 3)	
Frequent	Staphylococcus epidermidis Staphylococcus aureus
Less frequent	Klebsiella pneumoniae Enterobacter cloacae Pseudomonas aeruginosa Pscherichia coli Proteus mirabilis Alcaligenes faecalis Serratia macescens Peptostreptococcus Micrococcus Alpha–Hemolytic streptococcus Flavobacterium
Rarely	Fungi (Candida albicans)

In more than 50% of the infections Staphylococcus Aureus and Staphylococcus Epidermidis will be found. Infections with S. Aureus usually occur early after implantation, S. Epidermidis infections tend to appear much later, sometimes years after surgery. A number of factors predispose the pacemaker patient to infection (table 2). In the early infection bacterial contamination of the pocket can be regarded as causative, the pathogenesis of late infections is less clear. The incidence of pacemaker infection, new implants and replacements, are reported in recent clinical series ranging from 1 to 6%[2].

Abcess involving the pulse generator pocket is the most common infection, secondary infection of the leads is the next most common manifestation, clinical evident bacteremia and endocarditis occur rarely (0.5 – 1%)[3].

Sustained bacteremia in a patient with a transvenous lead should be considered as septicemia due to infective right sided endocarditis involving the mural endocardium of the tricuspid valve. This serious complication in the mostly elderly pacemaker population make the removal of all foreign material, pacemaker and lead(s), imperative to save the patient's life.

If traction fails to dislodge the lead, removal by open cardiotomy may be required.

Table 2

Pacemaker infections (adapted from reference 4)	
Causes	**Influences**
wound contamination at surgery	surgical technique use of surgical drain room location and equipment
blood–borne pathogenes	sepsis elsewhere temporary pacing system
wound breakdown	operative technique hematomas, effusions
system erosion	operative technique body build generator size
diminished defenses	diabetes mellitus corticosteriods malignancy

Analysis of recent studies of antibiotic prophylaxis for pacemaker implantation

Pacemaker pocket infection represents a serious complication of pacemaker insertion, however the role of antibiotics in the prevention remains controversial (table 3).

Table 3

Antibiotic prophylaxis for pacemaker implantation		
Before surgery	**After surgery**	
30 – 60 minutes	6 hours	12 hours
1 gr Flucloxacillin i.v.	do	do
500 mg erythromycin i.v.	do	do
or		
500 mg vancomycin i.v.	do	do

In the recent literature three controlled clinical trials of prophylactic antibiotics were reported[4,6]. The results of these prospective randomized trials are conflicting. Muers et al[4] studied 431 patients. These patients were randomly allocated to treatment with the combination of flucloxacillin 1 g and benzylpenicilline 600 mg intramuscular, one hour before operation, one hour and six hours after operation or no treatment. Nine primary generator pocket infections occurred, seven infections in untreated patients (n = 197) and two in treated patients (n= 234). Pocket cultures were positive in five instances, the organism being Staphylococcus aureus in four and Staphylococcus albus in one. They conclude that prophylactic antibiotics reduce significantly (p = 0.01) the incidence of acute early infections.

Ramsdale et al[5] prospectively randomized 500 patients either to receive or not receive prophylactic antibiotic treatment at the time of implantation. The antibiotic regimen for patients not allergic to penicillin was: cloxacillin 1 g together with amoxycillin 1 g intravenously one hour preoperatively plus ampicilline and flucloxacillin 500 mg orally every six hours for 48 hours starting one hour post–implantion.

Patients allergic to penicillin received a combination of vancomycin and erythromycin. In the 244 patients randomized to prophylactic antibiotic treatment were two pacemaker pocket infections observed. In the 256 control patients only one infection. In the three cases Staphylococcus aureus was

cultured. However 18 patients (36.6%), six having received antibiotics and 12 no antibiotics, developed superficial inflammations of their wounds requiring antibiotic treatment. None required generator removal for clinical infection. The authors conclude that in this large prospective trial they were unable to demonstrate a significant benefit from prophylactic antibiotic treatment at the time of pacemaker implantation.

However, in all patients, antibiotic spray containing neomycin, bacitracin and polymyxin B was applied into the pacemakerpocket before generator insertion. The application of this antibiotic spray can be regarded as an antibiotic prophylactic treatment and it can not be precluded that this procedure has influenced the result.

In a recent investigation of Bluhm et al, the study group was too small, both in the treated and untreated group of 52 patients no pocket infection was seen[6]. No conclusions can be drawn from these data. To our opinion, the study of Muers et al is in this respect the most valuable. This study does suggest a favourable effect of the prophylactic use of antibiotics in pacemaker surgery.

Conclusion and Recommendation

An infection after the implant of foreign material as an pacemaker, prosthetic cardiac valves, prosthetic joints, peritoneal or intra–cerebral, drains creates a serious threat for the patient. It is an accepted dictum that conservative therapy commonly fails in these conditions and all foreign material must be removed. Prophylactic antibiotics for implanting foreign material is generally recommended although statistical evidence that this treatment reduces the risk of infection is usually not present.

The role of antibiotics in the prevention of pacemaker infection continues to be somewhat controversial although the most pertinent prospective study advocates their use.

Muers et[4] al concluded that administration of prophylactic antibiotics at the time of pacemaker implantation is indeed beneficial, especially in the presence of intercurrent disease (diabetes, carcinoma), steriod therapy, anticoagulants and infection elsewhere.

Until now, the results of Muers et al supported the administration of prophylactic antibiotics for pacemaker insertion. Most pacemaker infections are due to staphylococci, the preventive antibiotic measures should aim to these micro–organisms.

Antibiotic prophylaxis is defined as short–term treatment of a transient bacteremia.

Principles for the application of antimicrobial prophylaxis are:

1. Treatment should be started as late as possible before surgery.
2. Parenteral administration is preferred, to ensure adequate blood levels when the implantation is performed.
3. Prophylaxis must not be maintained for more than 24 hours.
4. The choice of the antibiotic drug depends on the expected micro–organisms under the given conditions.
5. Preference is given to bactericidal over bacteriostatic drugs.

Recommendations

The rational of prophylactic antibiotics especially in new implants is that it might reduce the change of infections occurring as a result of wound contamination in surgery.

The prophylaxis must at least consist of a penicillinase resistent penicillin as flucloxacillin. Patients allergic to penicillin can be administrated vancomycine 1 g (table 3). However, flucloxacillin protects against staphylococcus but not against other occasional pathogens.

A second generation of the cephalosporines as cefuroxim or cefamandol have recently recommended as prophylactic antibiotics in patients undergoing cardiovascular surgery[8,9]. These antibiotics protect against staphylococci but also against gram negative strains.

With respect to the relative short pacemaker implantation procedure, 1 1/2 gram cefuroxim or cefamandol intravenously once given one hour before surgery will provide sufficient protection.

Patients allergic to penicillin should be administered vancomycin. Many clinical trials have been carried out to prove the superiority of one cephalosporin to another as prophylaxis in patients undergoing cardiopulmonary surgery. Results of few studies appear to be significant, cefazolin seemed to be less effective than cefamandol or cefuroxim.

Still we have to realise that antibiotic preventive measures affects wound infection to a much lesser degree than do mechanical factors and surgical technique.

Patients allergic to penicillin: vancomycin or erythromycin is advised. The phials with 500 mg vancomycin have to be diluted in 100 cc NaCl 0.9% or glu-

cose 5%. In patients with congenital or acquired valvular heart disease, particularly patients with prosthetic valves, should not be derogated from routine prophylaxis of infective endocarditis.

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Atrial Pacing Via Unilateral Persistent Left Superior Vena Cava

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PACE: 1986; 9: 594 – 596

Summary

Atrial pacing via unilateral persistent left superior vena cava. A patient who suffered from sinus node dysfunction and automatic atrial tachycardias underwent pacemaker implantation during which time a unilateral left superior vena cava was found. Despite the known difficulties in using this venous route, it was possible to place a transvenous endocardial screw–in lead in a stable position in the lower lateral wall of the right atrium. active fixation electrode, atrial pacing, unilateral left superior vena cava

Introduction

The absence of the right superior vena cava with persistent left superior vena cava is an uncommon venous anomaly.[1] Such patients may have symptomatic bradycardias and therefore require implantation of a pacemaker. However, difficulties concerning the lead stability in the right ventricular apex have been reported,[2,3] necessitating epicardial pacing[4] or the use of active fixation electrodes.[5] We succeeded in placing a screw–in electrode in a stable position in the right atrium. To our knowledge, this is the first report of permanent atrial pacing in a patient with unilateral left superior vena cava.

Case Report

A 72–year–old man was admitted in March 1985 because of dizziness, recurrent syncope, and signs of mild left ventricular failure. From age 40 to 65 he had been treated for tachyarrhythmias. On admission, physical examination was unremarkable except for the presence of jugular venous distention and scarce pulmonary rales. The electrocardiogram showed sinus bradycardia at a rate of 50 beats/min, with right bundle branch block and left anterior hemiblock morphology. Continuous electrocardiographic monitoring very frequently showed runs of supraventricular tachycardia (SVT) at a rate of 90 up to 150 beats per minute. These SVTs showed a typical "warming–up phenomenon," and suppressed the sinus node resulting in post–tachycardia pauses up to 3 seconds. Episodes of AV block did not occur.

Chest X–ray examination showed moderate left ventricular enlargement and mild pulmonary congestion. In retrospect, the right superior vena caval shadow was absent.

Electrophysiologic Study

After we obtained informed consent, we introduced three catheters via the femoral vein. Catheters were positioned at the high right atrial wall, at the septal leaflet of the tricuspid valve, and in the right ventricular apex. Unfortunately, a His bundle potential could not be recorded. During incremental atrial pacing, AV Wenkebach block occurred at a rate of 200 beats/min. During incremental ventricular pacing, VA conduction was intact up to 130 beats/min. The SVTs could not be terminated or initiated by programmed extrastimuli or rapid atrial pacing, but overdrive suppression was possible. An automatic focus in the lower right atrium or the AV node was suspected (mapping was not performed). The exact sinus node recovery time could not be determined because of the immediate recurrence of the tachycardia following overdrive suppression. Disopyramide, 3 mg/kg intravenously, was not able to suppress the SVTs and did not alter the Wenkebach point of anterograde conduction.

Based on the symptomatology and the electrophysiologic findings, we decided to treat the patient with a permanent AAI pacemaker in combination with antiarrhythmic drug therapy. Unexpectedly, during implantation, the lead had to be passed via a persistent left superior vena cava and the coronary sinus into the right atrium (Fig. 1).

After recognition of this venous anomaly, a screw–in electrode was chosen, and fixed in the lower atrial wall. The pacing threshold was 0.6 V and the "A" wave amplitude was 3 mV. Later on, venography confirmed the absence of the right superior vena cava.

Echocardiography at that time showed a marked dilatation of the coronary sinus with the pacemaker lead embedded in it.

Antiarrhythmic drug therapy with digoxin, disopyramide, and verapamil in high doses, alone and in combination, did not affect the tachycardias. However, the combination of amiodarone, 400 mg daily, and overdrive pacing at a rate of 80 per minute proved to be effective in suppressing all tachycardias. During a follow–up of 6 months, the patient's course has been uneventful. Syncope did not recur.

Figure 1 Chest X–ray of patient after implantation

Discussion

Normally, the left innominate vein develops as an anastomosis between the left and right anterior cardinal veins in the embryo. In 0.5% of the population, the left anterior cardinal vein persists and leads to the development of a left superior vena cava which empties in the coronary sinus.[6] In 10% of patients with persistent left superior vena cava, an anastomosis still exists, but the drainage is to the left.[7] This may lead to atresia or complete absence of the right superior vena cava.[8] Thus, the incidence of unilateral left superior vena cava is 0.05%.[1] This anomaly is often associated with other congenital cardiac defects,[1] sinus node dysfunction,[4,9] coronary sinus rhythm[1,3] and electrical instability with sudden death.[10] These arrhythmias may be the result of the abnormal development of the right and left horn of the sinus venosus and their embryonic pacemaker cells,[1] or it may be due to hypoplasia of the sinus node.[9]

Our patient presented with ectopic supraventricular tachycardias probably originating from the AV node region, suppressing the sinus node and resulting in symptomatic sinus pauses. The decision to use an AAI pacemaker was based on the following considerations: the presence of symptomatic sinus

node dysfunction, the presence of 1 : 1 atrio–ventricular conduction up to 200 beats/min even after disopyramide 3 mg/kg was given intravenously, which suggested intact AV conduction,[11] the ability to suppress automatic atrial tachycardias by atrial overdrive pacing, and the hemodynamic benefit of maintaining AV synchrony.

However, since the surface ECG showed right bundle branch block and left anterior hemiblock morphology, and since the H–V interval could not be determined during the electrophysiologic study, we recognized the possibility that extension to a DDD pacemaker system might be necessary in the future.

The unsuspected finding of a unilateral persistent left superior vena cava is not an impediment to atrial pacing provided that a screw–in electrode is used.

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Chapter IX

Cost Effectiveness In Cardiac Pacing

9.1. Costs of cardiac pacing

9.1.1. Introduction

Cardiac pacing is a costly but highly effective medical therapy. In a fifteen year comparative study of pacing costs (1965–1980) Langer et al[62] conclude: there is a reduction in costs caused by the prolongation of the pacemaker life–span, less frequent reinterventions and a reduction in hospital patient days. Inflation corrected annual pacing cost per patient fell from $ 2.590,– in 1965 to $ 1.407,–in 1980. However, since 1980 more sophisticated pacing modalities became available and the costs likewise increase when the patient receives a more complex pacing system.

Table 1 summarizes the present annual pacing cost in the Netherlands, the costs are calculated for four different pacing modalities assuming that the patient outlives his pacemaker. The cost of pacemaker therapy are the initial costs of the implanted pulse–generator and lead(s) but also the cost of surgery and follow–up. Outpatient follow–up is only a small fraction of the total costs of cardiac pacing.

Table 1

COSTS OF CARDIAC PACING [9,62]				
	AAI/VVI	**AAI/VVIR**	**DDD**	**DDDR**
pacemaker	8.000	9.000	12.000	13.000
lead(s)	1.000	1.000	2.000	2.800
hospitalizationand fees	2.500	2.500	3.500	3.500
first year follow–up	500	750	750	1000
follow–ups	900	1200	1200	1000
Total costs	**12.900**	**14.450**	**19.450**	**21.300**
Longevity in years	10	7	7	6
Total costs/year	1.290,–	2.093,–	2.807,–	3583,–

Table 1 cost of cardiac pacing in Dutch guilders

Average annual cost of a pacemaker implantation and following generator replacements for four different pacing modalities are given in figure 1.

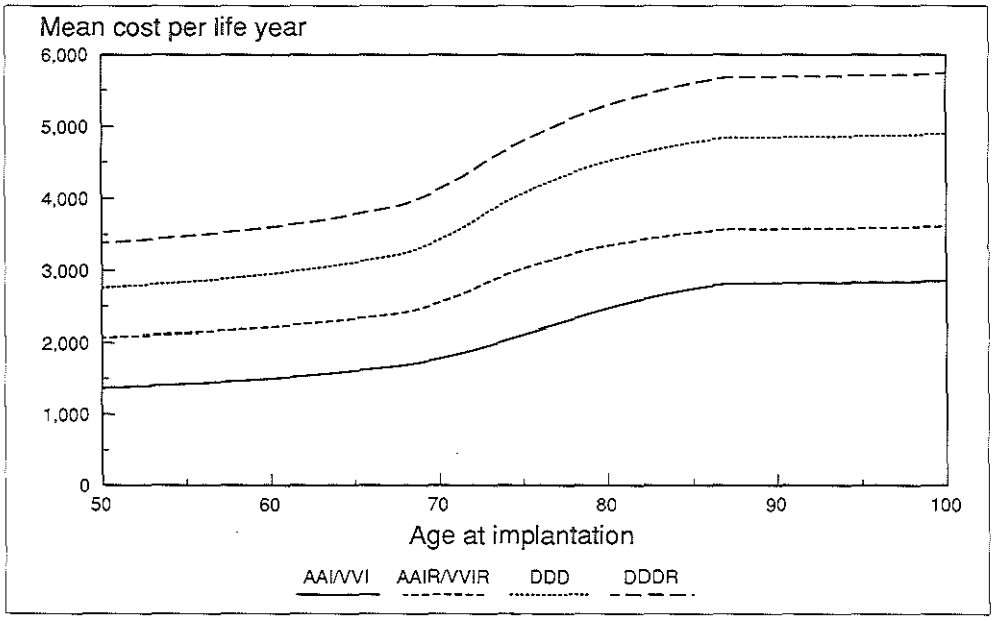

Figure 1. Average costs for four different pacing modalities

The average annual pacing costs are increasingly lower with a better patient survival and remains constant after the more expensive initial 10 years. Pacing therapy will therefore be more cost effective, expressed as the mean cost per life year, in the younger patient as a result of the better life expectancy (tabel 1)(figure 2). Cumulative pacing costs depend largely on patient survival and the applied pacing modality. However, the selection of a different and often more costly pacing mode, as will be shown in the next sections of this chapter, can influence the mortality and the quality of life of the pacemaker patient significantly. In the above mentioned calculations an important aspect of the cost–effectiveness of pacemaker therapy has not been discussed. Cardiac pacing can prevent syncope with the attendant risk of major fractures. Apart from obviating patient harm, it will result in important savings to the health care budget. Futhermore, due to pacemaker implantation some patients regain their independency rather than being looked after by the district–nurse.

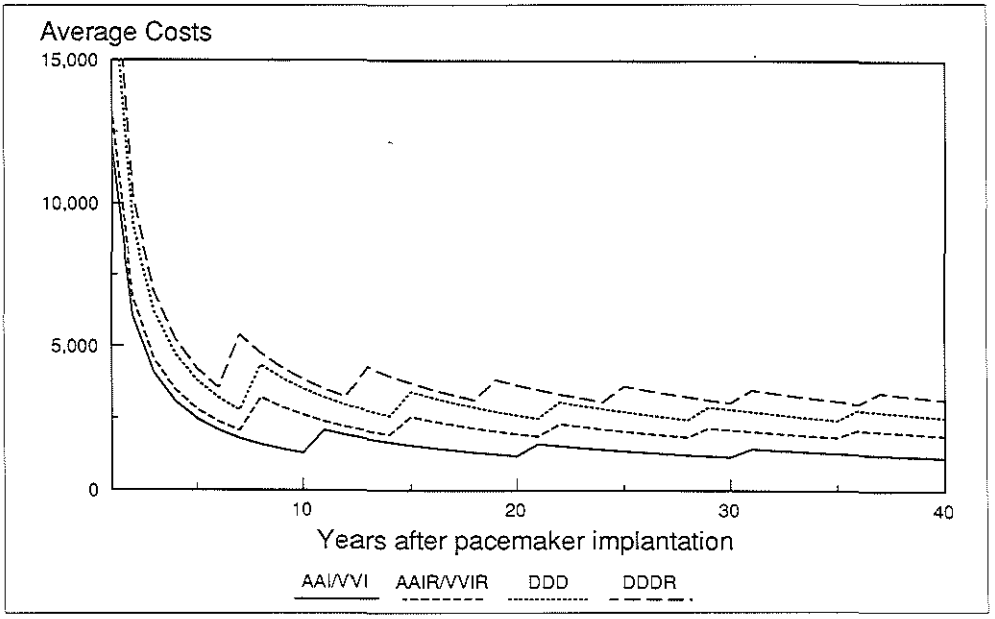

Figure 2. Mean cost per life year for four pacing modalities

9.2. Costs factors

9.2.1. Factors which increase pacing costs

The cost of cardiac pacing depends on several factors:

- System sophistication. The price of a dual–chamber rate–mediated system is approximately 200% of a simple ventricular system. In addition, increasing complexity of devices requires more frequent and lengthy follow–up visits .
- Dual–chamber and rate–mediated pacing systems have a shorter longevity than simple single–chamber systems, due to a higher power consumption. Dual–chamber pacing also requires a second lead.
- The price of technically similar pulse generators from different manufactures may be strikingly different and vary considerably from country to country. The prices are almost twice as high in the United States as compared to United Kingdom and 50% higher as compared to the Netherlands.

9.2.2. Factors which decrease pacing costs

- Programming. In more sophisticated, multiprogrammable generators, many reoperations can be avoided by reprogramming[4]. The flexibility of multiprogrammability can actually realize long–term savings, coupled with greater patient care and comfort.
- Ambulant implantation. Savings can further be realized by ambulant implantation of single or dual–chamber pacemaker in selected patients. In three recent studies[1–3] of patients undergoing ambulant surgery, specific problems were not observed.
- Pacemaker reuse. Efficient use of pacemakers is of major concern. Since patients who receive pacemakers are mainly elderly with limited life expectancy, the lifetime of the lithium pacemaker may exceed that of the patient [4–7,18]. Reuse of pacemakers is therefore worthwhile to consider[7,8]. However, actual savings from reuse are quite small due to costs of reconditioning, the shorter life of the reused pacemaker, hospitalization and medical costs[8]. Reuse is only of potential economical interest with expensive pulse generators with initial short implantation period[8]. In addition to these economic aspects there are also subjective elements which must be considered, problems about recall and replacement procedures, patient dissatisfaction with a second– hand pacemaker, complex reimbursement matters and legal questions concerning ownership. It appears therefore that reuse of pacemakers is unlikely to become widespread in the "western" world.

9.3. Benefit of cardiac pacing

9.3.1. Life expectancy of the pacemaker patient

Epidemiologic studies of pacemaker patients indicate that 40% of patients have their implantation between 70 and 80 years of age; the decade between 60 and 70 accounts for 25%, while the decade between 80 to 90 account for 25%, 5% are under 50 years of age and 5% over 90 years old. At each age more men are implanted than women[9–13,19,20].

Table 2 gives the life expectancy of the normal Dutch population according to the World Health Organization's demographic yearbook of 1989 and the recent study of Robin et al[25,60].

Table 2

Life expectancy		
Age	**Male**	**Female**
65	14.3	19.8
70	11.2	15.9
75	8.6	12.5
80	6.5	9.6
85	4.9	6.5

Age in years – Life expectancy in years
The life expectancy of the normal population According to the World Health Organisation's Demographic Yearbook [25] the life expectancy of the normal population is given.

9.3.2. Life–expectancy after pacemaker implantation

When survival of pacemaker patients is compared to the survival of the general population, it appears that once a pacemaker is implanted the prognosis has turned to normal[6,9]. There is a suggestion that survival may be better in the paced population with sick sinus syndrome[6,14–17,24]. However, patient selection can partially explain this difference because when the bradycardia–related symptoms are less clear, only patients with at least a reasonable life expectancy will receive a pacemaker system.

Health care reports from the United States show that pacemaker patients remain, consistent with their age, major consumers of health care but for reasons other than the pacemaker itself[19,25]. Similar to other elderly persons, each year approximately 10% of pacemaker patients undergo nonpacemaker– related hospitalization; in the half of the cases for cardiovascular reasons[9,19]. However, pacemaker–related or bradycardia–related hospitalizations are less than 2%.

9.4. Quality of life

Valuation of the result of medical therapy is partially subjective, this is particularly true for the assessment of "quality of life"[23]. Without any doubt, the treating physician, a dispassionate member of the family, the representative of the pacemaker industry and the agent of the health insurance have a different definition of "quality of life."

Nevertheless, absence of syncopal attacks or absence of congestive heart failure are certainly objective criteria for accepting improvement in quality of life for anyone who has observed patients in these conditions.

It may be questioned whether a cheaper non–physiological pacing system is sufficient, or must we choose for a physiological system which not only prevents syncopal attacks, but enables the patient to function more comfortably with less or even no complaints of tiredness or breathlessness. A more expensive physiological pacemaker may give such a patient a more productive life and undoubtedly a better quality of life.[35,39–41].

In the assessment of a pacemaker patient's quality of life, special designed questionnaires are used, next to exercise tests[21,22]. The questionnaires consist items of general well–being, physical activity, physical symptoms and social participation.

A statistically significant higher score in the quality of life (QOL) questionnaire and a significantly better exercise tolerance are regarded as an improvement in the patient's QOL.

Williams[63] combined the QOL with the expected life–prolonging effect of treatment and devised units in quality adjusted life year (QALY).

9.5. The benefit of pacing in A–V nodal disease

Information on patient survival following diagnosis of complete heart block is limited. Most generally one refers to the series of Johansson (1966) with probably the last well–designed study of untreated patients with complete heart block before the pacemaker era[26]. He reports 50% survival at one year and 44% at two years. Cabades et al[27] mention in their report on chronic complete heart block in untreated patients a survival of 50% after one year and 20% after 2 years. In a recent survey , Movar et al[28] reported a survival rate in complete or advanced A–V block of 80% at 5 years for the paced patients and 50% for the unpaced patients. At 10 years, respectively 60% and 10% (see Chapter III). The prognostic benefits of ventricular pacing in patients with A–V nodal

disease have shown to extend to all patients with second and third degree A–V block[61].

Prognosis in patients with complete A–V block as a result of intraventricular conduction disease is strongly related to the severity of the underlying heart disease[27]. Complete A–V block in patients with ischemic heart disease is more severe than in subjects with rheumatic valvular heart disease or complete heart block of unknown etiology[6,9,27].

In the Framingham study bi– or trifascicular heart block is often related to ischemic heart disease and carry high risk of sudden death, especially if ventricular ectopic beats are present[29].

Grimm et al[5] analysed symptoms, cardiovascular risk profile and spontaneous ECG pattern in 308 paced patients, of these, 61% suffered from other cardiovascular disease of which was 39% ischemic heart disease. In our own series of 599 paced patients (January 1985–July 1991), we demonstrated the presence of cardiovascular disease in 65%, 2/3 of these patients had ischemic heart disease. In patients with a conduction disorder of unknown etiology the prognosis is the same or even better in comparison with an for age and sex matched control group without cardiac disease[30,48].

In A–V nodal disease there is no conclusive evidence that any of the available pacing modalities results in a better patient survival. There seems to be a trend towards a better survival in DDD or DDDR paced patients in comparison to VVI or VVIR paced patients especially in the presence of retrograde A–V conduction[30,32,36,44,45]. However, exercise capacity, an important part of quality of life, was significantly better in the VVIR and DDD(R) group compared to the VVI group[31–43].

Dispite the subjective nature of quality of life surveys, in many studies it has been demonstrated that reprogramming of the pacemaker to the DDD mode, after a period of VVI pacing, resulted in a significant improvement in exercise capacity and subjective feeling of well–being[47,53–59]. A difference in the quality of life between VVIR and DDD pacing in patients with bidirectional A–V block is still a matter of debate[44–47].

In two recent studies[38,39], exercise capacity and general feeling of well–being have improved in the DDD group of patients as compared to the VVIR group of patients.[38,39]. When a ventricular pacemaker must be replaced, the patient should be assessed for potential chronotropic incompetence. When chronotropic incompetence can be demonstrated, upgrading the pacing sys-

tem to a rate–mediated or dual–chamber system should be considered.

In a summary of costs and benefits of various medical therapies, expressed in cost per extra QALY, pacemaker implantation for atrioventricular block was the most cost–effective[63].

9.6. The benefit of pacing in Sino–Atrial Disease

While pacemaker therapy has brought a dramatic reduction in mortality in patients with total A–V block, such an effect has not been demonstrated for patients with sino–atrial disease (sick sinus syndrome) under ventricular single–chamber pacing[14,15,24].

Hauser et al[4] and Witte et al[51] reviewed their experiences and noticed a 5–year survival of 65% in ventricular paced patients with sino–atrial disease. Rosenquist et al[50] showed a significant difference in mortality of sinus node dysfunction between two Swedish Centers where one center implants VVI units as a routine in this condition and the other implants AAI units. At four years, the survival in the VVI group was 63% compared to a survival of 85% in the AAI group.

In four other retrospective studies[6,14,15,24], differences in terms of the prognosis and antiarrhythmic effects between physiological forms (AAI, DDD) and ventricular pacing (VVI) were reported. In these studies the cardiovascular mortality is significantly higher (10.7% – 34%) under VVI pacing than the respective control groups with AAI pacemakers (3.2% – 6%) during comparable follow–up periods. Recent data of Witte et al[51] indicated during a follow–up of 8 years in two groups of 1242 patients with sino–atrial disease a survival of 89.1% in the AAI/DDD patient group, compared to a 77.4% survival in the VVI–paced patients. These differences are predominantly based on the higher incidence of atrial fibrillation and systemic emboli with their attendant lethal complications under VVI pacing. These recent reports have provided evidence of a favourable modification of the natural history of sino–atrial disease by AAI or dual–chamber pacing[16,17], even though these studies were not randomized.

It appears that life threatening conditions such as congestive heart failure and thromboembolism, that are associated with sick sinus syndrome, are not influenced or can even be aggravated by VVI pacing[48,50–53]. No studies are available which have prospectively investigated a life prolonging effect of physiological pacing in the sick sinus syndrome as compared to medically

treated or asymptomatic groups of patients. Prospective comparative studies between physiologic and ventricular pacing in the sino–atrial disease will presumably never be conducted because of the known adverse effects of VVI pacing.

The therapeutic consequence is that fixed rate (AAI, DDI) or rate variable atrial systems (AAIR, DDD and DDDR) should be selected in patients with the sino–atrial disease whenever possible.

According to Camm[16,49] several questions remain unanswered in sino–atrial disease.

1. Can anticoagulation reduce thromboembolic disease.
2. Does anticoagulation prolong life expectancy of such patients ?
3. Should all VVI devices be upgraded to atrial or dual–chamber pacing systems ?

Prospective randomized studies are needed to provide answers to these, for clinical management of patients with sino–atrial disease, important questions.

Table 3

Comparison of cost–effectiveness of various therapies	
Therapy	**Cost per year of life gained***
CABG for mild AP	75.000
Moderate hypertension	30.000
CABG for LMD	20.000
Cardiac transplantation	15.000
PTCA for unstable AP	7.500
Pacemaker implant for 3rd A–V block	1.200 – 3.000**
Thrombolysis for AMI (anterior)	1.900

** in dutch guilders*
***Dependent of pacing modality.*
Abbreviations: CABG= Coronary artery bypass grafting, AP= Angina pectoris, LMD= Left main coronary artery disease, PTCA= percutaneous transluminal coronary angioplasty, AMI= Acute myocardial infarction.
(Adapted from ref.[64])

9.7. Comparison of cost–effectiveness

In the recent literature[64] comparative data on the cost–effectiveness of various cardiovascular therapies were presented. These data are converted to

the cost of health care in the Netherlands (table 3).

9.8. Conclusion

These data demonstrate that cardiac pacing is an effective treatment of symptomatic bradycardias with respect to improvement of patient's survival and quality of life and can be very cost effective, particulary in the younger patient.

A major progress has been the demonstration of the importance of the maintenance of the atrial contribution in patients with sino–atrial disease.

Very little, if any, further improvement of life expectancy can be expected with the more sophisticated equipment which will become available in the future. Clinical progress must therefore be aimed at futher improving patient quality of life and the development of new indications for pacing.

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Summary

Since 1977, technological advances have made it possible, to incorporate a microprocessor in an implantable pacemaker. In 1980, the first devices with a microprocessor became available for patient use. At present, a single chip measuring a few square millimeters, contains more than a million active elements.

The development of these micro–circuits is very expensive and therefore economically risky for small and medium sized pacemaker companies. Large investments in funds, design and evaluation time forced the pacemaker industry to employ multi–purpose micro–circuits. Microtechnology renders the feasibility to produce almost fully programmable pacemakers and provide the physician with the ability to adapt the device to specific patients needs. Telemetry functions are bidirectional, from programmer to pacemaker and visa versa. Real time intracardiac electrograms can be analyzed and malfunctions of battery or lead performance can be detected. Telemetry and programming functions have significantly decreased the need for surgical reinterventions. Clearly, microtechnology has created the progression from single–chamber fixed rate stimulation to dual–sensor rate– mediated dual–chamber pacing. Optimal cardiac pacing is critically dependent on the pacing mode, the underlying conduction disturbance and the myocardial function. Predictors of patient survival, hemodynamic and electrophysiological factors and the possibility of an adequate follow–up are factors to be considered for selection of the optimal pacing modality.

In chapter I historical aspects of cardiac pacing are reviewed.

Definitions and technology in cardiac pacing
(chapter II)

Understanding of all current cardiac pacing modalities and indications, requires thorough knowledge of pacemaker nomenclature. In chapter II of this thesis, the universal five–letter code to indicate the various pacing systems is discussed and a list of both abbreviations and definitions, used throughout the thesis, is presented. Next, we will discuss some engineering aspects, as these may be relevant for the comprehension of the function and clinical application of cardiac pacing. The basic components of a pacing system: power source, electronic circuitry, and pacemaker lead are described and their function and

limitations discussed.

Finally, basic concepts concerning cardiac stimulation and sensing are presented.

Indications for cardiac pacing therapy

(Chapter III)

Advances in electronic micro–technology, surgical techniques, and pacemaker follow–up methods have expanded the indications for permanent cardiac pacing considerably. In symptomatic bradyarrhythmias the goal of pacemaker therapy includes prevention of Morgagni Adams–Stokes seizures, improvement of exercise capacity and amelioration of congestive heart failure. In the clinical evaluation of the prospective pacemaker patient, next to the patient history, physical examination and electrocardiograms, ambulatory monotoring and exercise testing are mandatory. In some patients, an electrophysiology study can be essential to relate symptoms to bradyarrhythmia.

Following the recently published guidelines on the indications for pacing from the combined working group of the American Heart Association and American College of Cardiology, we discuss the conditions in which there is generally agreement, or divergence of opinion to implant a pacemaker.

Temporary pacing remains controversial and will be addressed together with the therapeutic and prophylactic applications. A guideline is given for prophylactic use of temporary pacing, if bifascicular block complicates acute myocardial infarction.

Modes of cardiac pacing

(Chapter IV)

A pacemaker's mode of response to cardiac signals, combined with its pacing function is termed its mode of operation.

Various pacing modalities are classified in three distinct groups: single–chamber pacing; dual–chamber pacing and rate–modulated pacing. In general, a pacemaker mode, which aims to restore natural cardiac function, will be optimal for all patients. This requires the restoration of atrioventricular synchrony and rate adaptation during exercise and emotion (physiologic pacing).

Despite the widespread acceptance of dual–chamber pacing, there is still a place for atrial single–chamber pacing. Atrial pacing is a safe and reliable mode of permanent pacing in case of sino–atrial dysfunction. Subsequent de-

velopement of atrioventricular conduction disease in patients with normal atrioventricular conduction at implantation, is uncommon. The major indication for single–chamber ventricular pacing is the management of atrioventricular block complicating chronic atrial fibrillation.

Dual–chamber pacing offers the hemodynamic advantages of properly timed atrial systole and rate response in patients with normal sinus node function. The hemodynamic benefit of dual–chamber pacing over ventricular pacing is highly variable from patient to patient, depending on the underlying heart disease.

Pacemaker circus movement tachycardias (PCMT) were a troublesome complication of dual–chamber pacing. We studied retrograde conduction invasively before and non–invasively after DDD implantation and demonstrated that retrograde conduction remained stable in most patients with heart block during long–term follow–up. Using our findings we were able to prevent PCMT by means of adequate pacemaker programming. Many patients must be excluded from implantation of an atrial triggered pacemaker system, because of inadequate sinus node response, or recurrent atrial fibrillation.

In these patients, the pacing rate has to rely on another parameter of metabolic demand, in order to increase with exercise. The acceptable terms for this pacing modality include: rate adaptive, rate modulating, rate responsive and sensor driven pacing and will also be described in this chapter.

Considerations in the selection and use of cardiac pacing systems (chapter V)

When the choice of pacemaker mode for an individual patient is considered, the ideal is the restoration and maintenance of optimal cardiac function to enable the patient to be as active as possible. In the selection procedure hemodynamics, electro– physiologic parameters, and other (non)cardiac factors are important. Recent studies show that the majority of patients paced in a physiologic mode, independent of the underlying conduction disorder, have an improved quality of life, and decreased symptomatology as compared to single–chamber ventricular pacing. Evidence is accumulating of a considerable reduction in the high incidence of spontaneous atrial fibrillation and systemic emboli in patients with sinus node disease treated by a pacing system that maintains atrioventricular synchrony.

The most serious hemodynamic complication of single–chamber ventricu-

lar pacing is the pacemaker syndrome, characterised by a number of symptoms and signs which depend on the loss of atrioventricular synchrony.

The true incidence of the pacemaker syndrome is not known; it would appear, that a significant percentage of patients cannot tolerate ventricular pacing. The presence of ventriculoatrial conduction in patients treated with permanent ventricular pacing, is the major factor for complications and deaths related to atrial arrhythmias and cardiac failure.

Sensors in rate modulated cardiac pacing

(chapter VI)

In a rate mediated pacemaker three major aspects can be distinguished: the indicator, the sensor, and the algorithm for rate calculation. The sensor itself, detects indicator variation which in time reflects the patient's metabolic needs. Requirements for rate controlling biological sensors are: high sensitivity and specificity for metabolic demand, rapid change in exercise, long–term stability and low energy consumption.

The sensors are classified as physiologic or non–physiologic. A physiologic sensor is, in contrast with a non–physiologic sensor, directly tied to the autonomic regulatory process of the body. In this chapter our experience with the non–physiologic indicator activity and the physiologic indicator stroke volume are discussed.

Time intervals in rate modulated pacing

(Chapter VII)

Several intervals of the impulse propagation in the heart can accurately be measured by pacing leads; the duration of these intervals are a direct manifestation of sympathetic tone.

An advantage of time intervals used as metabolic sensors is that they can be used in a closed–loop system. In a closed loop–system the sensor responds only to metabolic demand and would ideally be totally self–regulatory. We investigated the possibility to use the interval from an atrial stimulus to the ventricular R wave (A–R interval) as indicator for physical stress. The changes of the A–R interval, during different kinds of exercise, were prompt and predictable in patients with sinus node dysfunction, but intact A–V conduction. In these patients the shortening of the A–R interval during exercise can be used as indicator for adaptive–rate pacing. Chronic pacing and sensing performance

of a pacing system, using the right ventricular pre–ejection period (P.E.I.) as input for metabolic demand was studied. Posture–related rate changes were observed. This first generation of P.E.I. pacing systems holds promise for adaptive–rate pacing.

Complications of cardiac pacing

(Chapter VIII)

This chapter will be confined to complications related to pacemaker implantations and component failure in the pacemaker system.

A five year experience comparing the complications in physiologic versus ventricular pacing is presented. Acute and chronic pacemaker complications are only slightly more frequent in the physiologically paced patients, as compared to the ventricular paced group. This difference is merely related to the atrial lead.

Pacemaker infection, and the clinical value of antibiotic prophylaxis for pacemaker implantation are discussed. Guidelines are given. A case of persistent left sided superior vena cava complicating pacemaker insertion is presented.

Cost effectiviness of pacing therapy

(Chapter IX)

Pacing is cost effective in terms of relief of symptoms, prolongation of life and improvement of the quality of life. Patients with pacemakers rarely need to be readmitted to hospital because of bradycardia or pacemaker related problems.

Samenvatting

De ontwikkeling van de microprocessor in 1977 heeft in de pacemakerindustrie een vrijwel volledige omwenteling teweeg gebracht. In 1980 werd de eerste microprocessor (chip) in een tweekamer pacemaker ingebouwd.

In de huidige pacemakers worden chips gebruikt die kleiner zijn dan een paar vierkante millimeter en meer dan een miljoen actieve eenheden kunnen bevatten. Het ontwikkelen en testen van deze micro–eenheden is zo kostbaar, dat de kleinere pacemakerfirma's het zich financieel niet kunnen veroorloven voor ieder pacemakertype een aparte chip te ontwerpen. Een oplossing bleek te zijn de ontwikkeling van microprocessors die op vele taken zijn voorbereid. Microtechnologie heeft het ontwerp van multi–programmeerbare pacemakers mogelijk gemaakt. In principe kan nu iedere pacemaker aan de individuele behoefte van de patient worden aangepast. Daarnaast is de pacemaker in staat patienten gegevens op te slaan en interne metingen te verrichten. Deze signalen en meetwaarden kunnen voor verdere analyse via de programmer zichtbaar worden gemaakt. Hierbij kunnen we denken aan de vorm en grootte van het intracardiale electrogram en aan weerstandsmetingen aan de geleider, batterij en electrische circuits. De grote betrouwbaarheid en de vele programmeer–mogelijkheden van de huidige pacemaker hebben het aantal heroperatie's bij pacemaker–patienten afgelopen tien jaar sterk doen afnemen. De microprocessor maakte de evolutie van de enkel–kamer pacemaker naar de dubbel–kamer dubbel–sensor pacemaker mogelijk. Of hartstimulatie in staat is zowel de kwaliteit als de kwantiteit van het leven te verbeteren hangt sterk af van de onderliggende hartziekte en geleidingsstoornis, echter ook van het type pacemaker. Wanneer voor een bepaalde patient voor een bepaald pacemaker systeem wordt gekozen, moet met meerdere factoren rekening worden gehouden. Deze factoren zijn: De patient's prognosis ad vitam, haemodynamische en electrofysiologische overwegingen, en de mogelijkheid tot regelmatige pacemaker–controle na implantatie.

In hoofdstuk I van dit proefschrift worden de historische aspecten van hartstimulatie belicht.

Definities en technische begrippen in hartstimulatie.
(hoofdstuk II)

Een grondige kennis van in de "pacemaker cardiologie", gangbare defini-

ties en technische begrippen is noodzakelijk voor een juiste toepassing van de vele mogelijkheden die de hartstimulatie de pacemakerpatient te bieden heeft. In hoofdstuk II van dit proefschrift worden achtereenvolgens besproken: de vijf letter–code voor hart stimulatie methode; de zogenaamde pacemaker mode; de verschillende pacemaker modes; en tenslotte wordt een lijst gegeven van afkortingen en definities die van belang zijn bij het lezen van dit proefschrift.

De bouw en functie van een pacemaker systeem worden behandeld. Een pacemaker systeem bestaat uit een pulsgenerator met een geleider en een electrode. De pulsgenerator is opgebouwd uit een lithium batterij en een electrisch circuit om enerzijds met vaste regelmaat impulsen van korte duur af te geven, en anderzijds de inkomende signalen van hartactiviteit te herkennen en te verwerken.

Indicaties voor pacemakerimplantatie
(hoofdstuk III)

De verworvenheden van de micro–electronica, de ontwikkeling van eenvoudige implantatie technieken, en de eenvoud van de pacemaker controle hebben het indicatie gebied van de hartstimulatie sterk verruimd. Het doel van hartstimulatie bij patienten met klachten en symptomen van een te trage hartslag bestaat uit het voorkomen van Adams–Stokes aanvallen, de verbetering van de inspanningstolerantie, en indien mogelijk het normaliseren van de hartfunctie. Bij de klinische evaluatie van de potentiele pacemakerpatient behoort naast de anamnese en het lichamelijk onderzoek, een electrocardiogram te worden vervaardigd, zowel in rust als bij inspanning, aangevuld met een continue 24 uurs registratie. Bij sommige patienten kan een electrofysiologische onderzoek pas uitsluitsel geven, of er wel, of geen indicatie bestaat, tot permanente pacemakerimplantatie. Van essentieel belang daarbij is dat de klachten, en de opgewekte ritme– en/of geleidingsstoornissen samengaan.

In 1984, en zeer recent in mei 1991, hebben the American Heart Association en the American College of Cardiology richtlijnen voor de indicatie tot permanente pacemakerimplantatie gepubliseerd. Deze richtlijnen worden in dit hoofdstuk overgenomen en besproken.

Er bestaan nog geen algemene richtlijnen voor het toepassen van een tijdelijke pacemaker in de cardiologische kliniek. In dit hoofdstuk worden enige prophylactische– en therapeutische indicaties voor tijdelijke hartstimulatie

behandeld. Tevens worden richtlijnen verstrekt voor de applicatie van een prophylactische–, tijdelijke pacemaker, wanneer een bifasciculair hart block als complicatie optreedt bij een accuut myocardinfarct.

Hartstimulatie methoden

(hoofdstuk IV)

Onder de stimulatie methode wordt verstaan: De wijze, en de plaats waar de pacemaker het hart stimuleert, en de wijze waarop de pacemaker reageert op de eigen hartactiviteit. De stimulatie– methoden kunnen worden ingedeeld in drie verschillende groepen: De enkele–kamer systemen; de tweekamer–systemen en de door een sensor gestuurde systemen. In principe dient voor iedere patient een stimulatiesysteem te worden gekozen, dat er op gericht is de natuurlijke functie van het hart te herstellen. Dit streven naar fysiologische hartstimulatie houdt in: een herstel van de atrioventriculaire synchronisatie, en de aanpassing van de hartfreqentie aan de metabole vraag van het lichaam tijdens inspanning en emotie. Ondanks alle voordelen die twee–kamer stimulatie te bieden heeft, is er nog steeds een duidelijk indicatie gebied voor enkel–kamer stimulatie. Atriale enkel–kamer stimulatie is een veilige en betrouwbare techniek bij patienten met het sick sinus syndroom. De kans op het ontstaan van een atrioventriculaire geleidingsstoornis, die bij implantatie van de atriale pacemaker niet aanwezig is, is klein.

De belangrijkste indicatie voor ventriculaire enkel–kamer stimulatie is behandeling van een traag ventrikel antwoord, mogelijk tengevolge van een atrioventriculair block, bij een patient met permanent atriumfibrilleren.

Twee–kamer stimulatie biedt duidelijke haemodynamische voordelen bij een patient met een atrioventriculair block en normale sinusknoop functie; namelijk het herstel van de atrioventriculaire synchronisatie, en een keurig gevolgd sinusritme, tussen de geprogrammeerde onder– en bovenfrequentie van de pacemaker. De mate waarvan een patient profiteert van een twee–kamer stimulatie, is erg afhankelijk van het onderliggende hartlijden. In de eerste generatie van de twee–kamer pacemakers was het optreden van pacemaker tachycardiëen een vrijwel niet te behandelen complicatie. De mogelijkheid tot retrograde geleiding door de atrioventriculaire knoop is van essentieel belang voor het ontstaan van pacemaker tachycardieen. Wij bestudeerden het gedrag van retrograde geleiding in tijd, bij patienten met atrioventriculaire geleidingsstoornissen na implantatie van een twee–kamer pacemaker. Wanneer ret-

rograde geleiding bij implantatie kon worden aangetoond, veranderde deze geleidings– eigenschap niet, gedurende meerdere niet–invasive electrofysiologische onderzoekingen, bij een patienten vervolg van gemiddeld 24 maanden. Met gebruikmaking van deze metingen werd de post–ventriculaire atriale refractair tijd van de pacemaker aangepast, en kon in alle gevallen het optreden van pacemaker tachycardiëen worden voorkomen.

In patienten met een, tijdens inspanning of emotie, slechte response van de sinusknoop, moet gezocht worden naar een andere indicator voor de metabole vraag van het lichaam. Methoden van hartstimulatie, waarbij de stimulatie frequentie wordt aangepast aan de metabole vraag van het lichaam, door middel van een andere indicator dan de sinusknoop, worden genoemd : Rate–responsive, rate–mediated, adaptive–rate, en rate–modulated. Ook deze methoden van hartstimulatie worden in dit hoofdstuk besproken.

Overwegingen in de keuze en het gebruik van pacemakers (hoofdstuk V)

Bij de keuze van een pacemakersysteem moet getracht worden de hartfunctie van de patient te optimaliseren, mede om een actieve levensstijl mogelijk te maken. Bij deze keuze zijn meerdere parameters van belang, te weten haemodynamische– en electrofysiologische parameters, daarnaast andere cardiale– en niet cardiale factoren. Recent onderzoek heeft aangetoond, dat de meeste patienten gebaat zijn met een fysiologisch pacemaker– systeem, zowel wat betreft de kwaliteit, als de kwantiteit van het leven. Vooral patienten met een sick sinus syndroom blijken, bij permanente rechter kamer stimulatie, een verhoogde kans te hebben op het ontstaan van atriumfibrilleren met embolische complicaties. Een ander groot bezwaar van enkel–kamer ventriculaire stimulatie is het optreden van het zogenaamde pacemakersyndroom. Het aanwezig zijn van retrograde atrioventriculaire geleiding maakt de kans op het optreden van een pacemakersyndroom groot, echter er spelen ook andere factoren een rol. In patienten met het sick sinus syndroom, bij wie in een hoog percentage retrograde geleiding aanwezig is, lijdt ventriculaire stimulatie tot sterk verhoogde kans op complicaties met een duidelijk verhoogd mortaliteits risico. Hierbij spelen het optreden van atriale aritmiëen met systemische emboliëen, en het optreden van hartfalen een belangrijke rol.

Sensoren in sensor gestuurde hart stimulatie
(hoofdstuk VI)

In een sensor gestuurde pacemaker kunnen drie verschillende aspecten onderscheiden worden: De metabole indicator, de sensor, en het algoritme dat de stimulatie frequentie aanpast. De sensor detecteert de veranderingen van de metabole indicator bij inspanning of emotie. Belangrijke eigenschappen voor een sensor zijn: Een hoge reactie snelheid bij veranderingen van de indicator, een, ook over een lange tijd, stabiele werking, en tenslotte een laag stroomverbruik. De indicator dient een hoge sensitiviteit en een hoge specificiteit voor metabole processen te hebben, die optreden ten gevolge van inspanning en emotie. De sensoren worden ingedeeld, naar het wel of niet aanwezig zijn van een directe verbintenis, met de door het parasympathische en sympathische zenuwstelsel bepaalde veranderingen, bij inspanning of emotie. Een indeling werd gemaakt naar fysiologische– en niet–fysiologische sensoren. Vooral de sensoren waarmee eigen ervaring is opgedaan worden in dit hoofdstuk behandeld. In het bijzonder worden de niet–fysiologische indicator "activity" en de fysiologische indicator rechter ventrikel slagvolume besproken.

Tijds–intervallen in sensor gestuurde hartstimulatie
(hoofdstuk VII)

Door stimulatie electroden kunnen de tijds–intervallen van de impulsgeleiding door de atria, het specifieke geleidingssysteem en de ventrikels nauwkeurig worden gemeten. De duur van deze intervallen wordt voornamelijk bepaald door directe invloeden van het sympathische– en parasympathische zenuwstelsel. Als indicator voor sensor gestuurde hartstimulatie kunnen worden gebruikt: Het rechter ventrikel pre–ejectie interval (P.E.I.), het A–R interval, en het Q–T interval. De, bij inspanning of emotie, optredende veranderingen in deze intervallen zijn snel, (P.E.I. en A–R interval) en proportioneel met de mate van inspanning. Daarnaast lijkt het een voordeel te zijn dat intervallen bij uitstek geschikt zijn voor toepassing in zelf regulerende hartstimulatie systemen. Immers, het gedrag van intervallen is vrijwel identiek aan dat van de gezonde sinusknoop en het staat onder dezelfde invloeden.

Wij onderzochten de mogelijkheid om het interval tussen een atriale stimulus en de ventriculaire spontane activatie (het A–R interval) te gebruiken als indicator voor inspanning en emotie. In een groep van patienten met het sick sinus syndroom, en intacte atrioventriculaire geleiding, werd de verandering

van het A–R interval gemeten op de fietsergometer onder verschillende belastingsgraad. De verandering in het A–R interval was snel en voorspelbaar, daarnaast lineair en proportioneel met het inspannings niveau. In deze groep van patienten is de verkorting van het A–R interval een goede indictor voor inspanning en emotie.

De eigenschappen van een sensor gestuurd pacemakersysteem op basis van het pre–ejectie interval van de rechter ventrikel werden in de acute fase en gedurende een follow–up van 18 maanden bestudeerd. Het P.E.I. is een uitstekende indicator van inspanning, echter daarnaast reageert het ook op andere fysiologische processen waar de haemodynamiek van de rechter kamer gevoelig voor is, zoals plotselinge houdings veranderingen.

Complicaties van hartstimulatie

(hoofdstuk VIII)

Dit hoofdstuk bepreekt de complicaties die op kunnen treden bij het implanteren van een pacemaker. Gelukkig zijn de, aan de implantatie gebonden, complicaties gering en kent de ingreep, ook bij de oudere patient, vrijwel geen mortaliteit.

Pacemakerinfectie en de klinische waarde van antobiotische prophylaxis, ter voorkoming van infectie bij pacemaker ingrepen, worden behandeld aan de hand van de eigen ervaring en recente literatuur gegevens. Aanbevelingen worden verstrekt. In de eigen pacemaker populatie werd onderzocht of een twee–kamer implantatie een hoger complicatie risico met zich mee brengt dan een enkel–kamer implantatie. Inderdaad blijkt er een lichte toename van complicaties op te treden bij implantatie van twee geleiders. Deze toename van complicaties wordt, vrijwel geheel, veroorzaakt door toepassing van de atriale geleider.

De haemodynamische voordelen van een fysiologisch pacemaker– systeem, met een aangetoonde verlaagde morbiditeit en mortaliteit in patienten met het sick sinus syndroom, wegen ruimschoots op tegen de nadelen die aan het gebruik van een atriale geleider kleven.

Tenslotte wordt in dit hoofdstuk een patient besproken bij wie tijdens de pacemaker implantatie een linkszijdige vena cava superior werd ontdekt. Met enige moeite werd in de infrolaterale wand van het rechter atrium een schroef electrode geplaatst.

De kosten en baten van hartstimulatie
(hoofdstuk IX)

Hartstimulatie is een zeer effectieve therapie bij de behandeling van de symptomen, veroorzaakt door stoornissen in het prikkel en geleidingssysteem. Daarnaast is duidelijk aangetoond dat permanente hartstimulatie de prognosis ad vitam van patienten met totaal AV block sterk verbeterd. Ook blijkt er sprake te zijn van een verbeterde levensverwachting, na pacemaker implantatie, bij enkele groepen van patienten met het sick sinus syndroom. De kwaliteit van het leven, ook bij de oudere patient, kan door toepassing van een fysiologisch pacemakersysteem sterk worden verbeterd.

Door nieuwe pacemaker technologie en een verbeterde implantatietechniek daalde, mede door de verkorte opname duur, de kosten van permanente hartstimulatie. In de tijdsperiode van 1965 tot 1980 was er een daling van meer dan 40% (voor inflatie gecorrigeerd). Sedert de komst van de fysiologische pacemaker– systemen zijn de kosten van hartstimulatie gestegen. Ondanks deze stijgende kosten blijft de pacemaker therapie een van de meest effectieve, gerekend naar kosten en baten, behandelings methoden in de moderne cardiologie.

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