

Electrical Stimulation of Excitable Tissue by Radio-Frequency Transmission *

WILLIAM W. L. GLENN, M.D., JOHN H. HAGEMAN, M.D.,** ALEXANDER MAURO, Ph.D.,
LAWRENCE EISENBERG, M.E.E., STEVENSON FLANIGAN, M.D.,
MARVIN HARVARD, M.D.

*From the Department of Surgery, Yale University School of Medicine, New Haven, Connecticut and
The Rockefeller Institute for Medical Research, New York, N. Y.*

THE STIMULATION of tissue by electricity has been the subject of study for nearly 200 years. Only recently, however, has serious consideration been given to the use of electrical stimulation as a permanent substitute for an impaired tissue function.

Two methods for applying an electrical stimulus to tissue are available: the direct method, in which the electrical power source is in direct wire contact with the tissue, a method with which we are not concerned in this paper, and the indirect method, in which the power source is at a distance from the tissue being stimulated. The basis for this latter technic is the well-known phenomenon of electromagnetic induction first described by Faraday in 1831. A time-varying current is passed through a primary coil and, in accordance with Faraday's laws, a time-varying potential is produced across the terminals of a secondary coil.

The inductive method was first used to stimulate tissue in 1933.^{4, 8, 16, 17} One or more primary coils surrounded an animal cage and activated one or more secondary coils buried within the body of an animal which was allowed free movement about the cage during stimulation. Although effective, this method has certain disadvantages, namely, the very large currents re-

quired in the primary coil and the limited wave form arising from the secondary coil.

A more sophisticated version of the induction method became available with the adaptation to inductive stimulation of high frequency radio waves by Newman *et al.*¹⁹ in 1937. Several years later, Grieg and Ritchie,¹¹ Mauro *et al.*,¹⁸ and Lafferty and Ferrell¹² also reported success in the remote stimulation of tissue by radio-frequency transmission. By changing the number of radio-frequency cycles transmitted (effective pulse width) and their amplitude, one gets, in effect, the equivalent at the tissue of a fluctuating d.c. pulse, with a duration and amplitude totally controllable from outside the body. An infinite variety of wave forms (envelopes) can thus be created which accounts for the versatility and adaptability of the radio-frequency method of stimulation (Fig. 1).

The present investigation is concerned with remote stimulation by radio-frequency induction of the heart, the diaphragm and the urinary bladder. In the case of the heart, we now have an extensive experience with the use of radio-frequency pacemaking and it is possible to make definite recommendations concerning its clinical application. The development of a radio-frequency electrophrenic respirator and bladder stimulator, or what might be called a micturitor, by Hageman, Flanigan and co-workers is still in the early stage and we can offer here only a preliminary report. A more de-

* Presented before the American Surgical Association, Hot Springs, Virginia, April 1-3, 1964.

** USPHS Fellow in Cardiovascular Surgery.

Supported by USPHS Grant 04651 and The Victoria Foundation.

tailed report will be published elsewhere.^{9, 13}

One major drawback to long-term electrical stimulation of tissue has been breakage of the electrode wires. We have therefore devoted much time to developing a fatigue-resistant electrode, which is reported in this paper in detail.

The Cardiac Pacemaker

Verzeano *et al.*²⁵ in 1958 investigated radio-frequency stimulation of the heart, using a conventional 200-watt radio transmitter and a large transmitting antenna surrounding the bottom of the cage (non-metallic) of a dog in whose chest was buried a small secondary, or receiving coil tuned to approximately the same frequency as the antenna. Also in 1958, Glenn and Mauro began investigating radio-frequency stimulation of the heart. They used a technique similar to that used earlier by Mauro to stimulate the motor cortex of the Rhesus monkey. The transmitting and receiving coils were closely coupled by being laid one over the other, separated only by the intact integument. Both the primary and secondary coils were tuned precisely to the carrier frequency. In their first experiments and clinical tests reported in 1959.¹⁰ Glenn and Mauro employed a vacuum tube, line powered radio wave transmitter. Portability, enabling the unit to be carried easily by the patient or the experimental animal, was achieved through the use of transistors in a design by Eisenberg *et al.*⁷

The block diagram (Fig. 2) illustrates

RADIO-FREQUENCY WAVE FORMS

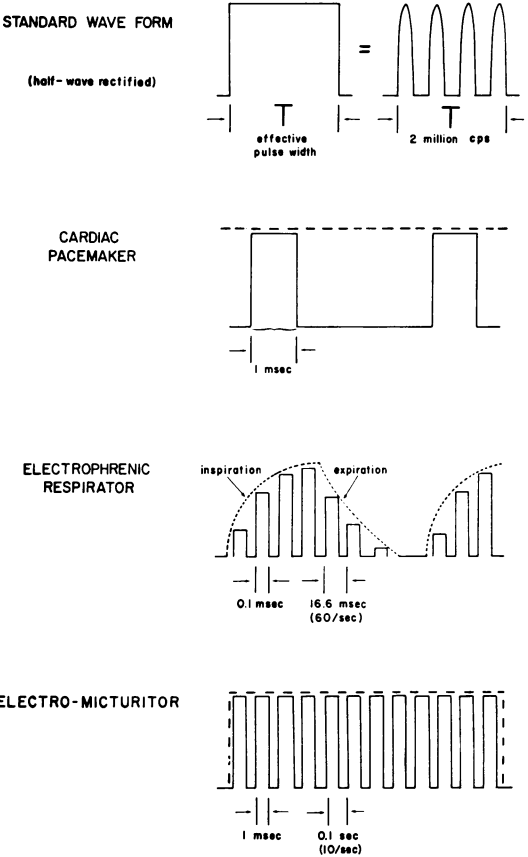
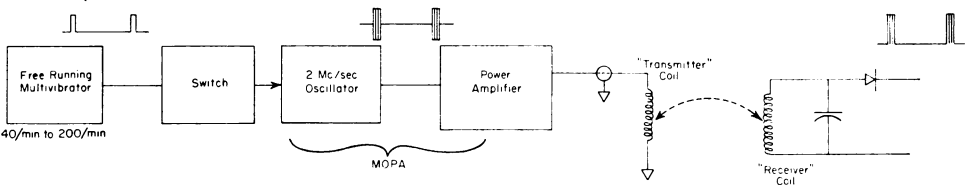


FIG. 1. Radio-frequency wave forms. It is apparent that by varying the effective pulse width and the amplitude of the R-F waves almost any wave contour can be created to meet the needs of the individual situation.

the fundamentals of the design of the transistorized radio-frequency cardiac pacemaker. The electronic circuits of the R-F transmitter, transmitting antenna and receiver are described in detail in a report by



Block Diagram of Pacemaker

FIG. 2. Block diagram of the R-F cardiopacemaker. (From Eisenberg *et al.*)

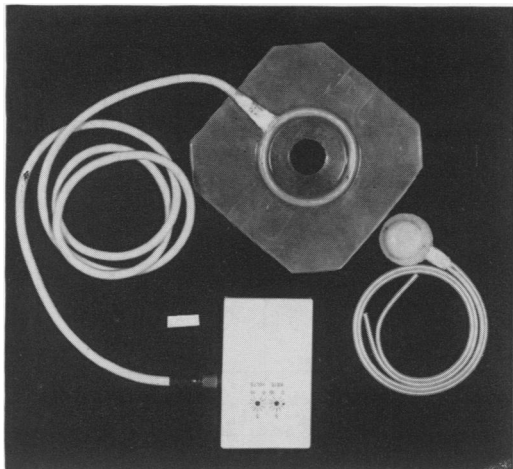


FIG. 3. The R-F cardiac pacemaker unit consisting of a transmitter which broadcasts a one millisecond impulse via the transmitting antenna coil. In use, the antenna patch is cemented to the patient's skin over the receiving coil, which is implanted subcutaneously. The attached electrode wires conduct the impulse to the heart.

Eisenberg *et al.*⁷ The pulse rate is determined by a free-running oscillator (an astable multivibrator). The radio-frequency master oscillator is normally inoperative, cut off by means of a switching transistor. The latter is turned on periodically at the pulse rate by the output of the free-running oscillator. Typically, the master oscillator is gated on for one millisecond out of each second and transmits a two-megacycle per second R-F burst to the power amplifier. The amplified signal is then inductively coupled to the receiver coil which is placed beneath the skin. The rectified radio-frequency waves are then applied to the myocardium through electrodes.

The design of the present model * (Fig. 3) is the result of the accumulated experience of five years of experimental and clinical trial with the radio-frequency technic. The electronic design and parts have undergone exhaustive testing and are, we believe, the most reliable available. The new unit is of rugged construction and

able to withstand complete immersion in water and a drop of at least ten feet to a cement floor without damage. The present battery uses a sodium hydroxide activator with a normal 500 ma. hour capacity which, assuming normal loading, is expected to last approximately ten months. (The mean threshold to stimulation of the myocardium with the radio-frequency unit, using Teflon coated multi-stranded stainless steel electrodes, has been determined in the experimental animal to be 1.4 ma. at 0.35 v. expressed as the unidirectional square wave equivalent.²⁸

Clinical Data. The first radio-frequency pacemaker receiver and electrodes were implanted in a patient with uncontrollable Stokes-Adams attacks on January 27, 1958.¹⁰ After operation the heart responded well to the pacemaker, but on the 21st postoperative day it stopped suddenly. Several days later the receiver was removed from the subcutaneous tissue and the bare end of the indifferent silver electrode was found broken at its junction with the Teflon insulation. (In retrospect, it is believed that the break was the result of electrolysis of the silver electrode.) Since that time 21 additional patients with complete heart block and Stokes-Adams attacks have had a radio-frequency pacemaker receiver and electrode implanted. In the majority of cases arteriosclerotic heart disease with or without myocardial infarction has also been present. In two patients, both children, the heart block was surgically induced; in one young adult it was presumably caused by a lupus erythematosus, and in another adult it was of congenital origin with Stokes-Adams attacks appearing for the first time at age 44. The patients ranged in age from 11 to 84 years, with an average age of 64.8 years.

The present status of these patients is as follows: Eleven patients are alive and have been paced continuously for four to 33 months. One patient is being paced 44 months after the initial receiver implant

* Manufactured by Airborne Instruments Laboratories, Division of Cutler Hammer, Deer Park, Long Island, N. Y.

though pacing was interrupted for a 21-month interval because of electrode wire breakage. One patient is alive but no longer requires electrical pacing. Ten patients are dead. In three of these, the electrode wires broke, the patients refused reoperation and died in Stokes-Adams attacks. Four patients died suddenly one to three months after pacemaker implantation: in two of these ventricular fibrillation may have been the cause of death as previous episodes of such fibrillation had been observed in both patients during illnesses: in the other two the cause of sudden death was not determined. The remaining three deaths were unrelated to the heart disease.

The management of patients with heart block followed in our clinic has been described elsewhere.²⁹ Prior to and during operation we prefer to control the patient's heart rate with a transvenous catheter electrode inserted into the outflow tract of the right ventricle. The heart is exposed through a left fifth intercostal space incision. The radio wave receiver is implanted in a small pocket made in the subcutaneous tissue usually about two to three inches below the thoracotomy incision in the mid-axillary line. It is important that the receiver lie no lower than the level of the eighth rib to allow ample space above the costal margin for attaching the antenna to the skin. Occasionally, in the female with large breasts the receiver must be placed in the midline overlying the sternum. The attached electrodes are brought through a subcutaneous tunnel into the thoracotomy incision and inserted into the myocardium with the aid of a small tracheostomy tube (Fig. 4). Two direct-wire electrodes are also inserted in the wall of the ventricle (after which the catheter electrode is removed), where they remain to allow control of the heart rate in the postoperative period until the wounds are healed sufficiently, and to allow application, with comfort, of the transmitting antenna over the receiver coil.

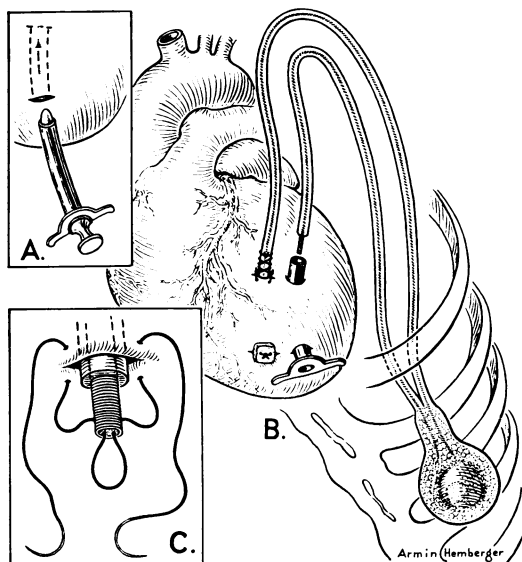


FIG. 4. Method of inserting electrodes into the myocardium.

Care of the radio-frequency unit by patient involves periodic 1) cleaning of the antenna applied to the skin, 2) replacement of the entire antenna assembly, and 3) replacement of the batteries supplying power to the radio-wave transmitter.

Cleaning of the Antenna Applied to the Skin. We have usually employed a Silastic-encapsulated antenna, held to the skin with ileostomy cement. Generally the antenna becomes loose after ten days to two weeks and must be removed completely from the skin with an appropriate solvent. The skin underlying the antenna is washed with warm soapy water and dried. Residual adhesive on the surface is removed with solvent before application of a new coat. An occasional patient develops asystole when the antenna is lifted off the skin. In such cases the antenna and skin must be cleaned and the adhesive reapplied without interfering with the coupling of the antenna and receiver. There may be a skin reaction beneath the antenna. In two cases a rash developed, from miliaria in one and local moniliasis in the other, several months after affixture of a latex-covered antenna to the

skin with ileostomy cement. In neither case was the reaction severe enough to preclude the use of a trimmed-down antenna patch. This was fixed to the skin with 3M * tape until the wounds healed under appropriate local treatment, at which time the antenna was reapplied without further trouble. Should skin reaction be a continuing problem, it may be possible to fix the antenna in a close-fitting garment to be worn by the patient.

Replacement of the Antenna. The normal life of the R-F antenna has been approximately three months. Wire fatigue and breakage has been a common cause of failure. When the antenna fails, it is exchanged for a new one. A recent modification in antenna design may prolong the useful life, but as a practical matter it is wise to have a second antenna on hand.

Replacement of the Batteries. In earlier models of the R-F pacemaker the useful battery life (with a stimulus rate of 60 to 70 and the threshold to stimulation minimal) was only five to ten days. With the present model, the battery pack used has a useful life of at least two months and in the immediate future a battery pack with a useful life of at least ten months will be available. The battery pack should be changed in the doctor's office.

The Electrode Problem

The initial success of pacing by radio-frequency transmission and by battery-powered implantable pacemakers has been marred by frequent interruption of electrical stimulation due to electrode breakage. Since the need for long-term electrical pacing of the heart was first recognized there has been a determined search for a fatigue-resistant, non-irritating electrode wire for implantation in the heart and other tissues. Single or multi-stranded wires of silver, gold, platinum and steel

have been tried but have shown an unpredictable response to stress when implanted in the body, with early breakage a recurring problem. Chardack *et al.*,⁵ has reported a Silastic-covered, coiled platinum-iridium electrode having greater fatigue resistance than an uncoiled electrode. The electrode has been adapted for use in several implantable pacemakers and in the radio-frequency receiver. However, in one of our patients, breakage of the wire occurred ten months after implantation in the heart and in a second patient four months after implantation. We therefore searched for an electrode wire having the desirable qualities of coiled platinum-iridium but greater resistance to fatigue. Tests in this laboratory on electrode materials have demonstrated that the single-strand Elgiloy wire encased in silicone rubber † had a high degree of resistance to breakage²⁴ but a considerably greater electrical resistance than a platinum wire. We investigated then a four-stranded coiled wire †† because it would have less electrical resistance and provide a margin of safety in the event of electrode breakage.

Elgiloy, a cobalt-nickel alloy, is a product of the Elgin National Watch Company. It is fatigue resistant, is readily coiled, and is one of the most corrosion-resistant metals known. Wible, *et al.* in 1957²⁷ used Elgiloy to make a prosthetic mitral and aortic valve: following implantation in the wall of the heart and aorta, it showed no evidence of tissue reaction to the metal. We implanted Elgiloy wire fragments in the anterior chamber of the eye in 12 guinea pigs and in the rectus muscle of five rabbits, and similar fragments of platinum-iridium in another 12 guinea pig eyes and the op-

† Silicone rubber manufactured by Dow Corning: We are grateful to Mr. Silas Braley for his generous assistance in all of this work.

†† In an independent investigation N. Braunschweig and A. G. Morrow are investigating a Silastic-enclosed, single coiled Elgiloy wire electrode.

* Minnesota Mining and Manufacturing Company.

posite rectus muscle of the rabbits. When the animals were sacrificed six weeks to nine months later there was no difference in the reaction of the tissues to the two substances.

Fatigue Tests. The fatigue testing machine was designed to subject the electrode to flex stress simulating that encountered on entering the heart. The electrode was clamped between two metal plates meeting at right angles, the horizontal plate fixed and the vertical oscillating at 1,800 cycles/min. The deflection of the vertical oscillation could be varied from 0.130" to 1.25". All specimens of wire were tested nearly simultaneously. The results, shown in Table 1, demonstrate the superiority as regards fatigue resistance of Elgiloy wire as compared with platinum-iridium wire.* All wires were embedded in Silastic rubber.

Electrolysis Tests. Although there has been no failure of the Elgiloy electrodes to date, electrode breakage due to electrolysis of the anode electrode may occur at some time in the future.^{6, 20} In recent tests, electrodes of Elgiloy wires were immersed in a physiologic saline solution and subjected to the passage of a constant current of 100 m.a. for three hours. The anode electrode lost nearly half of its weight by dissolution in this time but the cathode electrode was unscathed. Similar studies were done on pure platinum wire which was totally unaffected. We appreciate the fact that the current used in these experiments is far in excess of any encountered within the body, but it is important to note that even with such high currents the Elgiloy cathode electrode showed no sign of dissolution.

On the basis of these observations we believe that the ideal electrode system for long-term stimulation of tissue should include a stimulating cathode electrode of

four-stranded, coiled Silastic encased Elgiloy wires and indifferent anode electrode (implanted in the subcutaneous tissue) of a plate of pure platinum.

Clinical Application. To date five patients with Stokes-Adams attacks resistant to medical management have been treated with the radio-frequency pacemaker using the Elgiloy wire (0.006" Diameter) four-stranded helical coil electrodes.** Twenty-six days to six months after implantation of the electrodes there have been no complications.

The exact threshold current value was not determined in patients having an Elgiloy electrode, but it was always within the lower range of the radio-frequency transmitter. Except for one patient in whom there was a temporary rise in threshold between the fourth and twelfth postoperative days, the threshold current showed only minimal variation over a six-month period.

Phrenic Nerve Stimulation

It has been known for many years that certain patients with bulbar poliomyelitis have intact phrenic nerves which can be stimulated electrically. It is possible that these patients could be removed from an artificial lung if a satisfactory technic for chronic stimulation of the phrenic nerve were developed. Patients with chronic emphysema would likewise benefit from artificial stimulation of the phrenic nerve. Further, phrenic stimulation would aid patients in respiratory difficulty following operation, the need for which aid has become increasingly apparent in recent years, particularly with the advent of open-heart surgery.

Some years ago Sarnoff and colleagues made a detailed study of electrical stimulation of the phrenic nerve.^{21, 22, 23, 26} Based on the fact that the response of a muscle to stimulation of its nerve is in direct propor-

* Tests performed by Associated Spring Corporation, Bristol, Connecticut. We are grateful to Mr. William Johnson for his important technical assistance in these studies.

** Manufactured by Associated Spring Corporation, Bristol, Connecticut.

tion to the intensity of the stimulus, they reasoned that by varying the intensity, duration and rate of a stimulus applied to the phrenic nerve they could produce a reasonable imitation of normal respiration. They called the technic *electrophrenic respiration*.

Their experiments were done on the phrenic nerve in the neck. Generally the nerve was isolated, the bare end of a silver wire was placed around the nerve and the insulated part of the wire brought to the exterior to be connected to the stimulator. In one experiment, on a cat, Sarnoff used

TABLE 1. *Electrode Fatigue Tests**

Vertical Deflection (inches)	Millions of Cycles		Comments
	Platinum-Iridium	Elgiloy	
0.130	8.00 (broken)	56.00 (2 samples intact)	Bare helical coil.
0.130	83.00 (intact)	56.00 (2 samples intact)	Silastic tubing insulation.
0.250	0.200 (broken)	2.00 (5 samples intact)	Silastic tubing insulation.
	2.80 (4 samples intact)		
0.500	0.067 (broken)	2.00 (5 samples intact)	Silastic tubing insulation
	0.096 (broken)		
	0.096 (3 samples intact)		
1.000	0.024 (2 samples broken)	3.50 (insulation broken)	Silastic tubing insulation, Elgiloy broken after total of 6.0 million cycles.
		10.0 (2 samples intact)	Silastic tubing insulation.
		**10.0 (3 samples intact)	Silastic tubing insulation.
	0.268 (broken)	7.65 (intact)	***Silastic tubing filled with Silastic # 30885 gel.
	0.268 (broken)	7.65 (2 samples, Silastic tubing broken)	Silastic tubing filled with # 182 resin.
	0.093 (broken)	10.0 (intact)	Silastic tubing filled with Medical Adhesive.
1.250		*2.2 (broken)	Silastic tubing insulation
		*4.4 (broken)	
		*4.9 (broken)	
		4.3 (broken)	Silastic tubing insulation.
		8.8 (broken)	
		7.0 (Silastic tubing broken)	
		7.0 (2 samples intact)	Silastic tubing filled with RTV # 382.
		7.0 (intact)	Silastic tubing filled with Silastic # 30885 gel.
		7.64 (intact)	
		7.0 (Silastic tubing broken)	Silastic tubing filled with # 182 resin.
		7.5 (intact)	Silastic tubing filled with Medical Adhesive.

* Performed by M. Wm. Johnson.

** Heat treated at 900°F for 5 hours.

*** Filling of the core of the tubing was suggested by Morrow's experience with a coil of single strand Elgiloy.

The platinum-iridium electrode was a single strand of 0.010" diameter wire tightly wound into a helical coil and placed into a loosely fitting Silastic tubing 0.057" ID by 0.110" OD. The Elgiloy electrode consists of four parallel strands of 0.006" Elgiloy wire tightly wound into a helical coil and placed into a Silastic tubing 0.078 ID by 0.125" OD.

the induction method of Chaffee and Light^{4, 16} for remote control stimulation of the phrenic nerve, but believed this method suffered from having to have a large secondary coil implanted. (Also, as we have pointed out, with the induction coil method there is a definite limitation to the wave forms possible as compared to those possible with radio-frequency.)

These studies established several important facts: 1) That stimulation of the phrenic nerve at a rate slightly higher than the animal's own rate (and minute volume) caused the animal to cease promptly spontaneous respiratory activity; 2) Adequate ventilation was readily accomplished in the absence of spontaneous respiration by sub-maximal stimulation of one phrenic nerve; 3) Electrical stimulation of one phrenic nerve caused inhibition of the opposite diaphragm; 4) The result of the animal studies were confirmed in man.

Sarnoff developed an ingenious thimble technic that enabled him to stimulate the phrenic nerve in the neck through the intact skin and apply electrophrenic respiration in several clinical cases of ventilatory insufficiency.

Electrophrenic respiration never enjoyed much popularity as a therapeutic modality, probably because of the technical difficulty of applying it to patients. The advent of a practical method of remote stimulation of the heart by radio-frequency waves has caused us to renew our interest in electrophrenic respiration and to investigate the application of newer technics of induction to radio-frequency.

In the majority of experiments on dogs we have used a bipolar electrode (Fig. 5) of Elgiloy encased in Silastic, implanted in one phrenic nerve through the open chest, the attached radio-frequency receiver implanted in the chest wall beneath the skin and subcutaneous tissue. When the chest wounds have healed a week to ten days postoperatively, stimulation of the phrenic nerve by radio-frequency induction has

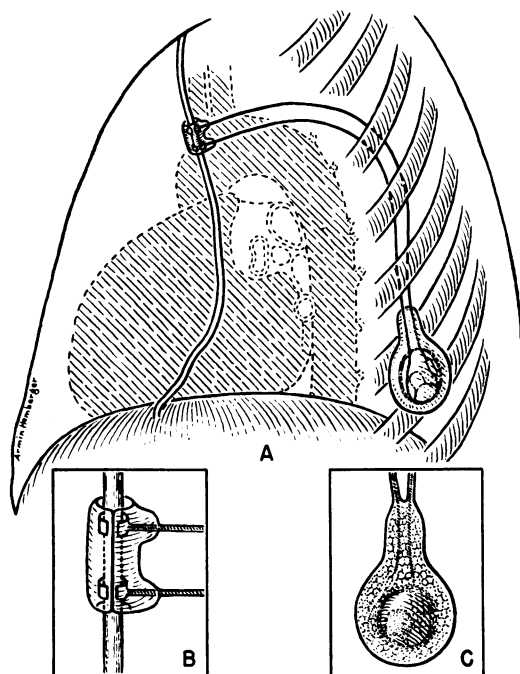


FIG. 5. Radio-frequency electrophrenic respirator: application of bipolar electrode to phrenic nerve.

been established through the application of the antenna coil to the skin overlying the receiver coil. The radio-frequency transmitter, designed for the cardiac pacemaker, was modified to provide a wave form that would stimulate normal inspiration and expiration.

Stimulation of the phrenic nerve by radio-frequency induction has been carried out in dogs at weekly intervals for as long as six months. A rise in threshold to stimulation has been observed in most animals, but in a few the threshold has remained low and contraction of the diaphragm could be elicited with one to two R-F volts.* Experiments are now in progress to determine the cause of the threshold rise and ways of preventing it.

* The stimulating current to the primary coil was a pulse of 0.13 milliseconds duration with a peak amplitude of 800 amperes. The resulting secondary current was a damped sinusoid wave with an 0.2 millisecond period and a peak amplitude of 10 milliamperes.

(R-F) ELECTROPHRENIC RESPIRATION

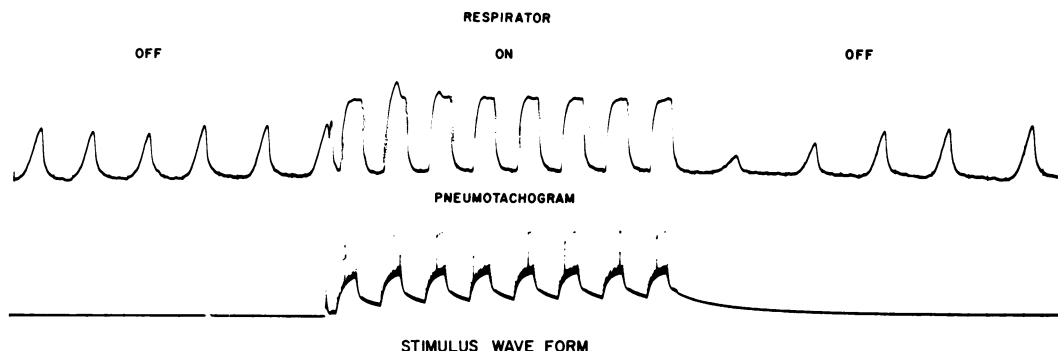


FIG. 6. Wave form of the R-F electrophrenic respirator. This form may be easily varied to mimic the normal respiratory curve more accurately.

The findings of Sarnoff, with respect to the prompt cessation of spontaneous respiration on starting electrical stimulation of the phrenic nerve, have been confirmed (Fig. 6). Ciné-fluoroscopy revealed an actively moving diaphragm on the stimulated side and an immobile diaphragm on the contralateral side. It was not unusual, however, for some intercostal activity to continue after the start of electrophrenic respirations, and in the animal made hypoxic by breathing nitrogen, spontaneous respiration promptly resumed in competition with electrophrenic respiration. It was also demonstrated that ventilation adequate to reduce the carbon-dioxide tension and raise the oxygen tension in the arterial blood of the heavily sedated animal could be provided by stimulation of a single phrenic nerve (Table 2).

Recently a portable transistorized radio-frequency electrophrenic respirator has been developed, and used continuously in a dog for 12 days (Fig. 7). It will now be possible to carry on continuous electrophrenic respirations and study the local and systemic effects of prolonged phrenic nerve stimulation. In one patient undergoing thoracotomy for aortic and mitral valve disease, electrophrenic respirations by R-F induction were established temporarily by applying monopolar electrodes

to the right phrenic nerve and the indifferent electrode to the chest wall. It was apparent that the success of this technic depended on maintenance of constant contact between the nerve and the electrode, and adequate safeguards to prevent leakage of the current to adjacent tissues.

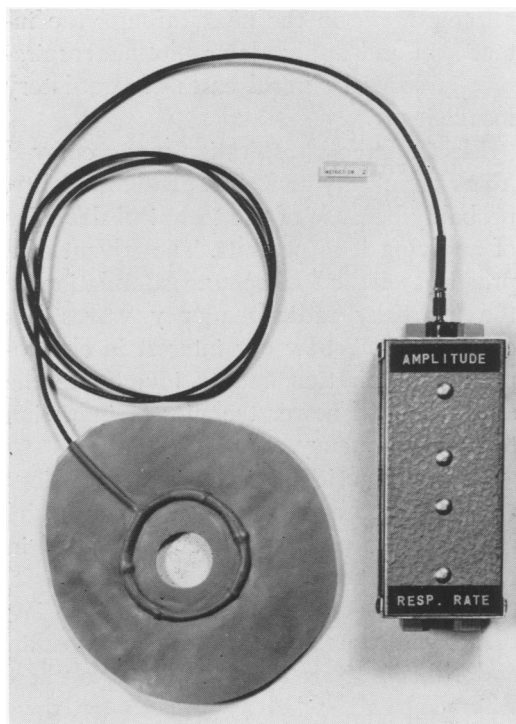


FIG. 7. Electrophrenic respirator: transistorized transmitter and transmitter antenna.

TABLE 2. *Electrophrenic Respirations in Dog Whose Spontaneous Respirations were Severely Depressed by Nembutal Anesthesia*

Experiment 292 wt 13 K							
Respiration	Rate min	Tidal Vol cc	Minute Vol cc	pCO ₂ mm Hg	pO ₂ mm Hg	O ₂ Sat vol %	pH
Spontaneous	7	280	1960	36.6	72.0	92.2	7.33
Electrophrenic	40	160	6400	30.4	94.0	96.3	7.40

Emptying of the Urinary Bladder by Electrical Stimulation

One of the most serious complications of paraplegia is urinary infection secondary to repeated catheterization to empty the urinary bladder. If a way could be found to empty the bladder at regular intervals without catheterization the lives of many patients with neurogenic urinary bladder retention could be prolonged. A number of investigators have already made important contributions to our knowledge of electrical stimulation of the bladder wall, by means of wires leading from the bladder to the exterior, or by simple induction, or by radio-frequency.^{1, 2, 3, 12, 14} From these studies it was found that the bladder could be evacuated completely by stimulation of the bladder wall provided the nerve supply (pudental) to the external urethral sphincter is cut. Pain in the pelvis and contraction of other skeletal muscles in and around the pelvis may be a serious attendant problem. It is not known at the present time which method of emptying the bladder is superior—stimulation of the bladder wall, of the vesical nerves or of the sacral nerve roots.

Preliminary studies in the laboratory demonstrated that in the paraplegic animal with the pudental nerve cut the bladder could be emptied by stimulation through shielded bipolar electrodes of either the sacral nerve roots (S2 or S3, bilaterally) or of the fundus branch of vesical nerves bilaterally, or of the bladder wall bilaterally through shielded disc electrodes applied in the region of the vesical nerves (Fig. 8, 9). The transmitter used was identical to that of the radio-frequency cardiac pacemaker

except that the number of pulses per second were increased from one to ten. The stimulus was usually applied for 20 to 30 seconds, or longer when needed to completely empty the bladder. When the sacral nerve roots or the vesical nerves were stimulated 1 to 5 R-F volts were required, whereas when the bladder wall was stimulated 5 to 20 R-F volts were required. There was usually less spread of the impulse to adjacent structures with direct bladder stimulation than with nerve root stimulation. The rise in intravesical pressure was about the same with both sacral root and vesical muscle stimulation (Fig. 10).

It is clear from the limited clinical ex-

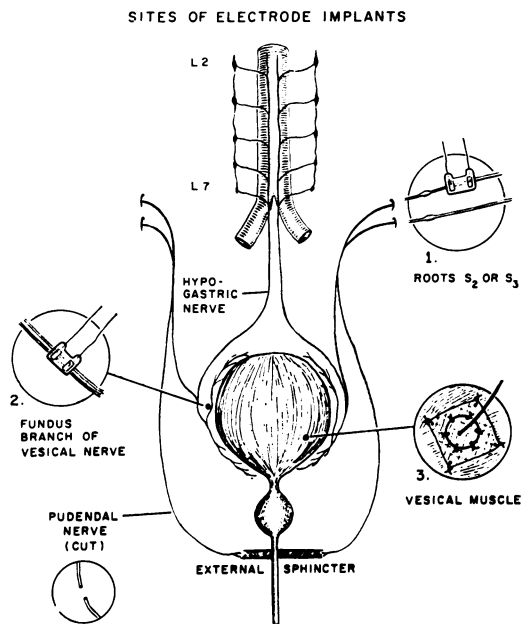


FIG. 8. Bladder stimulator. Electrode implant sites. All symbols imply that bilateral procedures were done.

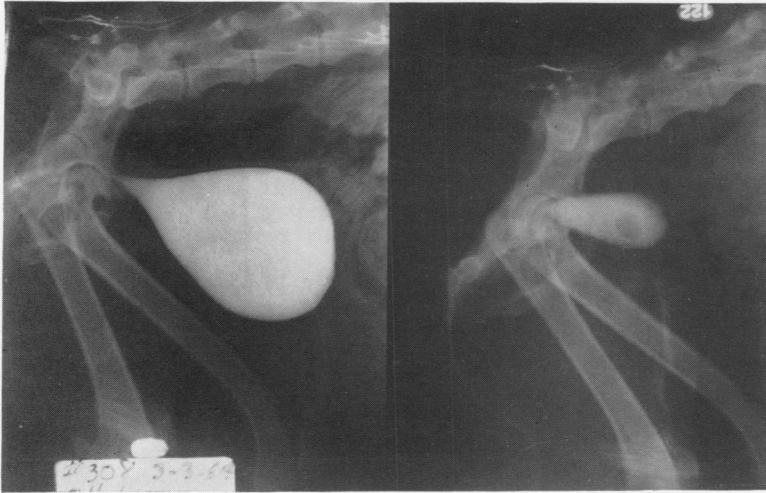


FIG. 9. Electro-mic-turition: emptying of bladder following sacral nerve root stimulation. The pudendal nerve has been cut. Similar results were found when the vesical nerve or the vesical muscle were stimulated.

perience of others with electrical stimulation of the bladder that a number of problems remain to be solved before this becomes acceptable therapy. To mention a few of the more obvious problems: the development of a bladder refractive to complete emptying by electrical stimulation; the difficulty of determining the best site for electrical stimulation; the prevalence of spread of the impulse to adjacent muscles and nerve structures; and the occurrence of pain on stimulation. Despite these obstacles to clinical application, recent experience in the experimental laboratory using radio-frequency induction is sufficiently encouraging to warrant continued intensive investigation in the hope that a satisfactory technic can be developed.

Discussion

Experience with the radio-frequency cardiac pacemaker during the past five years has pointed up its several advantages as compared to other implantable pacemakers.

External control of impulse rate and amplitude. In several patients this advantage has been a critical one. An increase in rate of only 10 impulses per minute was all that was required to bring back under pacemaker control the paced heart that had developed multifocal ventricular beats during the induction of anesthesia for a hernia

repair. Control of multifocal ventricular beats by increasing the pacemaker rate was possible in another patient who was febrile at the time. In other patients subjected to stress the pacemaker rate was deliberately increased in anticipation of the need for a greater cardiac output. In a few patients there was a rise in the threshold of stimulation and in such cases, because of the external location of the controls, it was a simple matter to increase the amplitude of the impulses.

External location of the batteries. This eliminates the need for reoperation when the battery fails or is worn out.

Simplicity of the implanted part of the unit. The implanted receiver consists of only a coil, a condenser and a diode to rectify the pulse wave. These are all firmly potted in Silastic rubber and have never been a cause of unit failure. Owing to the close coupling of the antenna and receiver there is virtually no danger of the receiver's picking up stray two megacycle impulses.

Ease of discontinuing stimulation (without compromising future use of the implanted components.) It may be desirable to discontinue pacing the heart should the block disappear, as has happened in three patients—one four months after surgical induction of the heart block, one a few days following resection of an aneurysm of a

left ventricle and one about two months after a myocardial infarction. Patients should have been free of block for at least three months before electrical pacing is discontinued.

In addition to those advantages applicable to cardiac pacemaking, another major advantage of stimulation by radio waves is the ease with which the amplitude of the radio waves and the effective pulse width can be modified to produce virtually any wave form that may be suitable for the stimulation of a particular organ or tissue.

The disadvantages of the radio-frequency unit are few, and generally unimportant. Skin irritation from the antenna has been seen occasionally but in our experience has been easily controlled. Decoupling of the antenna, resulting in loss of the pacemaker impulse, has never occurred accidentally except with breakage of the antenna cable, an accident that should be preventable. Cleaning of the skin and Silastic antenna shield can be accomplished with only momentary decoupling of the unit. The care of the external unit is soon mastered by the patient and his family and appears to them as no disadvantage when they understand the advantages of external control of the pacemaker and power source and the freedom from further operative procedures to replace a worn out unit.

Summary

Electrical stimulation of tissue by radio-frequency induction has been investigated in the laboratory and clinic for the past five years. Technics have been developed for the stimulation, by remote control, of the heart, the phrenic nerve, and the urinary bladder. In the course of these investigations, an electrode has been developed with remarkable fatigue-resistance properties.

Clinical experience in 22 patients with complete heart block who were treated with the pacemaker has pointed up the advantages of radio-frequency induction: 1) external control of the rate and amplitude of the impulse, 2) external control of power source, 3) simplicity of the im-

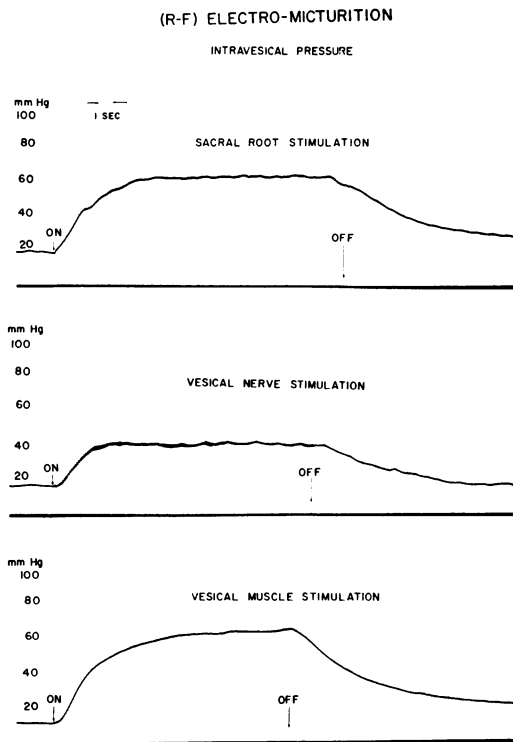


FIG. 10. Bladder contraction following submaximal stimulation of the sacral or vesical nerves or the bladder wall directly in the paraplegic animal. The bladder was filled with 5 cc. of saline solution per kilogram body weight before these studies were done.

planted components, and 4) ease of discontinuing stimulation without compromising the implantable components.

The variety of wave forms readily created with radio-frequency makes this technic adaptable to an infinite number of stimulation requirements.

Addendum

Recent experience has shown that when the monopolar myocardial electrode is used, electrocauterization will induce ventricular fibrillation. For this and several other reasons, bipolar electrodes are preferred. We therefore are investigating the use of bipolar Elgiloy myocardial electrodes with platinum tips.

References

1. Boyce, W. H., J. E. Lathem and L. H. Hunt: Research Related to the Development of an Artificial Electrical Stimulator for the Paralyzed Human Bladder: A Review. *J. Urol.*, 91:41, 1964.

2. Bradley, W. E., L. E. Wittmers, S. N. Chou and L. A. French: Use of a Radio Transmitter Receiver Unit for the Treatment of Neurogenic Bladder. A Preliminary Report. *J. Neurosurg.*, 19:782, 1962.
3. Bradley, W. E., S. N. Chou and L. A. French: Further Experience with the Radio Transmitter Receiver Unit for the Neurogenic Bladder. *J. Neurosurg.* 20:953, 1963.
4. Chaffee, E. L. and R. U. Light: Method for Remote Control of Electrical Stimulation of the Nervous System. *Yale J. Biol. Med.*, 7:83, and 7:441, 1934.
5. Chardack, W. M., A. A. Gage and W. Greatbatch: Correction of Complete Heart Block by a Self-contained and Subcutaneously Implanted Pacemaker. Clinical Experience with 15 Patients. *J. Thor. Cardiovascular Surg.*, 42:814, 1961.
6. Dittmar, H. A., G. Friese and E. Holder: Erfahrungen über die Langfristige Elektrische Reizung des Menschlichen Herzens. *Z. Kreislaufforsch.*, 51:66, 1083, 1962.
7. Eisenberg, L., A. Mauro and W. W. L. Glenn: Transistorized Pacemaker for Remote Stimulation of the Heart by Radio-frequency Transmission. *IRE Transact. Bio-Med. Elect.*, 8:253, 1961.
8. Fender, F. A.: Method for Prolonged Stimulation of the Nervous System. *Am. J. Physiol.*, 116:47, 1936.
9. Flanagan, S., J. H. Hageman, W. D. Widmann, W. W. L. Glenn, L. Eisenberg, A. Mauro and B. M. Harvard: Stimulation of the Paraplegic Bladder by Radio-frequency (R-F) Transmission. Submitted for publication.
10. Glenn, W. W. L., A. Mauro, E. Longo, P. H. Lavietes and F. J. Mackay: Remote Stimulation of the Heart by Radiofrequency Transmission. Clinical Application to a Patient with Stokes-Adams Syndrome. *New Engl. J. Med.*, 261:948, 1959.
11. Greig, J. and A. Ritchie: Simple Apparatus for Remote Nerve Stimulation in the Unanesthetized Animal. *J. Physiol.*, 103:8P, 1944 and 1945.
12. Habib, H. N.: Neural Trigger Points for Evacuation of Neurogenic Bladder by Electro-stimulation. *Surg. Forum*, 14:489, 1963.
13. Hageman, J. H., L. Eisenberg, W. W. L. Glenn and A. Mauro: Electrophrenic Respiration by Radio-frequency (R-F) Transmission. Submitted for publication.
14. Kantrowitz, A. and M. Schamaun: Bladder Evacuation in Paraplegic Dogs by Direct Electric Stimulation. *J.A.M.A.*, 187: 595, 1964.
15. Lafferty, J. M. and J. J. Ferrell: Technique for Chronic Remote Nerve Stimulation. *Science*, 110:140, 1949.
16. Light, R. U. and E. L. Chaffee: Electrical Excitation of Nervous System—Introducing a New Principle: Remote Control: Preliminary Report. *Science*, 79:299, 1934.
17. Loucks, R. B.: Preliminary Report of a Technique for Stimulation or Destruction of Tissues Beneath the Integument and Establishing of Conditioned Reactions with Faradization of Cerebral Cortex. *J. Comp. Psychol.*, 16:439, 1933.
18. Mauro, A., P. D. Wall, L. M. Davey and A. M. Scher: Central Nervous Stimulation by Implanted High Frequency Receiver. *Fed. Proc.*, 9:86, 1950.
19. Newman, H. W., F. A. Fender and W. Saunders: High Frequency Transmission of Stimulating Impulses. *Surg.*, 2:359, 1937.
20. Rowley, B. A.: Electrolysis—A Factor in Cardiac Pacemaker Electrode Failure. *IEEE Transact. Bio-Med. Elect.*, 10:176, 1963.
21. Sarnoff, S. J., E. Hardenbergh and J. L. Whittenberger: Electrophrenic Respiration. *Am. J. Physiol.*, 155:1, 1948.
22. Sarnoff, S. J., J. L. Whittenberger and E. Hardenbergh: Electrophrenic Respiration. III. Mechanism of the Inhibition of Spontaneous Respiration. *Am. J. Physiol.*, 155: 203, 1948.
23. Sarnoff, S. J., E. A. Gaensler and J. V. Maloney, Jr.: Electrophrenic Respiration. IV. The Effectiveness of Contralateral Ventilation During Activity of One Phrenic Nerve. *J. Thorac. Surg.*, 19:6, 1950.
24. Toole, A. L., E. Longo, A. Mauro and W. W. L. Glenn: Prolonged Electrical Stimulation of the Heart. *Surg. Forum*, 11:247, 1960.
25. Verzeano, M., R. C. Webb, Jr. and M. Kelly: Radio Control of Ventricular Contraction in Experimental Heart Block. *Science*, 128: 1003, 1958.
26. Whittenberger, J. L., S. J. Sarnoff and E. Hardenbergh: Electrophrenic Respiration. II. Its Use in Man. *J. Clin. Invest.*, 28:124, 1949.
27. Wible, J. H., L. F. Jacobson, P. J. Jordan, Jr. and C. G. Johnston: Spring Valve Prosthesis for the Control of Valvular Insufficiency. *Surg. Forum*, 7:230, 1956.
28. Widmann, W. D., L. Eisenberg, S. Levitsky, A. Mauro and W. W. L. Glenn: Ventricular Fibrillation Complicating Electrical Pacemaking: A Comparison of Direct Current and Radio-frequency Cardiac Pacemaker Stimulation. *Surg. Forum*, 14:260, 1963.
29. Widmann, W. D., W. W. L. Glenn, L. Eisenberg and A. Mauro: Radiofrequency Cardiac Pacemaker. *Ann. N. Y. Acad. Sc.*, III:992, 1964.