Radio Frequency Stimulation: A Research and Clinical Tool

Stimulation of excitable tissues by radio frequency induction methods is discussed.

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Deliberate electrical stimulation of excitable tissues began with Galvani (*1*) in the late 18th century and continued through the 19th and 20th centuries, with the techniques gradually increasing in degree of sophistication. Most experimenters of the past (and even current workers) used wires which extended through the body wall to the tissue, with an outside stimulator serving as the electrical source. The *clinical* use of electrical stimulation techniques is comparatively recent and has achieved its most widespread application in the last 5 years in the case of the cardiac pacemaker.

The induction technique—that is, the transfer of electrical energy through the intact body wall by electromagnetic induction—is not a new one. This technique is based on Faraday's law—namely, that if the amplitude of the current flowing through a (primary) coil varies with time, it will produce a voltage whose amplitude varies with time in an adjacent or secondary coil. As far back as the middle of the 19th century physiologists employed the *inductorium* or induction coil in their work. But it was not until 1933 and 1934 that a technique based on induction between a primary coil outside the body and a secondary coil within the body was developed, as reported by Loucks (*1a*), Chaffee and Light (*2*), and Fender and Scott (*3*).

In 1937 a more efficient variation of the induction method, called the radio frequency inductive method, was used by Newman and his coworkers (*4*). This method was then adopted by other physiologists and, more recently (*5, 6*), by clinicians for cardiac stimulation and other applications (*7*).

The radio frequency technique differs from the pure induction coil technique in that the use of tuned primary and secondary coils makes it possible to develop a stimulating waveform with whatever amplitude envelope one desires (Fig. 1). Consequently, this technique has the flexibility needed for stimulating different types of tissue. In a unit currently being manufactured, the life of the external battery is typically 9 months to a year, and the battery is small (see Fig. 2). The only components implanted in the body, in addition to the secondary coil, are a single capacitor and a silicon diode.

A single cycle of the radio frequency current normally used for tissue stimulation is of far too brief duration to produce stimulation. Typically this time duration is from 0.1 to 2.0 microseconds. But the insertion of a diode rectifier in one of the output leads results in half-wave rectified currents which cumulatively, cycle by cycle, produce a stimulating effect roughly equivalent to that resulting from a rectangular-shaped pulse of current whose amplitude is one-third the peak radio frequency amplitude.

Circuit Aspects of Radio Frequency Induction Stimulation

One of the important aspects of the radio frequency induction technique is the ease with which stimuli can be programmed. A schematic diagram of the programming circuitry is shown in Fig. 3. The lower section of the diagram illustrates the transistorized stimulating section. A free-running, low-frequency oscillator (blocking oscillator) determines the pulse rate and the pulse width. A transistor switch is turned on during the pulse interval, and this permits a radio frequency oscillator, normally turned off, to oscillate for the duration of the pulse. This radio frequency current is then amplified by a power amplifier which feeds the radio frequency signals to the transmitter coil. The radio frequency field is then coupled electromagnetically through the subject's intact skin to the receiver coil, is rectified, and is applied to the tissue.

The upper portion of Fig. 3 illustrates the modulator section. This section provides the modulating wave-

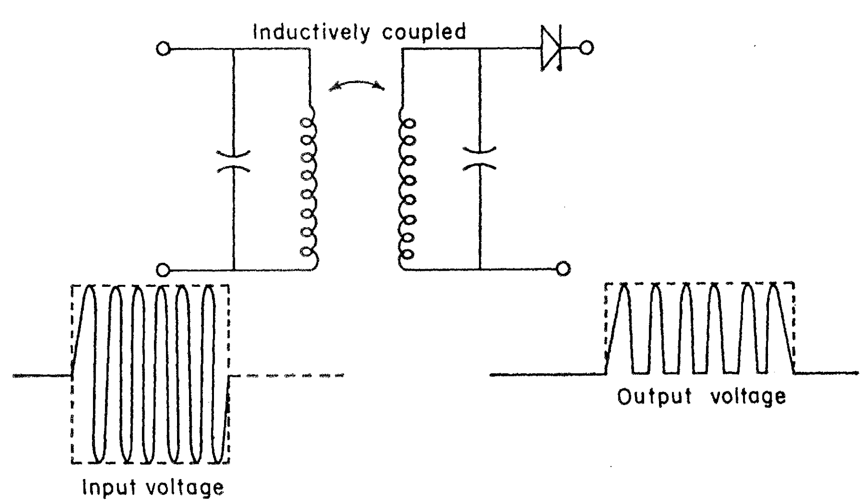

Fig. 1. Inductively coupled tuned primary and tuned secondary coils with rectifying diode. The input radio frequency signal is reproduced in form at the output of the tuned secondary coil with the negative-going half cycles removed by the diode.

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form which determines the shape of the envelope of the radio frequency amplitude. In stimulating the phrenic nerve, for example, to produce a continuously varying undulating contraction of the innervated diaphragmatic musculature, one requires a series of stimuli whose amplitude follows a continuously undulating variation with time.

Flexibility of programming is achieved by using two packages. One package produces the basic radio frequency current; the other package produces the desired modulating envelope. Clearly, one can adapt these packages (particularly in the case of experimentation with animals) for the diverse types of stimulation programs required (Fig. 4).

Practical Difficulties of Radio Frequency Stimulation

The most important problem is one which is common to all techniques of tissue stimulation, the problem of electrode breakage. Particularly in the case of cardiac stimulation, where the electrode wires are flexed some 60 to 80 times per minute, continuously, the mechanical stress on the wires is great. Further, there is an electrolytic decomposition of the electrode material which gradually erodes the electrode at the site of stimulation unless chemically stable materials such as platinum are used. As a result of our own experience, we discontinued using electrode wires made of 147 strands of Surgaloy wire (stainless steel), which broke repeatedly, and tried electrodes of Chardack's design (*8*), a helically wound platinum-iridium wire encased in Silastic rubber. This electrode, while electrolytically stable, did not, in our experience, have sufficiently long mechanical life, although it was considerably better in this respect than the stainless steel stranded wire.

Electrodes of single coiled Elgalloy wire (*9*) have been investigated by N. Braunwald and A. G. Morrow of the National Institutes of Health (*10*). These were demonstrated to be better able to withstand mechanical stress than either the Surgaloy or the Chardack electrodes. We have, in turn, developed our own four-stranded, helically coiled Elgalloy electrode, and we are currently using it clinically. However, we have found that Elgalloy disintegrates rapidly in Ringer's solution when current is passed through the electrode wires. Since only the positive electrode is affected, we have retained the negative electrode of the mechanically superior Elgalloy, using for the positive or indifferent electrode a short length of helically coiled platinum-iridium wire. One investigator, Camilli (*6*), has attacked this problem of electrode breakage in the course of cardiac pacing by suturing the secondary coil assembly directly to the heart and using an external radio frequency transmitting unit of much higher pow-

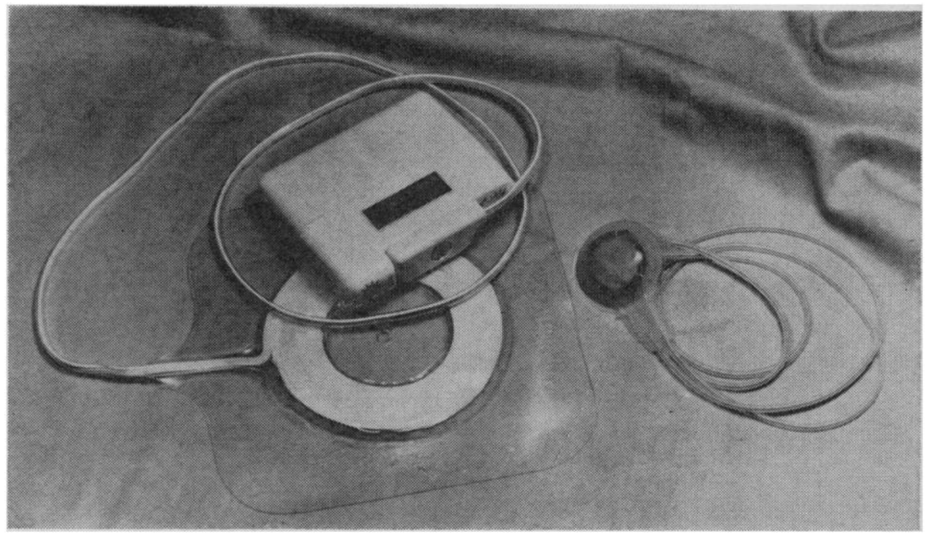


Fig. 2. Radio frequency cardiac pacemaker for clinical use, currently manufactured by Airborne Instrument Laboratories, a division of Cutler Hammer Corporation, showing (left) the transmitting coil and (right) the receiver coil assembly and electrodes, which are implanted in the body. Operating frequency, 2 Mc/sec.

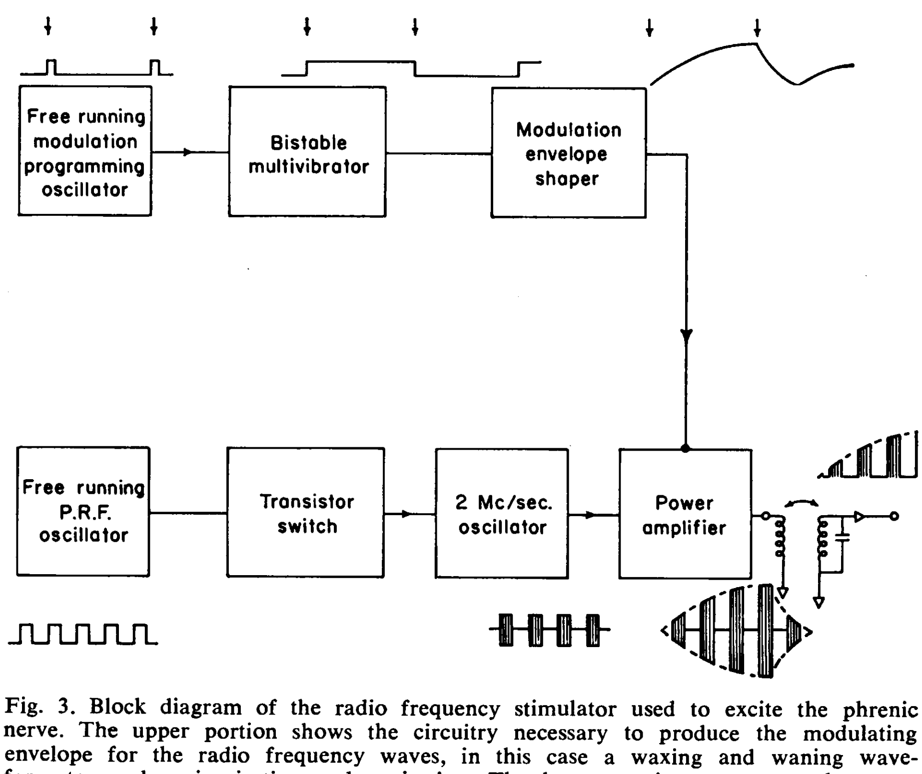


Fig. 3. Block diagram of the radio frequency stimulator used to excite the phrenic nerve. The upper portion shows the circuitry necessary to produce the modulating envelope for the radio frequency waves, in this case a waxing and waning waveform to produce inspiration and expiration. The lower portion represents the generating module of the stimulator. The radio frequency oscillator is turned on for 100-μsec intervals 60 times per second. The modulating waveform is supplied to the transistorized power amplifier and causes the amplitude of the radio frequency waves to follow a similar modulation with time. The stimulus is then coupled from the transmitting or antenna coil to the implanted receiver coil, and the rectified radio frequency waves are applied to the nerve.

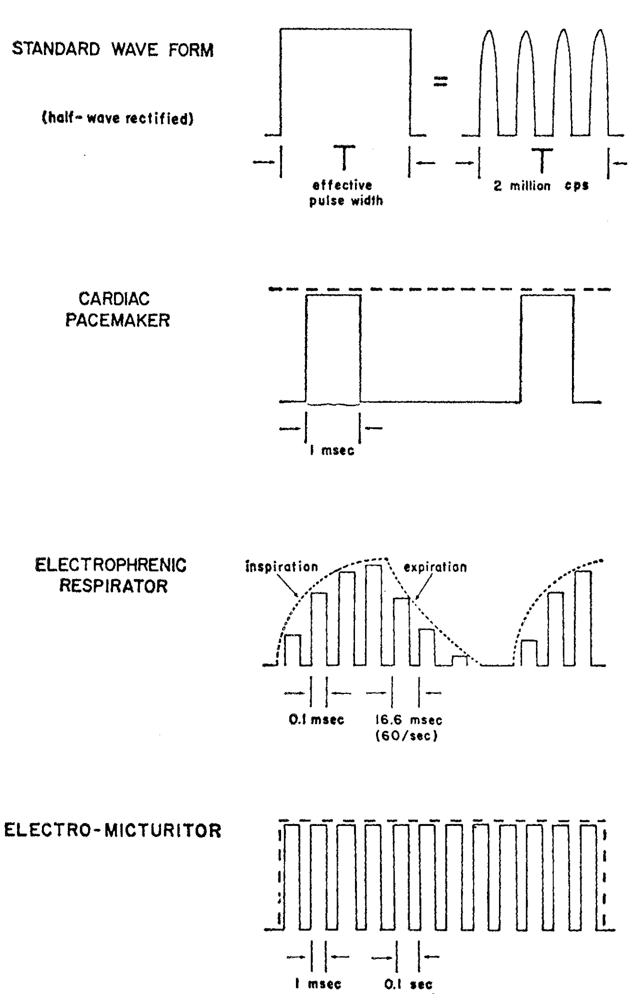
er than would otherwise be required.

The remaining problems have to do with the external or transmitting unit. They are the necessities of insuring against mechanical breakage of the transmitting-coil connecting leads, of making the unit shock-proof, in case it is dropped to a concrete floor, waterproofing it against accidental immersion, and of making it insensitive to changes in temperature over a specified range. We now believe that these problems have been overcome in a prototype commercial unit being manufactured by the Airborne Electronic Laboratories. In clinical situations there is a psychological problem, too, which is difficult to evaluate. In the case of the cardiac pacemaker, some physicians apparently prefer to use a unit which is totally within the body, without accessible controls. They feel that, with an external unit, the patient's preoccupation with the unit may be such as to outweigh the advantages. Our own experience indicates that less than 10 percent of the patients are sufficiently preoccupied with the external unit to make its use a problem.

Clinical and Laboratory Applications

Cardiac pacing. The advent of open heart surgery and the problems of surgically induced heart block (that is, cutting of the "conducting" path between the atria and the ventricles of the heart so that they contract at rates which are not synchronous) resulted in renewed clinical interest in electrical stimulation of the myocardium. Wierich and his associates (*11*) in 1957 reported the first clinical use of the "myocardial electrode" to stimulate the myocardium of a patient with induced heart block. A wire was led through the chest wall and sutured to the myocardium, an indifferent electrode being placed on the skin. In January 1959 the radio frequency inductive approach, as developed in 1948 (*12*) for cortical stimulation, was resurrected to effect stimulation of the myocardium in a patient with Stokes-Adams disease who did not respond to treatment with drugs (*13*). (In Stokes-Adams disease, heart block—that is, disassociation of contraction rates between the atria and the ventricles of the heart—is accompanied by seizures in the course of which the heart may go into standstill. Fainting, sometimes death, ensues.)

Since January 1959 we have used the radio frequency inductive technique for cardiac pacing in 26 patients. The average age of our patients is 62.2 years, but two were children under 15. In one of our patients the technique has been used continuously for over 36 months. In addition to the advantages already described, there have been certain clinical benefits, due to the external control over pulse rate and amplitude of the stimulus which the instrumentation provides. We have, for example, been able to discontinue stimulation, when this was desirable, without compromising future use of the implanted components. In one case in which the technique was used, surgically induced heart block disappeared 4 months after the operation and did not reappear. In this patient, electrical cardiac pacing was discontinued so that there would be no competition between the natural pacing mechanism and the external, electrical pacer. We



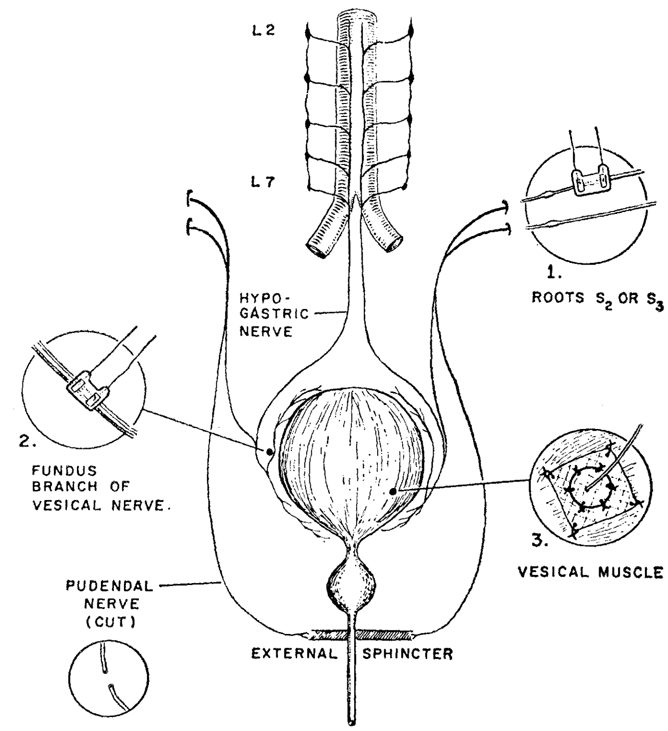


Fig. 4 (left). Modulating waveforms required for stimulating different tissues. The myocardium is stimulated by a 1-msec burst of radio frequency (rectified) waves of constant amplitude, recurring 60 to 70 times per second. For the phrenic nerve, an attempt is made to produce a contraction and relaxation of the diaphragm which is similar to normal respiration. In bladder stimulation a burst of waves of constant amplitude, lasting for several seconds, is used. Fig. 5 (above). Sites of electrode implants for producing contraction of the urinary bladder and voiding of urine. (Site 1) Roots of the sacral nerve; (site 2) the fundus branch of the vesical nerve; (site 3) the bladder wall in the region of the vesical nerves.

have reason to believe (*14*) that such competition under certain conditions might induce ventricular fibrillation.

In at least half our patients, symptoms of heart block have disappeared, at least temporarily. Since the receiver coil remains in place under the skin, pacing may be resumed at any time by repositioning the antenna coil over the receiver coil. In addition, we have lowered the venous pressure in a critically ill patient to the optimum level through external control of the cardiac rate. We have also been able to assist patients by increasing the heart rate during episodes of fever. [It is interesting to note that even the original induction coil method is currently being used for cardiac pacing (*15*).]

Bladder stimulation. A serious complication of paraplegia is urinary infection which often results from repeated catheterization of the urinary bladder. Emptying of the bladder at regular intervals without catheterization would undoubtedly prolong the lives of many patients. Studies made by many investigators have demonstrated that the bladder can be stimulated by the radio frequency induction method, either directly by means of wires to the urethral sphincter or indirectly via nerves to the bladder (*16*). We have found that the bladder can be completely evacuated more readily if the pudendal nerve to the external urethral sphincter is cut (*17*); by this procedure we forestall development of the situation wherein the bladder contracts but the external sphincter prevents the voiding of urine.

In our studies with paraplegic dogs we have found that we can produce evacuation of the bladder by three different types of stimulation (Fig. 5). Stimulating the roots of the sacral nerves produces complete voiding with the smallest radio frequency signal (peak, 2 to 5 volts), but there is concomitant twitching of the leg. Stimulating the vesical nerves requires about twice as much stimulating voltage (peak, 5 to 10 volts); it produces voiding but often results in twitching of the thigh. The third approach is stimulation with shielded disk electrodes at the bladder wall in the vicinity of the vesical nerves—that is, the so-called neural trigger described by Habib (*18*); a peak of 10 to 20 volts is required in this case. Usually there are no attendant twitchings. In the first and third approaches, severing or crushing of the pudendal nerve was carried out.

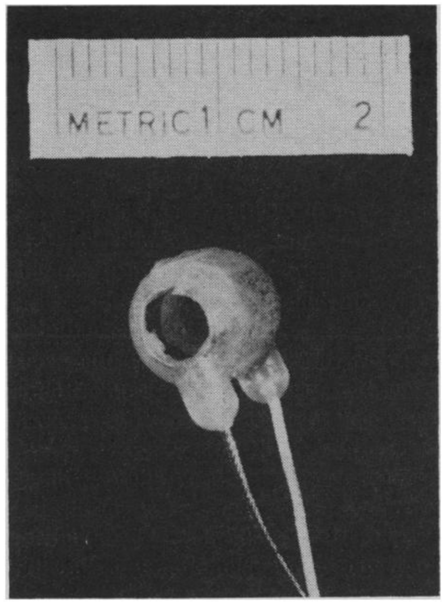


Fig. 6. A bipolar cuff electrode used for stimulation of the phrenic nerve. The electrode is made of an Elgalloy strip coated with Silastex rubber.

It is clear, from the limited clinical experience of others with electrical stimulation of the bladder, that a number of problems remain to be solved. The optimum site of stimulation in human patients may not be easily and consistently located. Whether severing of the pudendal nerve is necessary in all cases is not yet certain. There are also the possibilities that bladders will become refractive to electrical stimulation, and that stimulating currents will reach adjacent tissues, with resultant twitching or possible discomfort in some cases.

Phrenic nerve stimulation. Starting in 1948, Sarnoff and his colleagues (*19*) made a detailed study of the feasibility of electric stimulation of the phrenic nerves in connection with the respiratory difficulties of patients suffering from bulbar poliomyelitis. He reasoned that, by varying the intensity of a series of stimuli to the phrenic nerve so that peak values gradually increased and then gradually decreased, he could produce contractions of the diaphragmatic muscle which would be a reasonably good imitation of normal respiration.

Using electrophrenic stimulation by means of wires extending through the skin, Sarnoff found that the irregular spontaneous respiration of his patients could be completely suppressed and replaced by effortless, externally controlled respiration which contributed greatly to the comfort and recovery of the patients. Since there was difficulty in maintaining prolonged stimulation, the question then arose: Could stimulation of peripheral nerve tissue be effective over long periods? There was reason to believe that long-term stimulation was possible, as evidenced by the work of Fender (*20*) and of Lafferty and Farrell (*21*).

The technical difficulty of stimulating the phrenic nerve and lack of information about the feasibility of prolonged stimulation of this particular nerve by means of external wires probably is responsible, in part, for the dropping of work on electrophrenic stimulation after Sarnoff's early work. However, the radio frequency induction technique appears to have removed the technological obstacle.

It is our belief, subject to clinical verification, that certain patients with bulbar poliomyelitis have intact phrenic nerves which can be stimulated electrically. It might be possible to remove such patients from an iron lung if a satisfactory technique of electrophrenic stimulation could be developed. Other classes of patients who presumably would be assisted by such a technique would be patients with either chemical or physical damage to the higher respiratory center, obese patients who are physically unable to achieve adequate motion of the diaphragm and who thus develop an excessively high blood content of carbon dioxide, and patients in respiratory difficulty following surgery.

In our laboratories we have stimulated the phrenic nerves of dogs by radio frequency induction techniques for as long as 6 months. Generally the threshold of stimulation has remained low (peak value of 1 to 2 volts) and contraction of the diaphragm has been effectively controlled. Where the threshold of stimulation has risen, this has been due either to slippage of the electrode (see Fig. 6) or to pinching of the nerve. Where neither of these events has occurred, thresholds have been stable.

We have confirmed the observation of Sarnoff that stimulation of the phrenic nerve on one side of the body results in inhibition of the phrenic nerve on the other side and immobilization of the corresponding half of the diaphragm. In addition, De Villiers and his associates have noted (*22*), and the observation has been confirmed in our work, that after prolonged stimulation of one of the phrenic nerves, when stimulation is terminated, the nerve on the opposite side of the body resumes its normal function *but the nerve which has been stimulated* now shows no activity. After 12 to 72 hour this suppression due to prolonged stimulation disappears. The fundamental changes which are induced by prolonged stimulation, presumably at the level of the spinal cord, are now being investigated.

Conclusions

The radio frequency induction technique is now an important tool in physiological experiments and in the treatment of certain diseases. It has come to play an important role in the treatment of heart block in human patients, where medication has been ineffective. In the case of bladder stimulation, work with animals has shown that the voiding of urine can be induced by electrical stimulation. The successful use of this technique on human patients has yet to be consistently achieved, but there is reason to be optimistic.

Long-term electrophrenic stimulation appears to be feasible in laboratory animals. Applicability of the technique to certain classes of human patients awaits evaluation by clinicians.

In conclusion, we believe that the radio frequency induction technique, because of its flexibility, is useful for stimulating tissues of various kinds, particularly in animal experimentation.

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News and Comment

Congress and Science: Tensions Appear To Be Minimal as Annual Review Begins on Budget Requests

Two years ago, hazardous-duty pay might have been in order for government science administrators who were summoned to Capitol Hill. But congressional discontent about the costs of science has continued to subside from the high point that was reached with the gutting of the National Science Foundation budget for fiscal 1964. And when the administrators make their annual appearances during the next few months, it seems that they can expect a generally friendly reception.

There is, of course, no guarantee that affability will reign when the House Appropriations Committee holds its traditionally closed-door hearings on the proposed NSF budget, which is for $530 million, compared with the current $424 million. But the new budget seems to be responsive to the long-standing committee contention that NSF has been ignoring second-rank institutions while helping the rich get richer. NSF has countered with studies aimed at showing that there is reason and equity in its granting decisions, but now, in the proposed budget for fiscal 1966, starting next July, it is seeking funds that could be used to expand assistance to the second rank. For example, the new budget provides for 4145 NSF traineeships, compared with an estimated 2785 in the current year. At the same time, the number of NSF fellowships is reduced from 4940 to 4665. The significance of these allocations is that the traineeships are awarded directly by the institutions, thereby providing them with a lure for high-ranking students. On the other hand, the bulk of the fellowships are awarded directly by NSF, and the recipient is free to apply to the institution that he prefers—which is likely to be a top-ranking one. NSF is also seeking a good deal of additional money for its Science Development Program (*Science*, 10 April 1964), which is designed to provide development grants for institutions that appear to have everything but money for making the leap to higher quality. The first grants are yet to be made from the $28 million that is available for the program in the current fiscal year, but NSF apparently has big plans for this effort and is seeking another $40 million for the coming fiscal year.

In addition, the foundation has requested funds for a sizable expansion in the number of new research grants. This is an area that has been relatively static for 3 years. In fiscal 1963 the total was 2709; the following year it rose to 2892; and in the current year the number was 2900. Next year, however, NSF is seeking funds that would