Two to Three Years of Failure-free Testing of a Rechargeable Pacemaker in Experimental Complete Heart Block

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SUMMARY Six hermetically sealed single cell rechargeable mercury-zinc pacemakers (B.T.) that will run continuously for over 4 years between rechargings have paced dogs with complete heart block for 2 to 3 years. To maintain full cell capacity (over 1,000 mA hours) requires recharging for from 2–3 min/day to 60 to 80 hr once every 4 years, with any variation between these extremes being acceptable. Six realtime bench tests continue after over 7 years and accelerated tests have simulated a minimum of 50 years continuous pacing. Battery voltage is assessed by direct telemetry, eliminating the risk of patient intrinsic rhythm-pacemaker competition which is present with all current indirect (stimulation rate change) battery assessment techniques. The B.T. is an excellent 4–5 year primary pacemaker, fully rechargeable after several 4 year periods of battery rundown. A clinical test series has been initiated.

Since the first use of cardiac pacemakers, the objective has been to develop long-lived units. Alternatives to nonrechargeable mercury-zinc cells have included nuclear, solid state, and rechargeable power sources. Nuclear pacemakers do have a potential ten year life; however they are expensive and have a radiation hazard. Although studies are preliminary, solid state power sources (for example lithium iodide) appear to be reliable and long lasting; however, their low energy density necessitates a relatively large pacemaker to produce a unit lasting five to ten years. Early attempts by several investigators, and some recent efforts, utilized rechargeable nickel-cadmium cells and at present there is a commercially available rechargeable nickel-cadmium pacemaker. Basic disadvantages of the nickel-cadmium cells include a low initial capacity (less than 200 mA hours), high self-discharge rate, the necessity for frequent recharging for relatively long periods of time (90 min), and failure after a relatively short period of time (6–8 weeks) if not recharged. In addition, some investigators have felt that patients would object to recharging a pacemaker, as this act "reminds them of their disability" but this has been shown to be an unfounded concern, even with rechargeable units that have the limitations of a nickel-cadmium cell. Anxiety regarding the prospect of the next replacement operation, which often begins soon after implantation of a primary (nonrechargeable) pacemaker, is a far greater and more oppressive patient concern.

The objective of this study was to test in animals, a low drain, hermetically sealed, long lived, rechargeable pacemaker capable of years of pacing between rechargings and capable of a total life in excess of 20 years, so as to essentially eliminate reoperation for pacemaker pulse generator replacement. Marked reduction of recharging time was also sought to decrease patient inconvenience and increase physician acceptance. Using a high capacity rechargeable silver modified mercuric oxide-zinc cell and low current drain, low voltage circuitry, sealed in a hermetic container achieved all design objectives. This report details the results of chronic rechargeable pacemaker implantation in a series of dogs with surgically-induced complete heart block.

Methods

The pacemakers used in this study were of the fixed rate (asynchronous) type, although ventricular programmed units have also been developed. All electronic components were hermetically sealed in a seamless, stainless steel container, 3 by 1.5 by 0.5 inches including the connector (fig. 1). The rechargeable mercury-zinc cell and the induction recharging coil were hermetically sealed within a separate internal stainless steel case to prevent exposure of the other electronic components to either cell electrolyte or hydrogen.
gas. Through a right thoracotomy, six dogs had complete heart block surgically induced by a closed technique involving formalin injection into the bundle of His. Cathodal pacing was accomplished using a small surface area, ball tip electrode placed intramyocardially through a small stab wound in the epicardium of the left ventricle. A rechargeable pacemaker was then connected to the lead and implanted subcutaneously over the right lateral thoracic wall. The stainless steel case served as anode. The output of the pacemaker into a 1,000 ohm impedance was 4 V and 4 mA. Total cell drain, including a telemetry circuit, was 25 μA.

Recharging was accomplished through the intact skin, by placing an induction coil over the implanted pacemaker. To maintain the cell at full capacity (over 1,000 mA hours), recharging for 2 to 3 min of each day for pacing was necessary. Therefore during the first year following implantation, each of the six pacemakers was recharged once a week for 20 min. During the second year of the study, weekly recharging was continued in three dogs; the fourth was recharged once per month, the fifth once semiannually, while charging was discontinued in the sixth dog, to be resumed only after four years of continuous pacing. In previous body temperature bench tests of 13 pacemakers utilizing the rechargeable mercury-zinc cell, the average rundown time prior to requiring recharging was over 4½ years.

Each pacemaker had a built-in telemetry system which enables an operator (patient, technician or physician) to make simultaneous noninvasive percutaneous measurements of the cell voltage and stimulation rate of the totally implanted unit. In the six chronic animal studies, these measurements were taken immediately, six hours, and seven days after recharging, during the first year following implantation of each pacemaker. Weekly determinations of battery voltage and stimulation rate were continued in the three animals placed on an infrequent recharging schedule after the first year.

The rechargeable, 1,000 mA hour, silver-modified, mercuric oxide-zinc power source was approximately 36 mm in diameter and 6 mm thick. The chemistry of this cell is similar to that of the primary mercuric oxide-zinc cell (RM1) now used in over 90% of clinical pacemakers. The addition of 27% metallic silver to the mercuric oxide in the positive electrode serves three functions: 1) it aids in electronic conduction; 2) it prevents the formation of metallic mercury globules, assuring uniform recharging; and 3) it permits a rapid rise in cell voltage when all the mercury has been reconverted to mercuric oxide at the completion of recharging. Also, to aid in conduction during recharging, 7½% silver and 2½% epoxy are mixed with the zinc in the negative electrode of the rechargeable cell.

The rapid rise in cell voltage at the completion of recharging assists in the prevention of overcharging. While we have repeatedly overcharged new silver modified, mercuric oxide-zinc cells for up to 70 hours without any acute deleterious effect, and have then had the cells function normally or supranormally in accelerated tests (repeatedly cycled with initial capacities significantly in excess of 1000 mA hours), the effect of overcharging on function years after cell manufacture has not been determined. Thus until the late effects of this potentially abusive form of treatment are known, overcharging is best avoided.

Results

The six mercury-zinc rechargeable pacemakers have been chronically implanted in dogs with complete heart block for a total of over 160 months of continuous real time pacing, with no cell or circuit failures. The longest implanted pacemaker has been functioning for over 2½ years. There were no significant rate changes (73 plus or minus 2

**Figure 1.** The hermetically sealed rechargeable mercury-zinc pacemaker.

**Figure 2.** Mean pacemaker stimulation (heart) rates during the first year of implantation of six rechargeable mercury-zinc pacemakers in dogs with surgically induced complete heart block.
beats/min) as the pacemaker cell discharged and was recharged (fig. 2). Figure 3 shows cell voltages (mean plus or minus standard error) obtained from the six pacemakers during the first twelve months post implantation. The “super voltages” recorded immediately after recharging each pacemaker decreased to 1.52 V 6 hr after recharging was discontinued, due to rapid discharge of the silver in the positive electrode. After 7 days of pacing, the pacemaker cell voltages had dropped only an additional 0.08 V to a mean of 1.44 V. The variable initial voltage readings are not significantly different from the long-term readings and are related to early aging or breaking in of the electronic components, warming of the cell and electronics to body temperature following implantation, and to the cell becoming completely charged after one to two years on the shelf prior to implantation.

At present, the three animals being recharged weekly have shown no significant change in implanted cell voltages or stimulation (heart) rates over the entire period of study. In the pacemaker which has not been recharged for over a year, battery voltage has decreased less than 0.04 V. In the unit being recharged only once every six months, the cell voltage has decreased only 0.02 V from 1.40 to 1.38 V during the three completed six month cycles thus far examined. In the unit which is being recharged at monthly intervals, the cell voltages remain between 1.38 and 1.40 V during the weekly telemetry readings.

Discussion

The present study documents the continuous biological function of six rechargeable silver-modified, mercuric oxide-zinc pacemakers for from two to three years each, with no loss of cell capacity. The applicability of a wide range of recharging schedules has also been demonstrated.

We have previously studied a rechargeable pacemaker powered by the silver-modified, mercuric oxide-zinc cell in a series of simulated biological tests and have shown it to be superior to any power source now in use, including lithium, nuclear and rechargeable nickle-cadmium batteries.

Accelerated tests in vitro have demonstrated that this rechargeable cell, with its high initial capacity and minimal cell discharge, is capable of long life, even when placed under severe stress. The high initial capacity (over 1,000 mA hours) and low energy drain allow recharging schedules to be established to fit individual patient needs. While some patients may prefer to recharge 2-3 min daily (about as much time as it takes to brush your teeth) others may prefer 15 to 20 min weekly, 80 min monthly, 8 hr semi-annually, or 60 to 80 hr once every four years.

The longer the period between pacemaker recharging, the greater becomes the “energy debt” and the time required to achieve full recharging increases. While total rundown of any rechargeable cell would be expected to damage it, periodically recharged mercury-zinc cells that were initially totally discharged, continue to function after over 7 years actual time.

In addition, accelerated tests have shown this cell capable of a minimum of six complete total discharge cycles without loss of capacity; this is equivalent to 24 years of continuous cardiac pacing without pacemaker power source replacement. A rechargeable mercury-zinc pacemaker is ideally suited to patients with high stimulation threshold requirements, as more frequent recharging of a high output unit is far superior to frequent (often yearly at present) pulse generator replacement surgery with standard primary pacemakers, or to frequent prolonged recharging, as would be required with rechargeable nickle-cadmium pacemakers.

With the rechargeable pacemaker used in this study, direct readout of both the cell voltage and heart rate by telemetry eliminates the necessity for indirect monitoring techniques that utilize stimulation rate changes to determine pacemaker status. Thus demand units do not have to be converted to the fixed rate mode to assess battery voltage, as with all presently available remote transtelephonic or office/clinic monitoring techniques.

Therefore the attendant risk of pacemaker-natural rhythm competition, the problem the demand pacemaker was originally designed to circumvent, is eliminated with our unit. The telemetry system used in the six rechargeable animal units is already in use for telephone monitoring of the first four human patients to receive the rechargeable mercury-zinc pacemaker.

The rechargeable silver-modified, mercuric oxide-zinc pacemaker has been documented to have the capacity to consistently function (six of six units), continuously in a biological environment (dogs with complete heart block) for two to three years without loss of cell capacity, and without circuit or hermetic seal failures, with all units continuing to pace normally. In simulated biological tests at 100°F, continuous actual time pacing for over seven years has been consistently demonstrated (six of six units). In accelerated tests at body temperature, the mercury-zinc cell has consistently simulated continuous pacing for a minimum of 50 years (120 of 120 cells). No other currently available pacemaker power source can approach these achievements and clinical testing of the rechargeable silver-modified, mercuric oxide-zinc pacemaker has been initiated.
Noninvasive Evaluation of Regional Myocardial Perfusion in 112 Patients using a Mobile Scintillation Camera and Intravenous Nitrogen-13 Labeled Ammonia

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SUMMARY  The short half-life positron emitter $^{13}$N, as labeled ammonia ($^{13}$NH$_3$), was evaluated as a myocardial imaging agent. Regional myocardial uptake of $^{13}$NH$_3$ correlated with the distribution of labeled microspheres in experimental myocardial infarction. Using intravenous $^{13}$NH$_3$, myocardial scintigraphy was performed in 85 cardiac patients and 27 normal subjects. Ninety-five scintigrams were suitable for analysis. Eighteen of 24 normal subjects had homogeneous myocardial images; six had inhomogeneous images attributable to early technical problems. Perfusion defects were observed in the scintigrams of 82% (57/65) of patients with coronary artery disease, being most common in patients with myocardial infarction (27/28). Six sequential studies showed changes in perfusion consistent with the clinical course of each patient. Scintigraphic abnormalities were also observed in 4/6 patients with valvular heart disease.

$^{13}$NH$_3$ myocardial scintigraphy is a valid and sensitive method of assessing regional myocardial perfusion and is especially useful for sequential imaging at short intervals.

THE INTRODUCTION OF RADIOPHARMACEUTICALS which localize in the myocardium at levels dependent upon regional blood flow has made possible the noninvasive assessment of regional myocardial perfusion using a scintillation camera. Experience with this new technique was initially limited by production difficulties and unsatisfactory imaging characteristics of the available radio-nuclides.

In 1971 Hunter and Monahan observed myocardial uptake of $^{15}$N-labeled ammonia during animal metabolic studies and suggested that it might be a useful agent for imaging the myocardium. Subsequently, myocardial uptake of $^{15}$NH$_4^+$ was demonstrated in man. Because of the advantages of using a short half-life isotope we evaluated $^{15}$N-labeled ammonia as a myocardial imaging agent for the assessment of regional myocardial perfusion. The relationship between myocardial uptake of $^{15}$NH$_3$ and regional perfusion was determined in animal studies, following which a clinical imaging study using this agent was carried out in 112 patients to determine the myocardial scintigraphic patterns in the normal subject and in patients with cardiovascular disease.

References
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