THE DESIGN AND TESTING OF A VAPOR-DEPOSITED CARBON-COATED TITANIUM PACEMAKER ELECTRODE

by

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Also I love dogs

ABSTRACT

The occurrece of rising thresholds and exit block in artificial cardiac pacemaker therapy are thought to be due to fibrous tissue encapsulation of the implanted electrode. A vapor-deposited carbon-coated titanium electrode was made for use in pacemaker therapy. It was thought that due to the high degree of biocompatibility exhibited by pure carbonaceous materials following implantation of this electrode in the heart, threshold would remain constant. It was foudn that, in dogs with chronically induced heart block with implanted vapor-deposited carbon-wired titanium electrodes and constant rate stimulators, the threshold did indeed rise as a function of time following impantation.

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I. INTRODUCTION

The Heart

The heart is responsible for circulating blood throughout the body. It does so by contracting and forcing the blood out ot its chambers and then relaxing, allowing its chambers to fill with blood before contracting again. This rhythmic mechanical activity is largely the result of a highly specialized electrical conduction system within the heart which transmits electrical impulses in various directions throughout the heart. Electrical impulses excite cardiac muscle fibers, causing them to contract. When this conduction system is impared the heart ceases to operate in a rhythmical, efficient manner and it sometimes becomes necessary to provide artificial electrical stimulation to pace the heart effectively. The heart is a four-chambered pump organ. The larger of these chambers are the two ventricles; which pump the blood to the lungs and to the rest of the body. The smaller two chambers, the atria, serve as primers to the body. The smaller two chambers, the atria serve as primers to the ventricles (see Fig. 1). To discuss how the heart operates as a pump, it is necessary to first examine the physiology of the heart muscle tissue itself.

Electrical potentials exist across the membranes of essentially all cells of the body. These potentials are termed membrane potentials and are a consequence of a number of factors; namely, the membrane's selective permeability to various ions, particularly Na^+ and K^+, the voltage and chemical gradients associated with ions and active transport mechanisms within the cell which allow the "resting potential" to be maintained

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The Heart

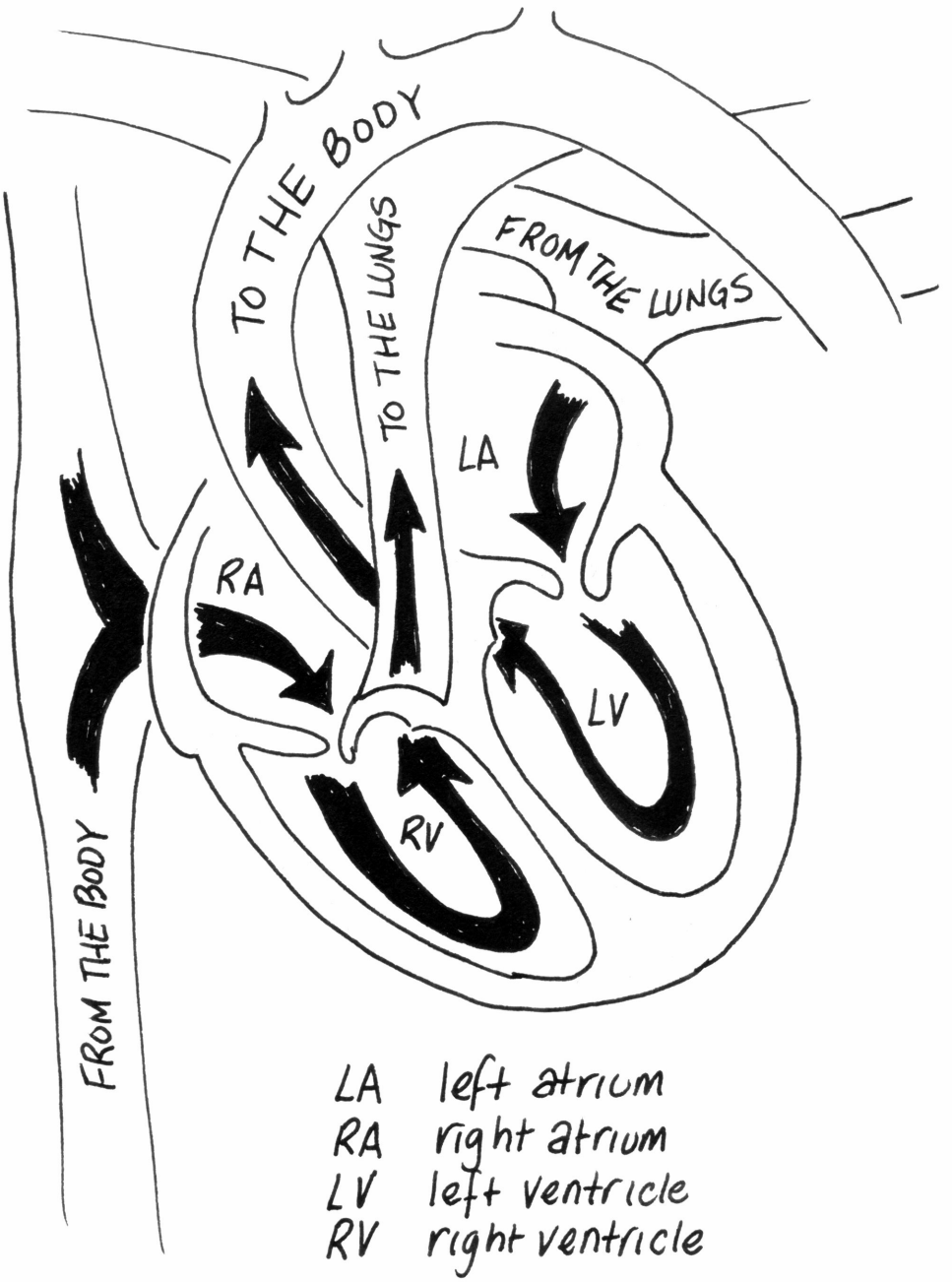
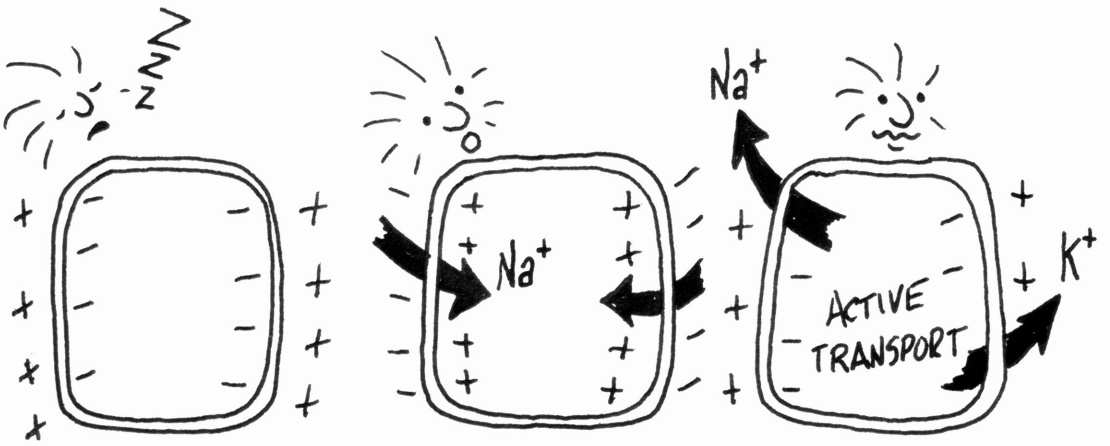


FIGURE 1

against concentration gradients. In its resting state the membrane potential renders the interior of the cell negative with respect to its exterior, the membrance is said to be polarized. Resting membrane potential of normal cardiac muscle tissue is around -80 to -85 mv.[20] In the case of excitable tissue such as muscle, nerve, and, in particular cardiac muscle, electrical stimulation of a resting membrane, if it is of sufficient magnitude can promote a change of the membranes selective permeability. The membrane permeability change allows for the rapid fluction of the intra- and extra- cellular ionic concentrations, so that the cell's interior becomes more positive with respect to the exterior. The cell is now said to be depolarized. In the heart depolarization is achieved when electrical stimulation causes the membrane to reach threshold, which is the potential which must appear across the membrane in order to ellicit the response described. In cardiac cells the threshold is about -55 mv. During depolarization the cell's membrane potential changes to about +20 mv.[20] It is during depolarization that the muscle cell contracts. Following depolarization K^+ ions flow out of the cell, reestablishing the membrane potential; this is repolarization. During repolarization the cell relaxes (Fig. 2). In cardiac tissue the cells transmit the electrochemical responses along their membranes so that the excitation of one cell will cause excitation of its neighboring cells; in this way, a wave of depolarization is spread across the excitable tissue.

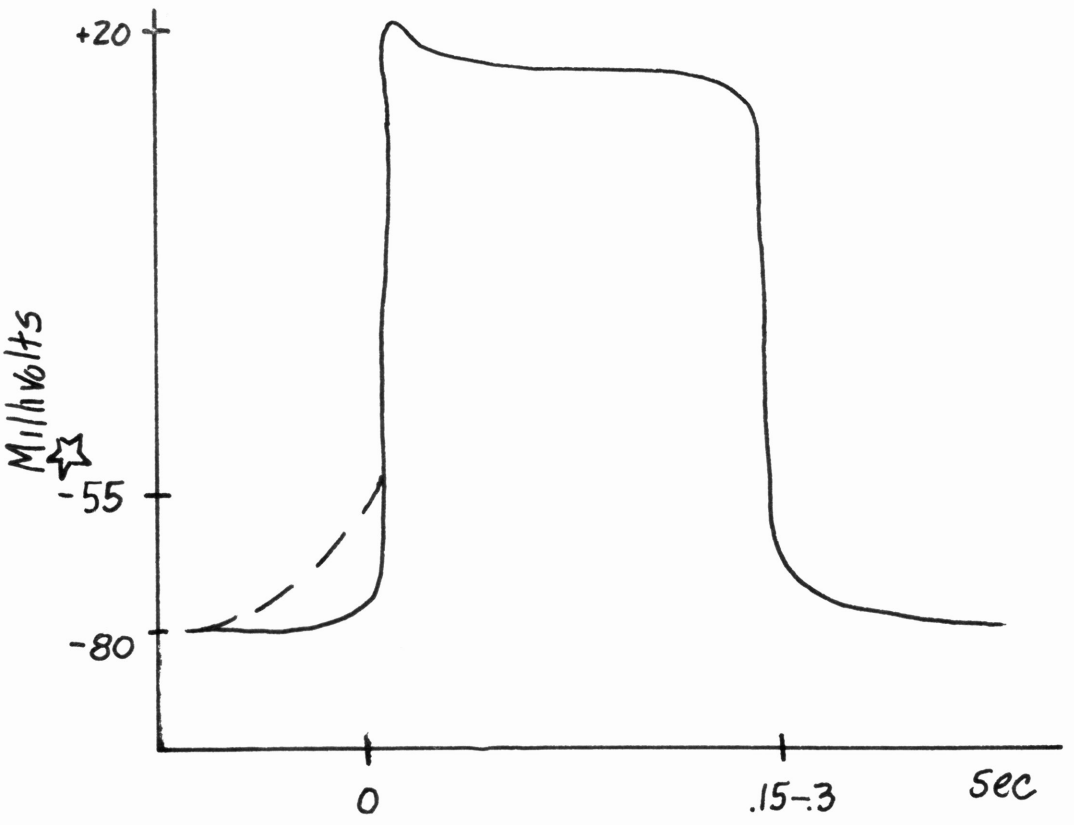
The heart is composed of three major types of cardiac muscle tissue: atrial muscle, ventricular muscle and specialized excitable conductive muscle fibers. The specialized conductive fibers contract fairly feebly compared to the atrial and ventricular muscle. Instead they provide



Polarized Resting State

Depolarized Excited State

Repolarized



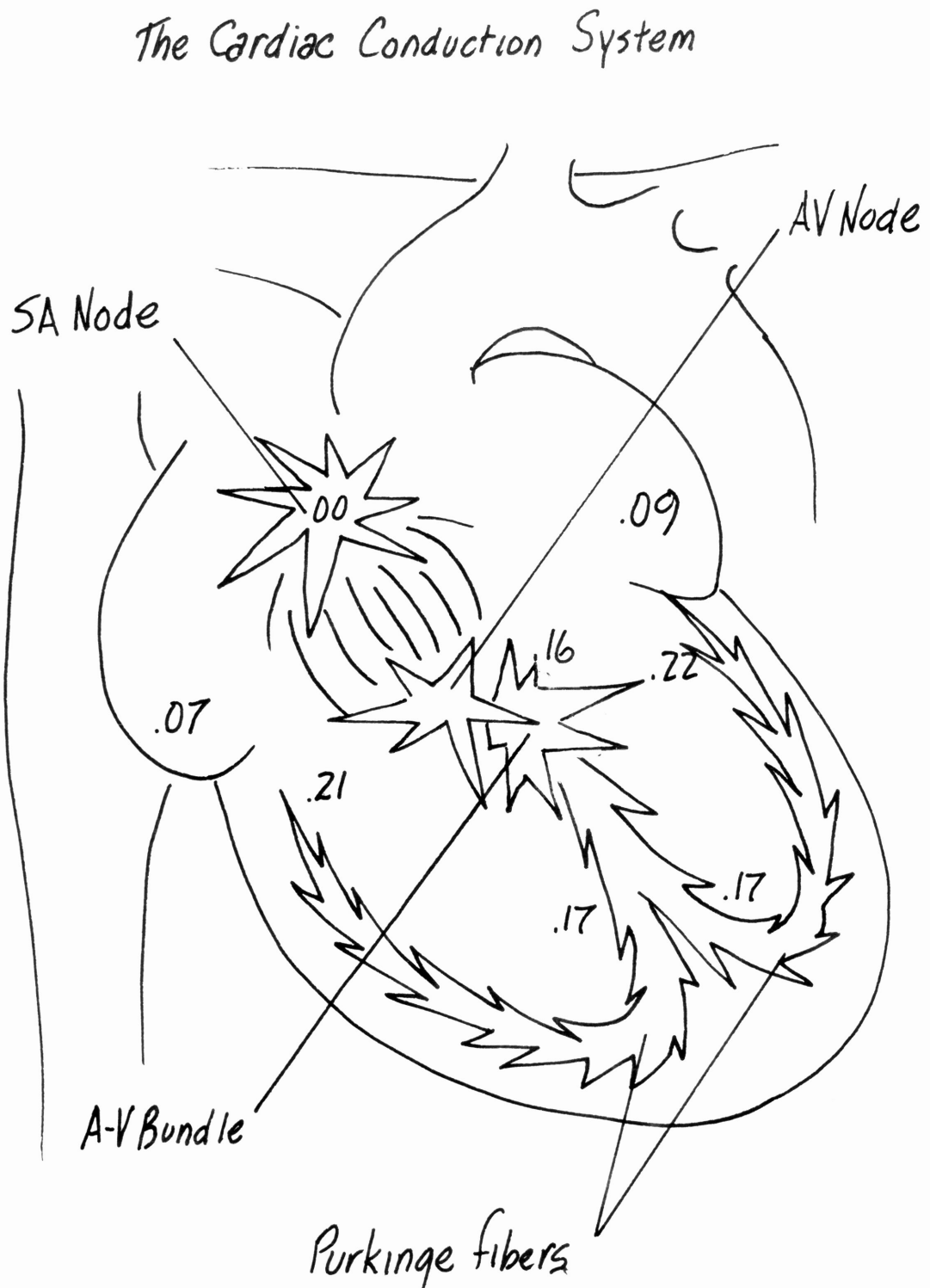
Cardiac Action Potential

☆ threshold

FIGURE 2

an excitation and transmission system for rapid conduction of impulses throughout the heart. All three kinds of tissue, especially the specialized conductive tissue, exhibits the capacity of self-excitation, a process which can cause automatic contraction. The cellular membranes in these tissue are somewhat more permeable to positive ions (Na^+ in particular) this alllows for these ions to diffuse into the cell, during the resting state. The inside of the cell then becomes more and more positive with respect to the outside and eventually the threshold potential appears across the membrane and the cell will "fire" or depolarize. The electro-chemical impulse it ellicits during this firing will spread throughout the tissue. This tissue is then said to have been "self excited". The cardiac tissue which displayes this self-excitation to the greatest extent is the specialized conduction system. The tissue exhibiting the fastest rate of excitation sets the rate for all the rest of the muscle.

The conduction system is divided into various nodes and bundles of tissue located throughout the heart: the sinoatrial (SA) node, the atrioventricular (AV) node, and the left and right bundles of Purkinge fibers (Fig. 3). The SA nodal tissue exhibits the fastest rate of self-excitation and thus is responsible for the excitation of the rest of the heart tissue. It is for this reason referred to as the natural pacemaker of the heart. From the SA node the electrical activity travels to the AV node where, due to the low velocity of conduction in this tissue (.01 n/sec) the impulse is delayed before passing.[20] This allows for the impulse to travel through the atria causing them to contract and fill the ventricles with blood before the electrical signal is transferred to the ventricles. Then the electrical impuse travels to the AV bundle which conducts is rapidly through the left and right Purkinge fibers. These



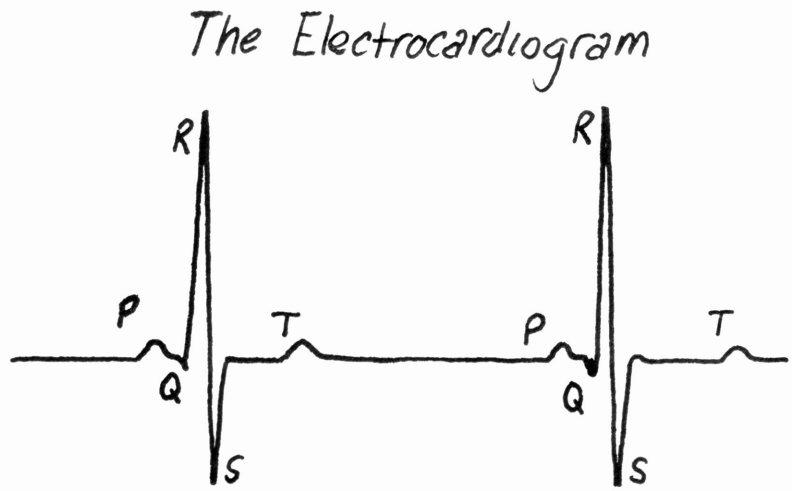
Numbers indicate time in seconds after SA node initiates the impulse that the fibers at the location receive.

FIGURE 3

fibers conduct the impulse to all parts of the ventricles causing them to contract. The velocity of conduction in this tissue is very rapid (2.4 to 3.0 m/sec), and it takes only .06 sec for the impulse to travel from the AV bundle to the most remote fibers in the ventricles. This means that the ventricles contract essentially as a whole unit. They remain contracted for approximately 0.3 seconds. In summary, the impulse for contraction is initiated in the right atrium, in the SA node. The atria contract, forcing the blood into the ventricles. The impulse wave passes through the ventricles and causes them to contract, forcing the blood in their chambers to the lungs and to the rest of the body.

As the transmission of the electrical impulse passes through the heart some of the current is spread into the tissues and eventually to the surface of the skin. If electrodes are placed on the skin, these currents can be recorded. This type of recording is called an electrocardiogram (ECG) (Fig. 4). For a normal cardiac conduction system the electrocardiogram has a characteristic wave shape. The general shape describes the direction of conduction in the heart. A change in the pattern of the wave of depolarization through the heart will alter the shape of the waves in the normal ECG, i.e. abnormal cardiac rhythm can be detected on an ECG recording.

The heart rate is usually controlled by the autonomic nervous system which transmits impulses from the brain and spinal cord. It operates by altering the ionic concentrations in areas surrounding various receptor sites associated with the SA and AV nodes thus causing the heart rate to slow down or increase. In a resting individual the heart rate is dependent on the natural leakiness of the membranes to Na^+ ions and associated effects of the autonomic nervous system.



2 heart beats

P-wave indicates atrial depolarization and contraction

QRS complex indicates ventricular depolarization and contraction

T-wave indicates repolarization

The ECG is measured by placing electrodes in skin which sense cardiac electrical activity.

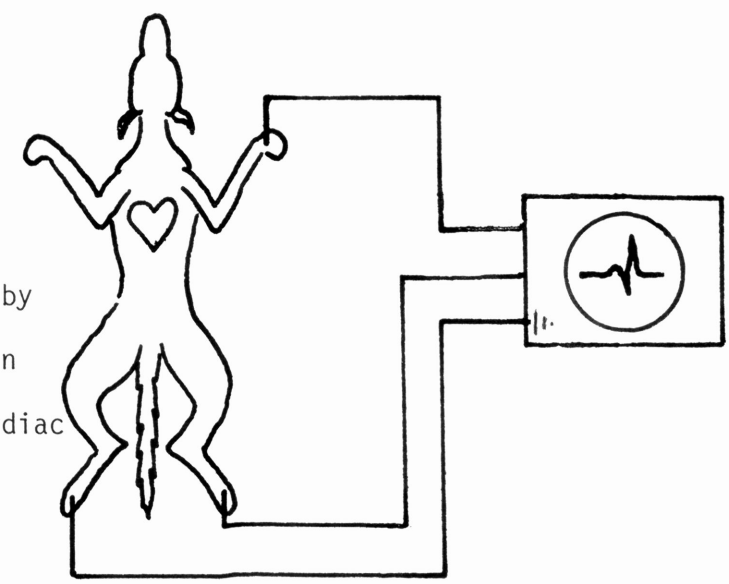
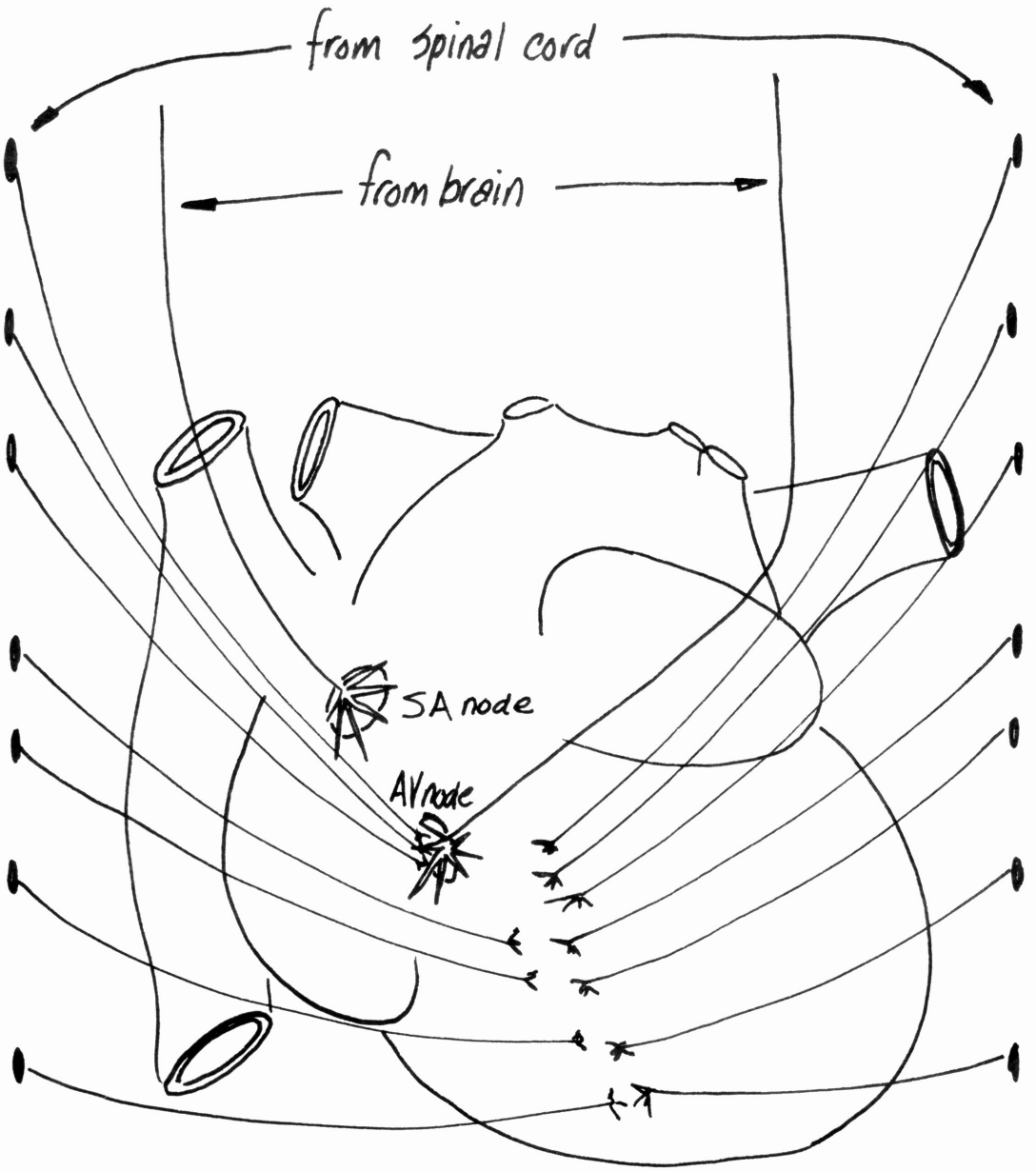


FIGURE 4



Autonomic Nervous Control of the Heart

FIGURE 5

Abnormal cardiac rhythm can be the result of abnormalities within the specialized conduction system. One common type of abnormality is called heart block, in which the transmission of the impulse through the heart is blocked at some point in the conduction system. One place for the block to occur is between the SA node and the AV node. There are varying degrees of heart block. These range from complete heart block, or 3rd degree, in which the signal does not pass from the SA node to the ventricle at all, to first degree heart block where the signal is simply delayed longer than normal before passing on to the ventricles. As a result of the heart block the natural pacemaker is usually efficient as far as the atria are concerned but ineffective with respect to the ventricles since the signal is blocked before it reaches them. However, due to the natural leakiness of the membranes in the ventricular tissue the ventricles may continue to contract but at a slower rate than the atria and also independently of them. The effects of heart block and certain other cardiac conditions can be corrected through artificial pacemaker therapy.

Cardiac Pacemaker Therapy

Cardiac pacemaker therapy is the term used to refer to the ability to cause characteristic rhythmical contraction of an otherwise impared heart. More specifically, it refers to the ability to promote depolarization and subsequent contraction of cardiac muscle cells through means of an external source of electrical stimulation.

Cardiac pacemaker therapy began its successful use in humans in 1952 when Zoll[46] placed electrodes on a patients chest and through the application of high energy stimuli, attempted to treat symptoms of the periodic occurrence of heart block. This technique provided only

temporary treatment and caused burns on the skin and other painful side effects. In 1957, Weirich, Gott, and Lillihei[44] stimulated the heart temporarily through conductive wires sewn directly onto the myocardium, which deliver an externally derived stimulus. Then, independently, in 1959 Chardak[17] and in 1960 Sennings[35] described fully implantable pacemaker generators which operated through electrodes sewn on the myocardium. Clinical application of permanent implantable pacemaker systems followed in 1961. Since that time considerable experience in the use of artificial pacemakers has amassed and refinements and new developments have been made on almost every facet of cardiac pacing in order to alleviate problems encounted in practice and in response to the various different type of cardiac disorders.

A pacemaker system refers to a pulse generator and an electrode lead assembly which delivers the generator derived stimulus to the heart. Pacemaker systems can be categorized according to major different functional characteristic modes of operation, electrode lead configuration, materials, and power supply types.

The mode of operation of the generator refers to the particular technique employed in a generator to develop the stimula necessary to pace the diseased heart, the mode employed is dependent on the type of disorder. There are two basic modes, asynchonous (constant rate and competitive) and synchronous (non-competitive). Asynchronous generators deliver stimulus at fixed rate regardless of any natural cardiac pacemaker activity, therefore it competes with natural pacemaker activity. Synchronous pacemakers use sensing circuits which trigger of inhibit the generator output in response to natural cardiac depolarization waves so that this mode is non-competitive with natural cardiac activity.

A three-letter coding system has been developed which allows for the indentification of the mode of operation of a particular pacemaker generator.[33] This coding reveals the chamber in which the stimulating electrode is placed (first letter), the chamber in which a sensing electrode is placed (second letter), and the mode of response (third letter). This coding is defined in the following table.

Table 1. Pacemaker Coding System.

CHAMBER PACED		CHAMBER SENSED	MODE OF RESPONSE	
Ventricle	(V)	(V)	Inhibited	(I)
Atria	(A)	(A)	Triggered	(T)
Double Chamber	(D)	(D)	Not Applicable	(O)

As an example of the use of this code: VOO describes fixed rate asynchonous ventricular stimulated pacemaker, and VAT describes a ventricular paced, atrial triggered pacemaker.

Of all the types of pacemakers, asynchronous has the simplest circuit design with fewer components and therefore less susceptible to failure.[16] This type of pacemaker lacks the complex sensing circuit incorporated in the non-competitive systems. The sensing circuits detect the natural activity of the heart in a form of electrocardiogram (described above). The generator is either triggered or inhibited to provide stimuli depending on characteristic waves of the ECG. The type of generator employed and the location of sensing and stimulating electrodes is dependent upon the nature of the cardiac disorder. For example, the location of the block in the case of heart block disorder would obviously determine the location of the electrodes. The non-competitive generator

generator circuits employ more sophisticated circuits and therefore are more susceptible to failure. They are also more susceptible to external sources of electromagnetic interference.[22,16]

There are basically three types of non-competitive systems which operate in response to sensing: P-wave triggered, QRS-wave triggered, and QRS-wave inhibited. The P-wave indicates natural atrial depolarization and contraction. These generators provide stimulation to the heart when a P-wave is sensed and at a fixed rate on the absence of a P-wave. The QRS-wave complex indicates depolarization of the ventricles. QRS-wave triggered generators operate in the same manner as P-wave triggered generators operate in the same manner as P-wave triggered except that they respond to the QRS-waves. The QRS-wave inhibited generator provides fixed rate stimulation in the absence of natural ventricular activity. Clearly there are many possible variations of generator modes with regard to the location of electrodes and response to the location of electrodes and response to sensing (if any).

The electrode-lead assembly must provide mechanical as well as electrical integrity to the system. It is characterized on the basis of construction and configuration. The lead and electrode are susceptible to fracture in that they are constantly subjected to flexing due to the rhythmic motion of the heart itself, motion due to respiration and general body motion.[19,14] The repetitive flexing is referred to as fatigue. The fatigue life, the number of repetitive cycles of flexing which a lead or electrode can withstand before fracture, is a property of the material from which it is made. Fatigue life can be enhanced by various conformational designs. The lead should be made of highly conductive wire and well insulated. Typically platinum, stainless steels, and Elgiloy (nickle-

cobalt alloy, Elgin Watch Co., are used. To resist fracture due to fatigue multistranded wires, wire ribbons wound around nonconductive cores, and single strand coils have been employed in lead wire design. The insulation is usually provided by teflon or silicone rubber sleeves.

It is essential that the electrode achieve stabilization in the heart muscle.[12,15,16,25] The most successful screw-in electrode.[26] The Chardack electrode is the last three turns of a coiled lead wire which are separated to allow for the ingrowth of cardiac tissue. Whe sutured in the myocardium, the sutureless electrode is a slightly larger helical coil which is screwed into the heart muscle and also allows for ingrowth of tissue to provide stability.

The configruation of the electrode lead assembly refers to the location of the stimulating and indifferent electrode with respect to the heart. Terms used to describe electrode configuration are unipolar and bipolar, and endocardial vs myocardial stimulation. When both electrodes are positioned on or within the heart the configuration is bipolar, if only the stimulating electrode is placed on or in the heart and the indifferent electrode is placed elsewhere (usually on the generator housing) the configuration is unipolar. Endocardial electrodes are placed transvenously, usually via the cephalic vein, to the right ventricle Whereas, myocardial electrodes are placed directly on the myocardium in either the left or right ventricular wall. In either case the electrode must make contact with the heart muscle tissue (Fig. 6). Endocardial electrodes are more susceptible to displacement and subsequent failure of the system than myocardial electrodes but they offer the advantage of being much easier to implant surgically since placement of myocardial electrodes usually involves thoracotomy.[4,12,19] Although complications

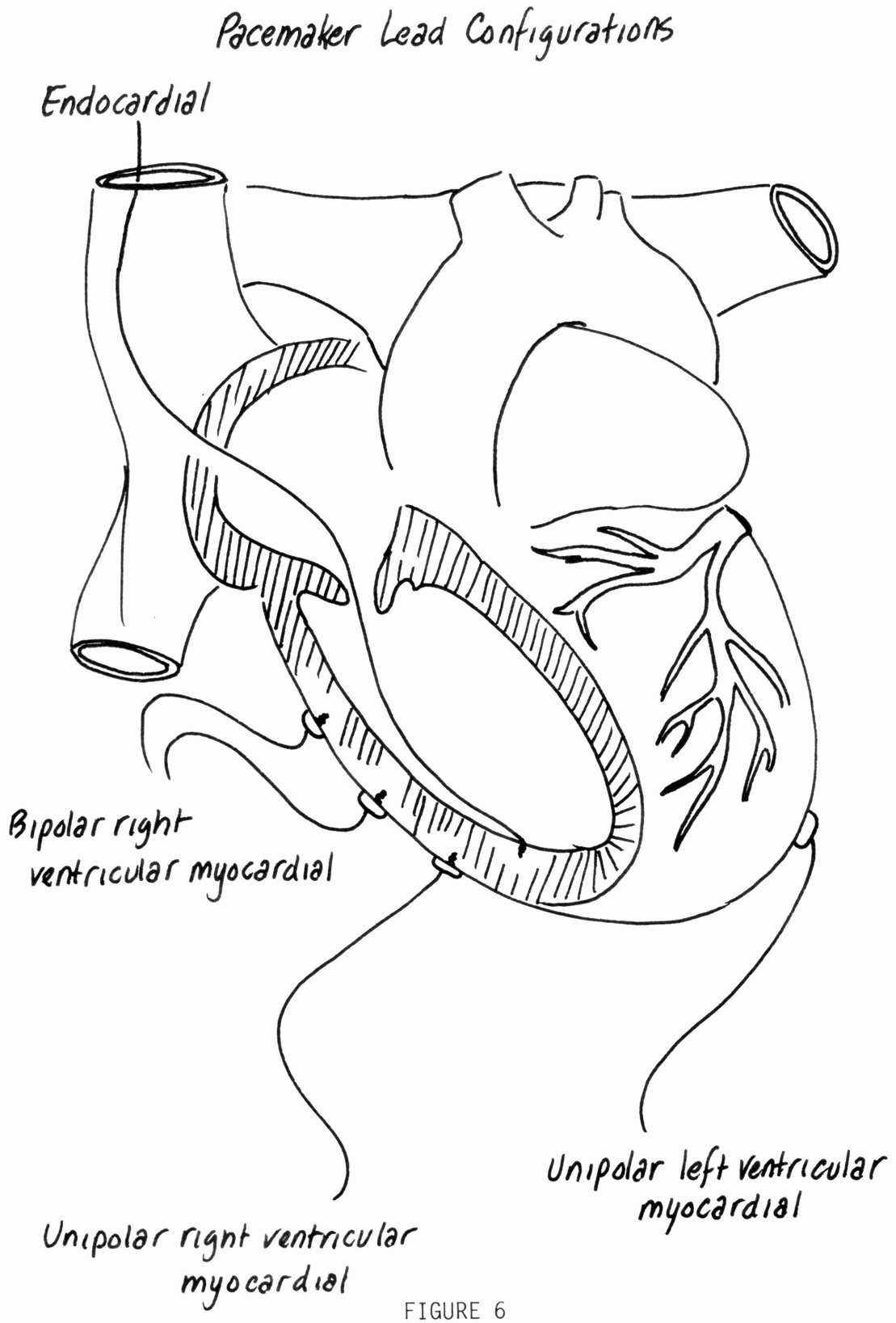

Pacemaker Lead Configurations
Endocardial
Bipolar right ventricular myocardial
Unipolar right ventricular myocardial
Unipolar left ventricular myocardial

FIGURE 6

other than those related to pacemaker therapy following surgery are greater for myocardial than for the endocardial approach, there appears to be greater occurence of pacemaker related failure with the endocardial electrodes. The thick wall of the left ventricle makes it the more favored site for myocardial implantation than the right ventricular wall. Whether endocardial or myocardial pacing techniques are employed is dictated, by the general health and age of the patient, the nature of the cardiac disorder, and the experience of the surgeon.

Unipolar techniques are usually favored over bipolar techniques, especially in the case of endocardial pacing.[12] Post-operative analysis of pacing is easiest in unipolar pacing due to the greater spacial separation of the electrodes.[9] Also larger anodes can be provided in unipolar techniques, this is advantageous in that corrosion is usually associated with the anode in metal electrode systems. In unipolar techniques the stimulating electrode is most often established as the cathode.

Assume that the integrity of the generator circuit and the electrode lead assembly remain intact, pacemaker longevity is dependent upon the power source. Types of power sources available include conventional mercury-zinc cells, lithium-iodine cells, rechargeable nickle-cadmium cells, and radioisotope cells which employ plutonium 238 or promethium 147. Logevities of the available power supplies range from 18 months (minimum for mercury-zinc cells) to more than 10 years (maximum for radioisotope and lithium-iodine cells). Pacemaker lifetime, however, is also a function of circuit design electrode design, and pulse duration and shape. The lithium-iodine cells are presently the most popular power source due to safety consideration, simplicity, and dependability.

Complications in Artificial Pacing

Certain complications may occur in any of the various artificial pacemaker systems. The problems are associted with the surgery itself, component failure, or failures at the electrode-tissue interface. The most obvious surgical complications are infection and hemorrahage.[39] Component failure can occur in any of the various components of a pacemaker system. Some of these complications were previously described.

Complications arising at the electrode-tissue interface include displacement of the electrode, myocardial perforation, and exit block. Displacement of the electrode can occur anytime following implantation, and is usually associated with poor initial implantation. Myocardial perforation, the extrusion of the electrode into the chamber lumen, is also a result of poor surgical implantation. Exit block, on the other hand, is less a consequence of surgical technique but is a potential problem in all systems.

Exit block occurs when the electrode-lead assembly remain intact and in position and the generator output remains constant but the amount of current needed to stimulate the heart has exceeded the generator output.[19,31] The minimum amount of current (or voltage or energy) needed at the electrode-tissue interface to cause depolarization and contraction of the heart is called the threshold. A progressive increase in thresholds is always observed following implantation of artificial cardiac pacemakers.[21,39] The threshold rises significantly for a few months until it usually levels off to some value around three to five times the value at implantation. Exit block is the complication in cardiac pacing which has stimulated this investigation. In particular it is the rising thresholds observed at the electrode-tissue interface which are of major interest.

Threshold

Threshold describes the amount of current or voltage at the electrode needed to excite the cardiac tissue. In cardiac pacemaker therapy it is desirable to have the lowest possible threshold in order to increase pacemaker longevity and to reduce the occurrence of failure due to exit block. It has been determined that threshold is a function of many variables encountered in pacemaker therapy. Some of these variables are the following:[15,16,25,42]

1. Electrode material (polarization and corrosion);
2. Stimulation site;
3. Pulse duration and shape;
4. Electrode surface area and configuration;
5. Stimulus polarity;
6. Drugs and electrolyte balance;
7. Maturity of the electrode.

With respect to electrode material, threshold is related to the general reactivity of the metal and the polarization voltage developed during the passage of current through an area.[15,18] When a voltage is applied across a pair of metal electrodes in saline, ions collect around the surface of the electrode inducing a potential gradient which opposes the flow of current thereby increasing the current or voltage needed for stimulation. It is generally desirable to chose a metal with a high tolerance to corrosion in saline, such as platinum, for use as an electrode in pacing however more reactive metals, such as Elgiloy and stainless steel are successfully utilized in many pacemaker systems.[15,23,28,42]

Stimulation site refers to the position of the electrode in the heart.[15,21,25,34] As previously described, the electrode is positioned in either the endocardium or the myocardium. Endocardial electrodes are placed transvenously through the superior vena into the right ventricle. Myocardial electrodes are placed in either the right or left ventricular wall. With respect to surgical approach the transvenous technique is favored over the myocardial technique which involves thoracotomy.[4]

Threshold of stimulation vary according to the duration of the stimulating pulse. The voltage and current thresholds decrease with increasing pulse duration.[13,15,32] However, the energy requirements at threshold are highest for short durations then reach a minimum at durations between .2 and 1.0 msec, before the energy threshold increases again with longer pulse durations. Therefore it is generally considered most efficient to employ pulse durations between .2 and 1.0 msec.[11,13,25,38] Also pulse shape has an effect on threshold. It has been determined that an optimal pulse shape is one that is a combination of a ramp pulse and trailing edge rectangular pulse, but for simplicity most systems use a square wave stimulus.

It has been well documented that the surface area of the stimulating electrode is a very significant factor in relation to threshold requirements.[15,38,42] The smaller the surface area the lower the threshold. This is in accord with the theory that it is the current density at the tissue interface which determines the threshold. Clearly then for a given current to the electrode the smaller the surface area the greater the current density (current per unit area). It has also been noted that for a larger area. Fibrillation threshold refers to the threshold that is needed to cause waves of depolarization in the heart to spread in all

directions rather than in the direction of that for normal cardiac rhythm. This further strengthens the support for the use of smaller surface area stimulating electrodes in artificial pacemaker applications.

The threshold can be affected by the polarity of the stimulating electrode, i.e. whether it is used in cathodal or anodal stimulation.[43] Lower thresholds are observed with cathodal stimulation. This observation is probably due in part to the fact that, for metal electrodes subjected to a potential gradient, corrosion is greater at the anode.[15,31,43]

Certain drugs can drastically alter the thresholds needed from cardiac pacemakers. Some drugs such as epinephrine and digitalis can make the heart easier to excite while other drugs, such as lidocane, can significantly reduce the excitability of the heart. Drugs operate on the autonomic nervous system which in turn effects the rhythmicity of the heart by causing alterations in the ionic concentration at the ionic concentrations at the cellular level in the heart. The ionic mechanisms at the level lead to depolarization of the cardiac muscle tissue. Therefore, electrolyte balances at the electrode are important factors in regard to threshold.[41]

Maturity refers to the length of time following implantation that the electrode remains in one position. At implantation the threshold required is termed acute. As mentioned previously the threshold rises until it levels off at some value, termed the chronic.[15] It was originally though that the observed rise is due to the increases impedance of fibrous scar tissue which develops surrounding the electrode. This was disproved by Meyers and Parsonet when they showed that the threshold is virtually independent of impedence at the interface.[27] It is now accepted that the rising thresholds are due to the effective increased surface area

of the electrode caused by the fibrous encapsulation of it. The stimulable cardiac tissue is further from the electrode itself in that the conductive fibrous tissue has increased the apparent size and surface area of the electrode. Increased surface area lowers the current density and therefore increases the required threshold. It is suggested that the threshold rise could be eliminated and significantly lower chronic thresholds could be achieved by minimizing the fibrous scar tissue growth following implantation.

Biocompatibility of Carbon

Almost anytime a foreign material is introduced to the body, the natural defense mechanisms set out to protect against the invader. A chronic response to such an invasion is the growth of fibrous tissue which typically walls out or encapsulates the intruder. There are some materials for which this response is very lower or even totally absent. These materials are referred to as being highly biocompatible. A variety of pure carbonaceous materials exhibit this biocompatibility and are therefore a particular interest in this study to eliminate rising thresholds in cardiac pacemaker systems.[3,24,30a,43]

Carbonaceous materials vary greatly in their appearance and mechanical properties, for instance the differences between graphite and diamond. The more poorly organized crystalline structures of carbon are of particular interest in biological implant studies.[3,37] These are the turbostatic carbons. One type of turbostatic carbon of interest is the vapor deposited carbon (this type of carbon has structural, physical, and compositional properties which are identical to the group of carbons called LTI carbons). The vapor-deposited carbons are formed by evaporating carbon atoms from a carbon source heated by a high energy electron beam

and depositing the carbon on a cool substrate such as a metal, polymer, or a ceramic which is held at some distance from the carbon source. The coating thus achieved is less than one micron thick and the mechanical properties of the substrate are not altered nor is its gross surface topography.[3]

In order for the vapor-deposited carbon films to be effective in biological applications they must adhere strongly to their substrates. High bonding strengths have been reported with the carbon films and titanium and titanium alloys.[36]

II. OBJECTIVES

The objectives of this investigation are the following:

1. To design a vapor-deposited carbon-coated metal electrode for use in cardiac pacemaker therapy.
2. To implant this electrode in dogs hearts and to determine threshold as a function of time following implantation.
3. To study the biocompatibility of the electrode with surrounding cardiac muscle.
4. To attempt to correlate compatibility, or lack-thereof, with changing thresholds.

III. MATERIALS AND METHODS

The study involved two separate approaches. The first involved periodic stimulations of healthly dogs' hearts to determine thresholds following implantation for a period of up to ten (10) weeks. The second involved constant stimulation of hearts in which chronic complete heart block had been induced, with periodic (monthly) sampling of thresholds. In both series of experiments the same electrode design was employed.

The Electrode

The electrode used in this study was a three-turn helical coil of .5 mm diameter Titanium (99.97% pure) wire with an overall diameter of 3 mm diameter and an overall length of 4.3 mm. This configuration which is identical to that developed by Hunter, et al., was selected because of its clinical acceptance and ease of implantation.[26]

The electrode was carbon coated by General Atomic, Corp. (now CarbonMedics, Inc.) of San Diego, Ca., using a vapor deposition process. Compared to other metals, Titanium has a relatively high electrical resistivity, and exhibits a minimum degree of corrosion in body fluids, and has a high bonding strength with the carbon coat.[27,25]

Procedures

In the first phase of experimentation, the end of the electrode was mechanically deformed into a square peg so that it could be covered with .30 guage tinned copper wire through a wire-wrapping technique. This was necessary in that the titanium could not be soldered to the lead. The lead wire (.22 gauge multi-stranded copper wire) was soldered to the wire-wrap wire. The entire lead was then covered with silastic tubing and sealed at both ends with commercially available RTV silicone rubber.

The assembly was cleaned in ethanol and sterilized.

Four mongrel dogs were used for this study. Each dog was anesthetized with sodium pentobarbitol and a thoracotomy performed through the fourth intercostal space. Lidocance was sprayed topically over the heart muscle in order to reduce the excitability during the implantation of the electrode in the left ventricle. Implantation involved a clockwise torquing motion to screw the electrode into the myocardium. The lead was then routed subcutaneously around to the dorsal portion of the neck where it exited the skin. Following surgery, strength-duration curves were obtained to determine thresholds. The exposed lead wire was connected to a Grass model S44 stimulator in the circuit shown in Figure 7. The pulse width was set and the stimulation voltage increased until artificial pacing was achieved as observed on the ECG. The voltage was then reduced until stimulus strength was the minimum needed to sustain artificial pacing. Thresholds were obtained once a week following surgery. The dogs were sacrificed at two week intervals to evaluate the biocompatibility of the electrodes.

The second phase of experimentation, the electrode was spot-welded to an Intermedics Elgiloy lead wire. The weld was encased in epoxy, silastic tubing was slipped over the lead and weld joint and the entire assembly was sealed with RTV silicone rubber. The electrode-lead assembly was cleaned ultrasonically and in ethanol and then sterilized (Fig. 8).

The surgical procedure in this phase included inducing chronic complete heart block by injection of 37% formalin into the AV bundle; a procedure described by Steiner and Kovalik.[40] No lidocane was used so that threshold could be determined immediately following implantation.

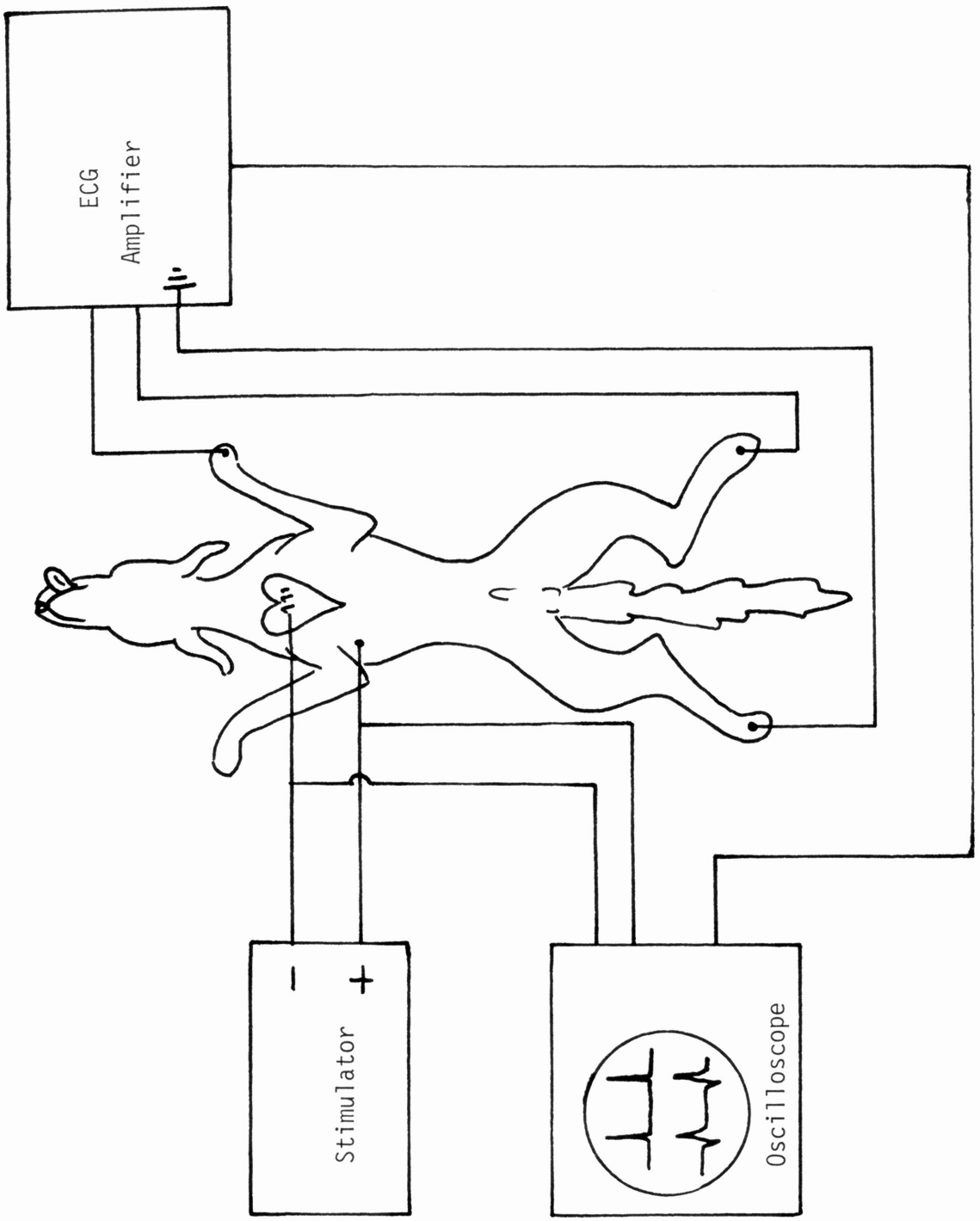


FIGURE 7

PACEMAKER SYSTEM

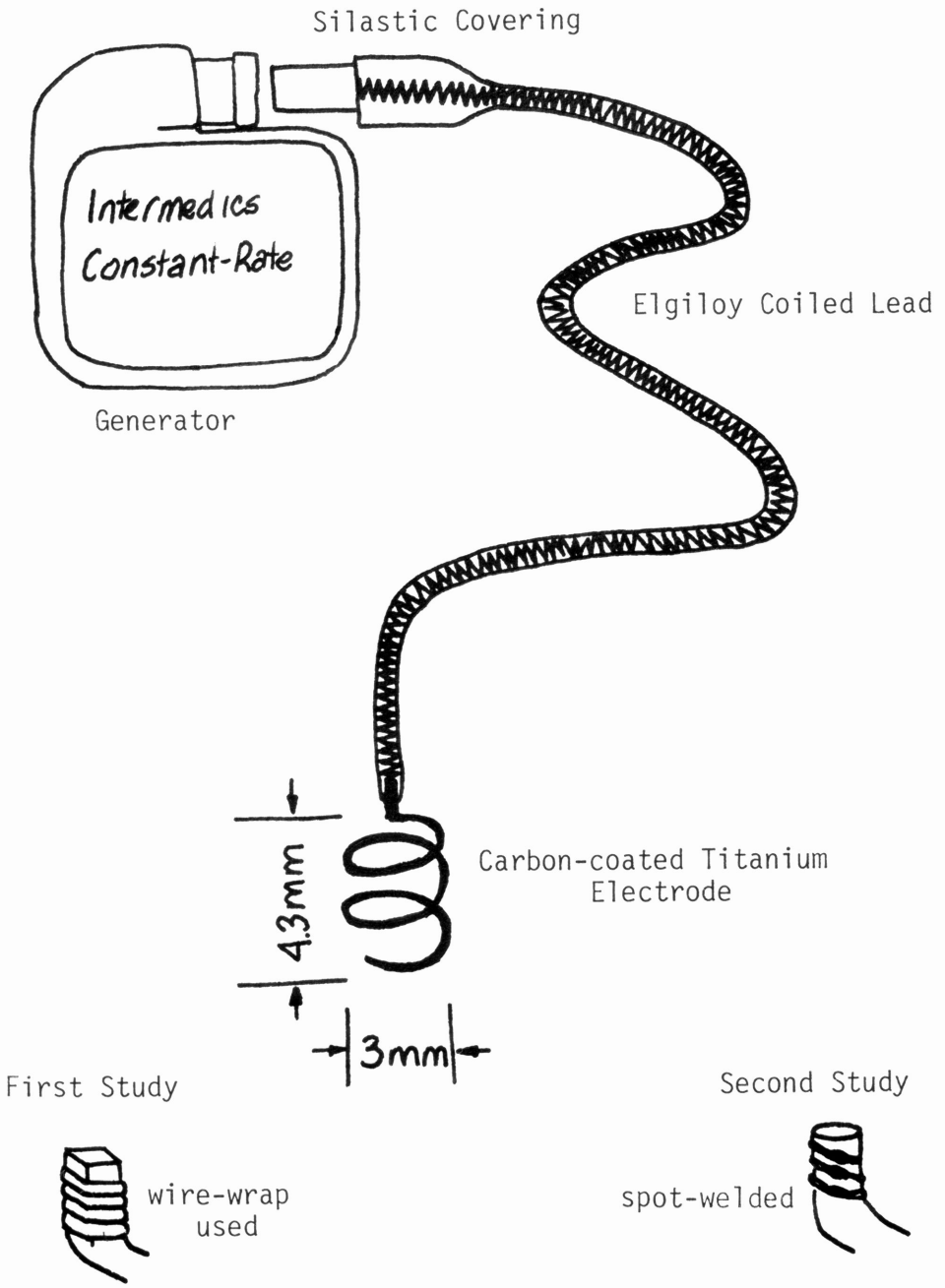


FIGURE 8

The lead was connected to an Intermedics constant-rate pacemaker generator placed between the muscle layers of the abdomen.

Strength-duration curves were obtained immediately following implantation and at monthly intervals following surgery. Threshold was determined in the manner described previously (Fig. 7). Two dogs were used in this phase of the study and were sacrificed at the end of four months to determine biocompatibility of the electrode.

IV. RESULTS

First Phase

Of the four dogs used in this study, three broke their lead at the skin surface. The relationship between voltage threshold and electrode maturity for the one dog which did not destroy its lead is shown in Figure 9. Figure 10 shows a typical voltage threshold and associated ECG. Due to the inexperience with pacemaker systems and their related measuring techniques, data obtained during the first weeks is suspect of measurement error. Histologic evaluation of the tissue at the interface of each electrode revealed many neutrophils, indicating localized infection. Fibrous tissue reaction was not present.

Second Phase

Figures 11 and 12 show the relationship between voltage thresholds and pulse duration obtained at implantation and at monthly intervals following surgery for both of the dogs with chronically implanted pacemakers. A notable increase in threshold is observed following implantation. Histologic evaluations of the tissue surrounding the electrode have not yet been completed.

Results of phase one

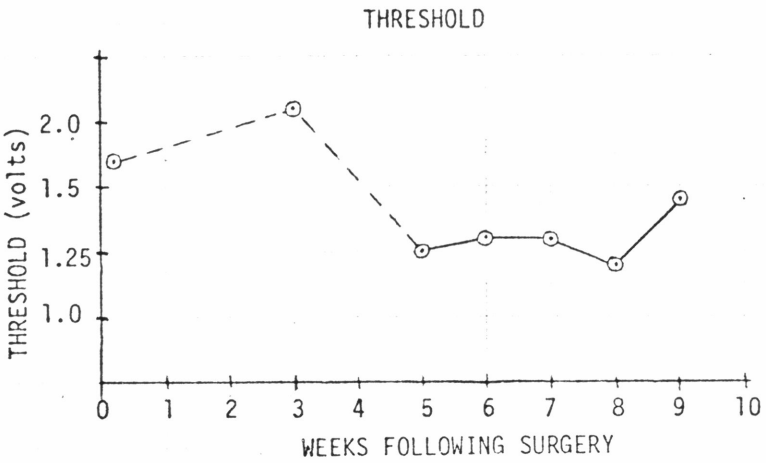


FIGURE 9

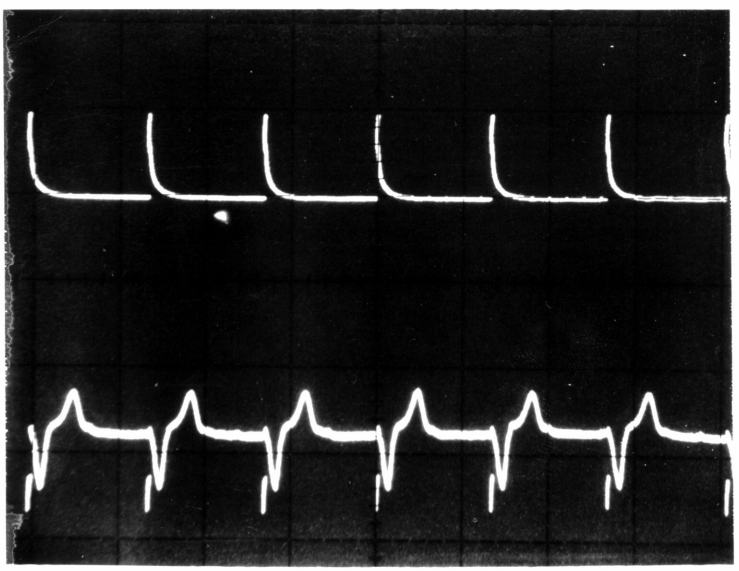


FIGURE 10

Results of second phase

("Pointer Sister") Dog 1

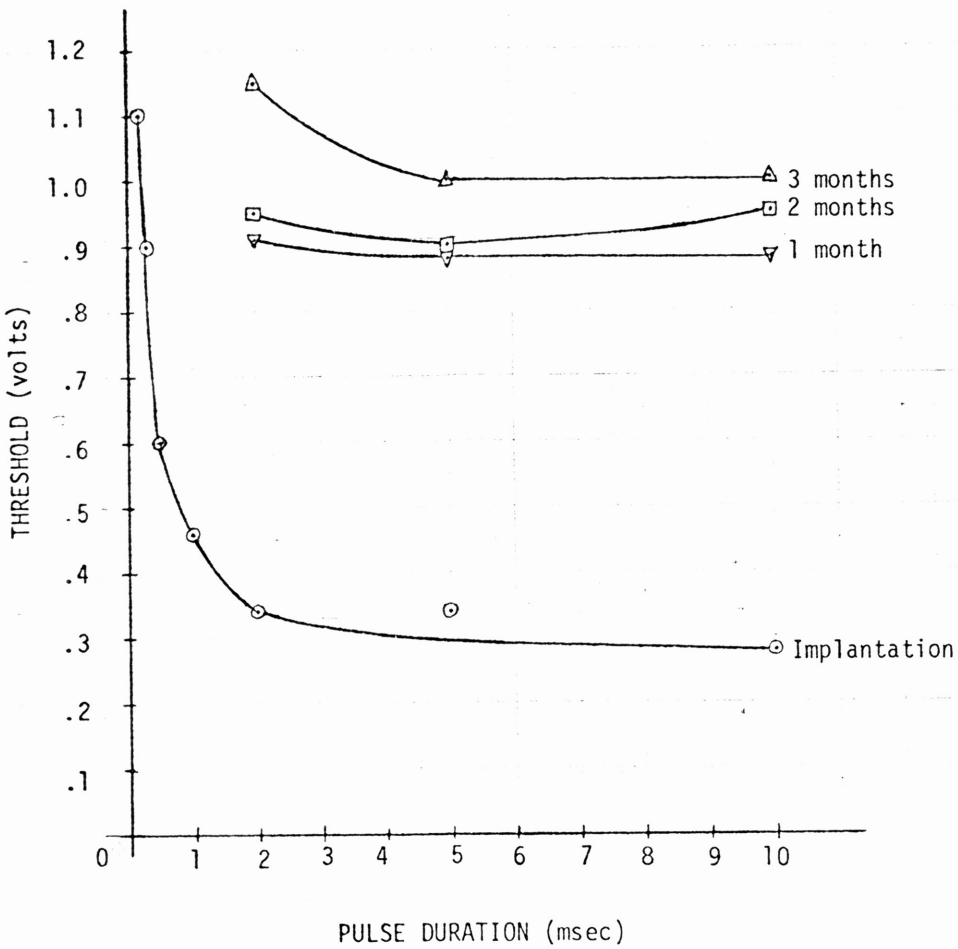


FIGURE 11

Results of second phase

("Val") Dog 2

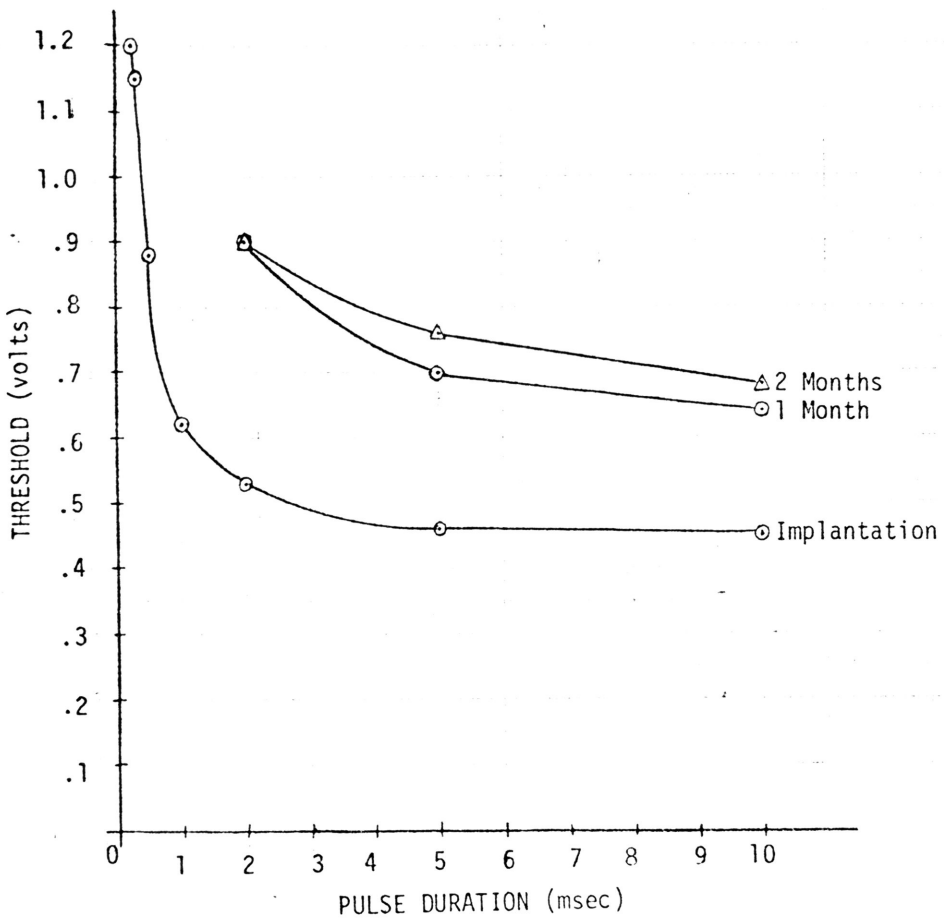


FIGURE 11

V. DISCUSSION AND CONCLUSIONS

Because of the large number of neutrophils observed of histologic evaluation of the electrode-tissue interface, the results from the first study are inconclusive. This study did, however, serve as a valuable learning experience on the part of the investigators in the following ways:

1. The susceptibility of the lead to failure was greatly increased by transcutaneous passage. The dogs chewed or scratched at the leads causing breakage of these assemblies.
2. The transcutaneous passage of the lead served as a channel from the skin surface to the heart for bacterial infection. This was indicated by the localized infection observed surrounding the implanted electrode and at the skin surface. Difficulty encountered with bandaging the neck and thorax of dogs made other efforts toward protection against infection virtually useless.
3. The threshold measurement data indicated the need for the establishment of more stringent measurement controls.

This study stimulated the desire to establish a more controlled experimental approach in order to determine the biocompatibility of the electrode with respect to fibrous tissue growth. This resulted in the second phase of experimentation.

The modifcations made on the basis of the experience gained in the first phase are the following:

1. The electrode and lead were totally implanted.
2. Continuous stimulation of cardiac muscle was employed.
3. Threshold was evaluated at monthly intervals.

Results from the second phase of experimentation showed the characteristic rising thresholds reported by other investigators. Histologic evaluation of the tissues surrounding the implant have not been performed and therefore the cause for the rising thresholds can not be determined. Nevertheless, on the basis of the observed rising thresholds, conclusions can be speculated with regard to possible outcomes of the histological evaluation; by first considering that no scar tissue encapsulation of the electrode is observed and, second, that scar tissue is observed.

If no fibrous encapsulation of the electrode is observed it could be concluded that rising thresholds are not a function of the fibrous tissue growth as was theorized. In this case rising thresholds would probably be due to polarization effects or reduced excitability of the myocardium.

If, on the other hand, fibrous encapsulation is ocurring around the carbon-coated electrode only speculation could be made concerning the relationships among biocompatibility, artifical stimulation, and scar tissue growth. Futher studies would then have to be performed before conclusions could be drawn. Since previous biocompatibility studies of passive LTI carbon implants have shown minimal scar tissue reaction, the scaring reaction would most likely be the result of either artifical stimulation or mechanical injury.

It is well recognized in implant studies that injury to tissues surrounding implants can be caused by mechanically induced stresses.[7,8] To test whether this is ocurring in the pacemaker system the following series of investigations is suggested:

1. Implantation of leadless carbon-coated electrodes in the hearts of laboratory animals in order to evaluate the effects of

mechanical action of the heart alone on the electrode.

2. Implantation of electrode-lead assemblies in laboratory animals' hearts to test the effects of mechanical stresses induced by heart motion, respiration, and general body motion.
3. Implantation of non-stimulating (passive) electrode-lead-generator systems, with the generator being in a stable position unable to migrate, to test the effects of mechanical stresses due to stresses developed in the lead between the electrode and generator.

It has been proposed by Klafter, et al. that the relatively high energy stimuli applied to the heart by artifical pacemakers causes insult to the tissue to the tissue around the electrode and enhances the fibrous tissue response.[30] There is no data to date, however, to support this hypothesis. To test the effects of the stimulation on fibrous tissue growth this study could be repeated with one modification. Threshold could be checked as a function of time following implantation for both anactive stimulating condition and a passive non-stimulating condition. This modification in experimental design calls for totally implantable systems. The measuring circuits and conditions, electrodes and leads used in both cases would have to be identical. Along with the information regarding the threshold obtained in this type of study, and the known biocompatibility of carbonaceous materials, the results of the combined series of suggested investigations would give the information needed to assess the reason(s) for fibrous tissue growth and rising thresholds observed in cardiac pacemaker systems.

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