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IMPLANTATION OF ECG ELECTRODES, EEG ELECTRODES AND TEMPERATURE THERMISTORS IN THE MONKEY (MACACA MULATTA)

ARMED FORCES RADIOBIOLOGY RESEARCH INSTITUTE
Defense Atomic Support Agency
Bethesda, Maryland

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IMPLANTATION OF ECG ELECTRODES, EEG ELECTRODES AND TEMPERATURE THERMISTORS IN THE MONKEY (MACACA MULATTA)

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FOREWORD
(Nontechnical summary)

In clinical medical practice, sensing devices to measure various physiological parameters can be applied to the body surface of the patient. In biological investigations employing laboratory animals, these surface devices are frequently rendered useless because of muscle movements. The only methods available to the research biologist to eliminate these movements are anesthesia, severe restraint, or implanted sensing devices. Investigations concerned with the study of behavior and physiology concurrently cannot use anesthesia or severe restraint. Either one of these two methods would suppress the animal's movements entirely, thus eliminating all behavioral activity.

The present report describes instrumentation and methods for implanting sensing devices to record the electrocardiogram (electrical activity of the heart), body temperature, and the electroencephalogram (electrical activity of the brain) of a moderately restrained monkey. The devices described herein provide an accurate and consistent signal for long-term monitoring and do not markedly alter the behavior of the subject. The instrumentation and techniques were designed for use in a variety of behavioral programs in which a concurrent physiological monitor was desired in the preirradiated and postirradiated monkey.

ABSTRACT

Methods and procedures of bioinstrumentation for the long-term monitoring of the electrocardiogram, body temperature, and the electroencephalogram are discussed. These techniques were designed specifically to facilitate psychophysiological investigation of preirradiated and postirradiated monkeys. The instrumentation herein described has performed satisfactorily throughout an exposure to a gamma-neutron radiation pulse of 5000 rads with no appreciable decrement.

I. INTRODUCTION

Many of the investigations at the Armed Forces Radiobiology Research Institute (AFRRI) into the psychophysiological effects of radiation exposure can best be performed using implanted sensing devices. The nature of this research dictates that these implantable devices have certain attributes. First, each device must provide an accurate and consistent signal capable of being transmitted, via hard wire and booster amplifiers, for distances of approximately 200 feet (Trageser and Kavanaugh).[3] Second, the implanted device will have to remain in the subject up to 30 days, and therefore should provoke a minimal tissue response during this period. Third, neither the implanted device nor the external leads should markedly alter the behavior of the subject. Finally, the technique of fabrication and implantation should be simple enough to enable a large annual production of implanted subjects.

Physiological sensing devices which satisfy these criteria have been developed at the AFRRI for monitoring the electrical activity of the heart (electrocardiogram, ECG), body temperature, and the electrical activity of the brain (electroencephalogram, EEG) of a moderately restrained monkey. Although numerous methodologies[1] have been presented for implanted sensors, the instrumentation and implantation techniques described herein are essentially modifications of work by Gorman.[2]

To date, 20 monkeys (both sexes) have been implanted with physiological sensors. Fifteen of these animals were prepared for recording only the ECG, while five were implanted with combinations of ECG, temperature, and EEG sensors.

This paper describes the bioinstrumentation techniques employed for these parameters at the AFRRI.

II. ELECTROCARDIOGRAM

Prior to implantation of the electrodes, the animals are conditioned to behavioral chairs for periods varying from 1 to 4 weeks (Figure 1). On the day preceding surgery, all animals are fasted for approximately 18 hours; however, water is available until 2 hours before administration of the anesthetic.

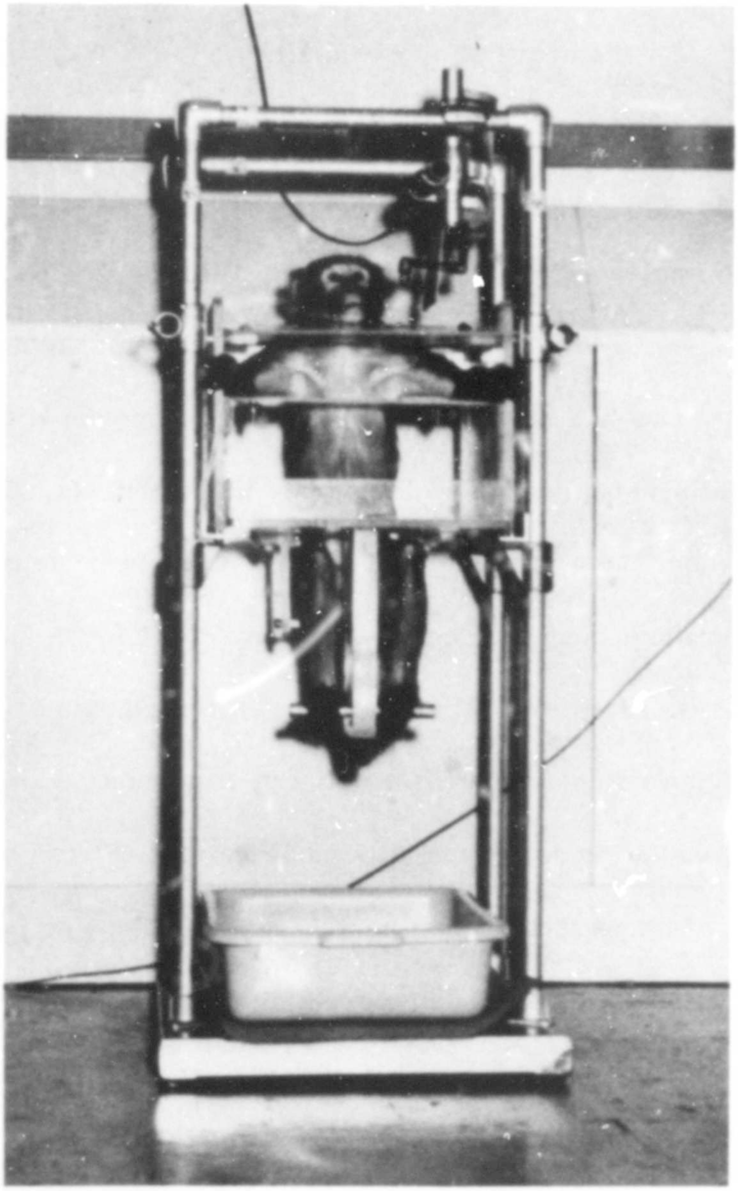

Figure 1. Behavioral chair and subject

Preparation of the monkeys for surgery consists of anesthetizing the subject with intravenous pentobarbital sodium. A calculated dose (30 mg/kg) of the anesthetic is given, the loss of the palpebral and the pedal reflexes indicating a satisfactory degree of anesthesia. With the subject completely immobilized, the hair is clipped from the dorsal surface of the body and the animal then freed of all debris and waste material. The monkey is then taken to the surgical room and prepared for surgery, utilizing conventional procedures.

The electrodes (Figure 2) for recording the ECG consist of Teflon coated stainless steel wires, which are attached to the spine of the right scapula and the wings of the right and left ilia. The Teflon coating of the wire is complete except for a small looped area at the points of attachment. The three electrode wires terminate in a 3-pin Amphenol connector, molded in a medical grade elastomer.* The central connector

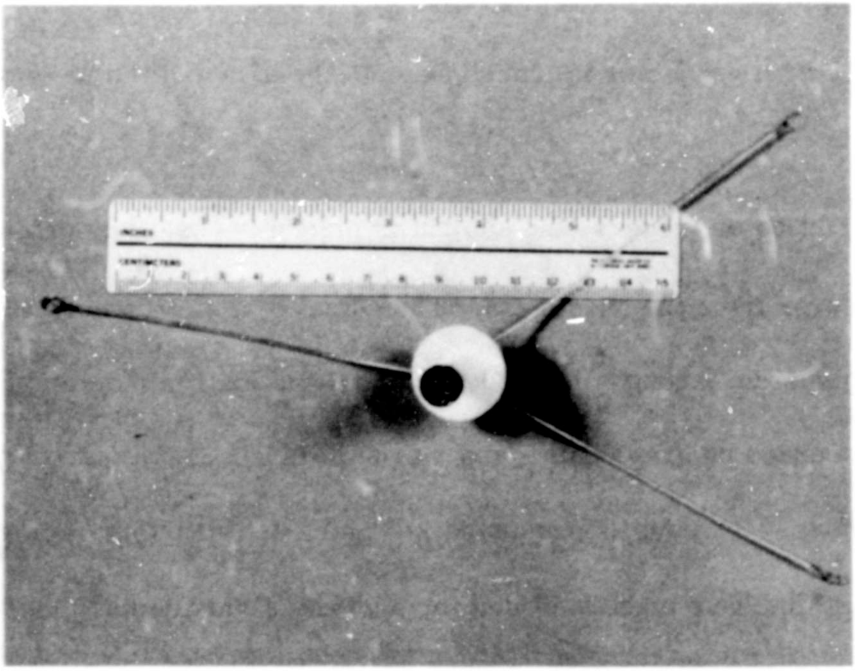

Figure 2. Electrocardiogram sensing apparatus

* Silastic 382 Medical Grade Elastomer.

is positioned at the level of the last rib, at which point it is allowed to extend through the skin for attachment to the recording system. Support for the central connector is achieved by the molded flanged base of the elastomer support, which is positioned under the skin at the point of exit. The lengths of the lead wires vary according to the size of the subject. The entire unit is sterilized in a 1:1000 dilution of benzalkonium chloride solution, U.S.P., prior to implantation.

To surgically implant this device, an incision (approximately 2.5 cm) is made through the skin at each implantation site and at the exit point of the central connector. By tunneling beneath the skin with hemostatic forceps, the stainless steel wires are drawn from the terminal point of the central connector to the implantation locations. The stainless steel wire loops which serve as the electrodes are then anchored to the spine of the scapula and wings of the ilia with 2-0 silk suture. The flange of the central connector is placed beneath the skin and the incisions are closed (Figure 3).

On completion of surgery, the subject is placed in the behavioral chair and allowed to recover from the anesthetic. The output of the electrodes is fed directly to a recording system through electrode couplers and high gain ac amplifiers. These signals are recorded on graph paper and magnetic tapes. A sample of the ECG obtained from these electrodes is presented in Figure 4. With this bioinstrumentation, electrocardiograms have been recorded for periods of one month. Tissue reaction and infection have been minimal and because of the restraint offered by the behavioral chair, intentional damage to the electrode apparatus by the subject is minimized.

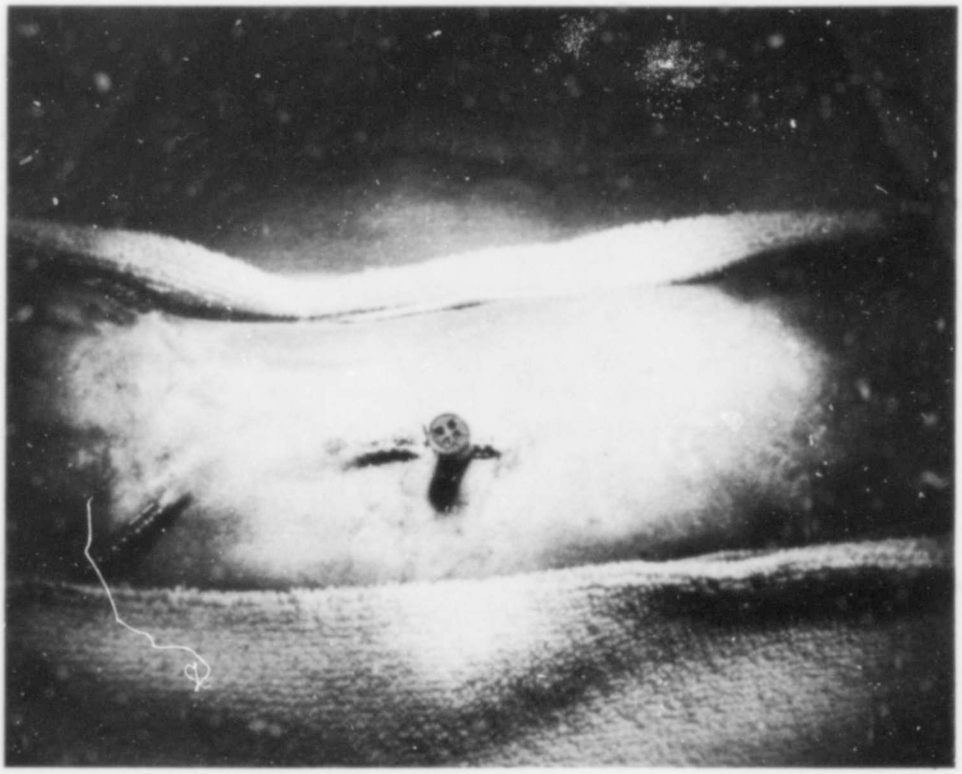

Figure 3. Central connector of electrocardiogram apparatus and implantation sites

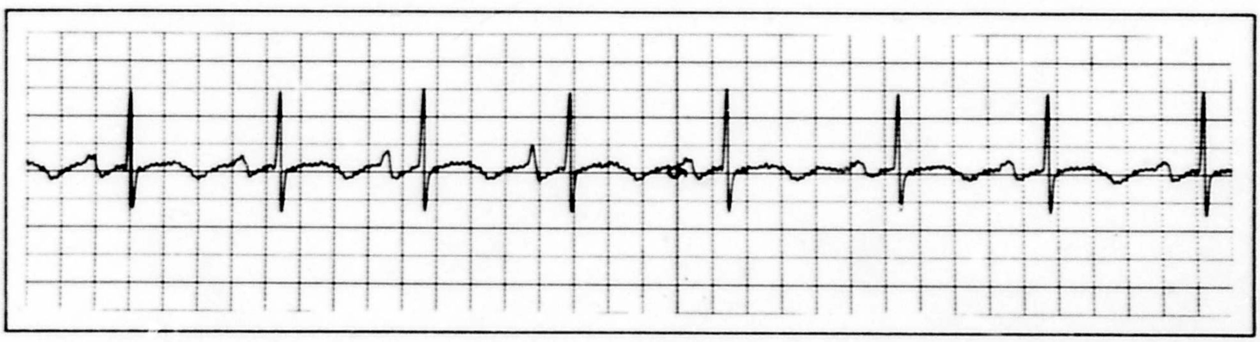

Figure 4. Electrocardiogram recorded from right scapula (negative) to left ilium (positive) at 50 mm/sec

III. BODY TEMPERATURE

To record the subject's body temperature, a temperature thermistor,* coated with silicone rubber to prevent body fluid contamination, is placed subcutaneously over the abdominal musculature. The connecting wires for the thermistor are also implanted subcutaneously for attachment to the previously described central connector (modified for 5-pin connection) of the ECG device. To date, only subcutaneous temperatures have been recorded with this thermistor unit; however, by increasing the length of the implanted connecting wires, this unit is suitable for recording temperatures from other anatomical locations. The implantable temperature apparatus is shown in Figure 5.

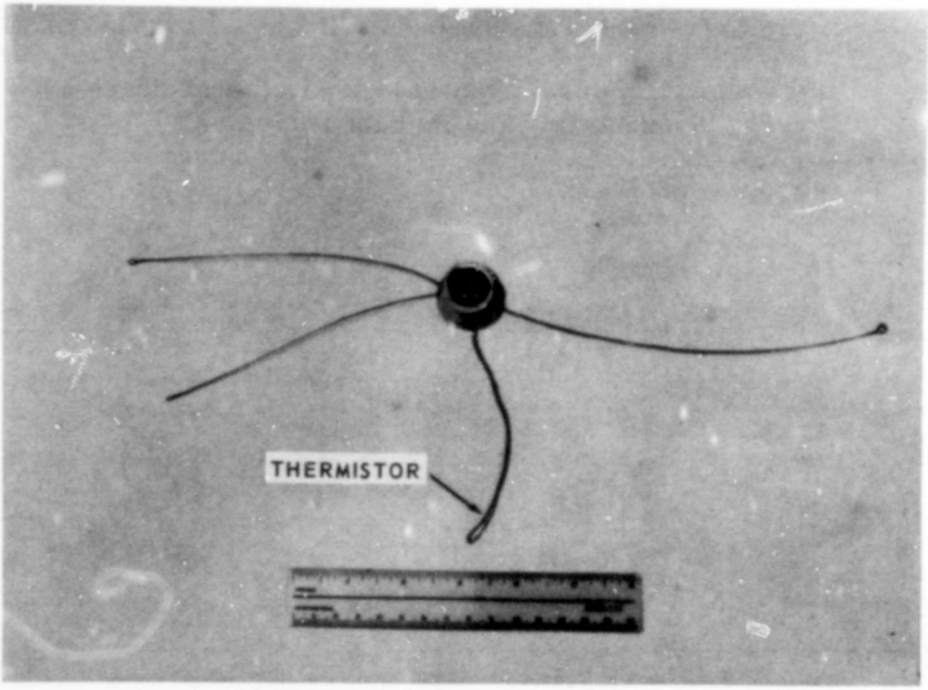

Figure 5. Electrocardiogram sensing apparatus with temperature thermistor

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* Yellow Springs temperature thermistor #44005, Yellow Springs Instrument Company, Yellow Springs, Ohio.

Implantation of the temperature thermistor is conducted concurrently with, and uses the same procedures as, the ECG implants. The electrical output of the temperature thermistor is transmitted to the recording system through a temperature bridge, electrode couplers, and a dc amplifier. The temperature data are recorded both on magnetic tapes of the Data Acquisition System and on graph paper through an auxiliary recorder. This system of recording body temperature has been employed utilizing four monkeys and has provided continuous recording for periods of 3 weeks. These periods could have been extended had the subject not been utilized in studies employing lethal doses (5000 rads) of gamma-neutron radiation. On the death of the animals, the thermistors are recovered and tested for accuracy. The preirradiation and postirradiation calibration curves have been accurate to within $\pm$ 0.2°C.

Two types of silicone rubber have been used with adverse effects. RTV-102,* used in two monkeys, becomes pervious to body fluids and is difficult to apply. RTV-11,† also used in two monkeys, has ideal physical properties, but causes inflammation after implantation as evidenced at necropsy by exuberant tissue granulation around the thermistor. Another compound, RTV-615,‡ exhibits physical properties similar to RTV-11, and is reported to be more readily applicable to biomedical purposes. It is presently under study as a possible solution to the tissue reaction problem.

Prior to the studies utilizing the monkey, four thermistors were employed in a pilot investigation to determine the radioresistance of these instruments. Thermistors

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* General Electric RTV-102 Silicone Rubber.
† General Electric RTV-11 Silicone Rubber.
‡ General Electric RTV-615 Silicone Rubber.

alone were surgically implanted in each of four anesthetized rats. One animal was used as a control while the other three were exposed to 5, 10, and 20 thousand rads, respectively, of pulsed gamma-neutron radiation from the AFRRI-TRIGA reactor. The resulting preirradiation and postirradiation voltage output of the four thermistors is shown in Table I. These figures indicate that the thermistors are not affected significantly by these levels of radiation. Their output remains steady, thereby allowing correction factors to be applied after necropsy. All thermistors have been calibrated before and after irradiation and all have read to within ± 0.2°C without applying a correction factor.

Table I. Thermistor Calibration*

Temperature (degrees C)	Control		5000 rad		10,000 rad		20,000 rad	
			pre-irradiation	post-irradiation	pre-irradiation	post-irradiation	pre-irradiation	post-irradiation
48.5	0.178	0.175	0.174	0.175	0.178	0.175	0.178	0.173
46.5	0.154	0.154	0.154	0.154	0.154	0.154	0.155	0.154
44.5	0.133	0.133	0.134	0.132	0.133	0.133	0.135	0.132
42.5	0.108	0.110	0.108	0.110	0.108	0.111	0.110	0.109
40.5	0.087	0.087	0.089	0.088	0.088	0.088	0.088	0.088
38.5	0.061	0.063	0.063	0.062	0.063	0.063	0.063	0.062
36.5	0.033	0.036	0.036	0.036	0.034	0.037	0.036	0.035
34.5	0.006	0.008	0.009	0.009	0.008	0.009	0.009	0.008

* Calibration data pre- and postirradiation expressed in volts.

IV. ELECTROENCEPHALOGRAM

Surgical procedures similar to those previously described are followed in implanting the EEG electrodes. The system for detecting the electrical activity of the cortex consists of a central 7-pin Amphenol connector and five stainless steel dural electrodes. The Amphenol connector is imbedded in a Teflon holder designed for attachment onto the calvarium. A single stainless steel electrode passes from the central connector through the supporting Teflon and terminates on the dura. This electrode serves as the indifferent electrode. Four additional electrodes complete the EEG sensing apparatus. These electrodes are made of stainless steel rods 0.35" in diameter held in place by Teflon holders. The four outer electrodes are attached to the indifferent electrode holder by four pieces of Teflon coated stainless steel wire to form a four-armed array (Figure 6). To implant this apparatus, the subject's head is positioned in a stereotaxic instrument, incisions are appropriately made through the scalp, and the underlying tissues are reflected to expose the bone surface. The electrode placements, for the purpose of this study, are located as follows:

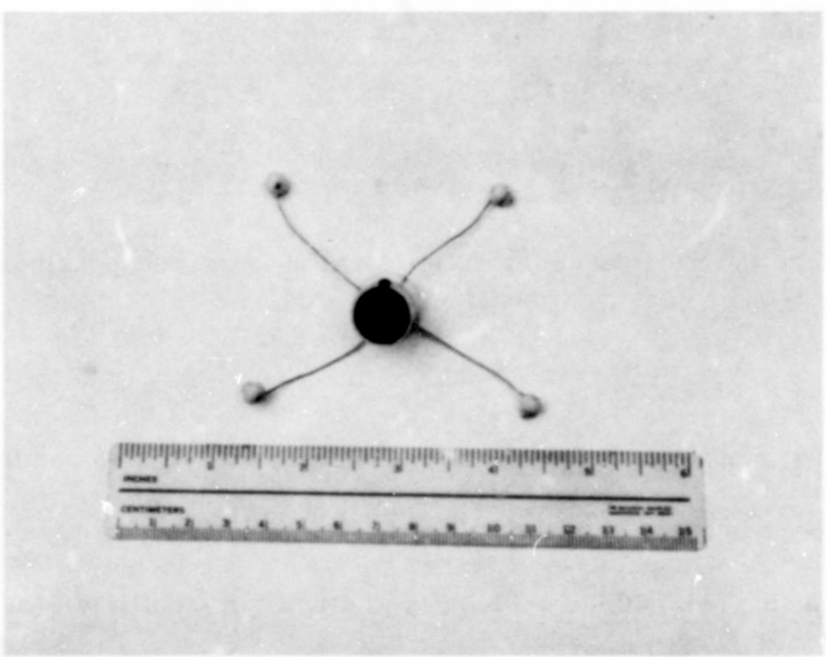

Figure 6. Electroencephalogram sensing apparatus with central connector and electrodes

(1) on the apex of the calvarium, sufficiently lateral of the midline to avoid the cranial sinus; (2) left frontal region; (3) right frontal region; (4) left posterior parietal region; and (5) right posterior parietal region (Figure 7).

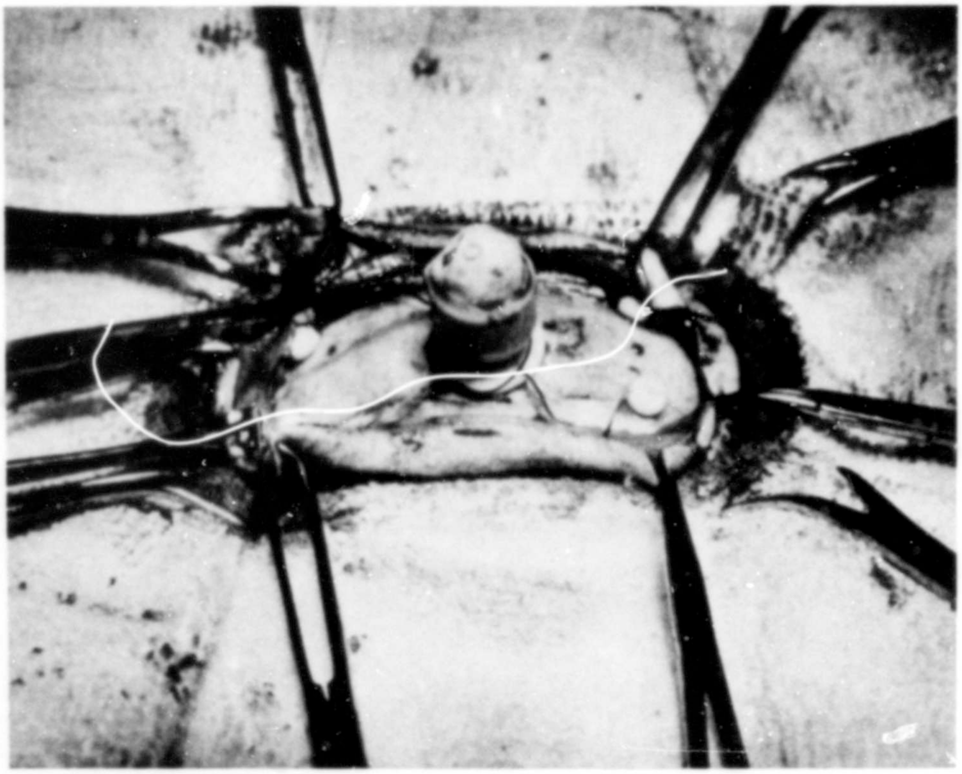

Figure 7. Surgical implantation sites of electroencephalogram sensing apparatus

In our first monkey, all the electrode holders were drilled and tapped. In subsequent animals, however, only the holder in the apex of the calvarium has been drilled and tapped. This holder is chamfered slightly so that it will self-tap into the calvarium. The other electrodes are designed to press fit into a drilled fenestration without tapping or turning.

The general procedure followed is to drill and tap the apex penetration, and then drill the other four openings. The apex holder which has all of the other electrodes attached to it by the stainless steel wires, is self-tapped into the apex opening. When a firm attachment is obtained, the outer four electrodes are snapped into place. The electrodes from these holders are designed so that they would terminate on, but would not pierce, the dural membrane. A single depth dimension for all electrodes suffices for most of the animals since the dura is quite flexible. In the event the length of the electrode exceeds the depth measurement, a small Teflon washer is inserted between the calvarium and the electrode holder.

The subject is placed in the behavioral chair and allowed to recover from the anesthetic. The animal's hands, as previously mentioned, are restricted to prohibit it from reaching the sensing implants. The output of the electrodes is fed directly to the Data Acquisition System through electrode couplers and high gain ac amplifiers. A recording of cortical activity as detected with a left frontal to left parietal and a right frontal to right parietal electrode combination is pictured in Figure 8.

This apparatus has been tested on five monkeys for a period of one month with sampled recording throughout this time. Neither tissue reaction to the appliance nor infection were encountered and it is anticipated that a much longer period could be monitored without difficulty. This method of bioinstrumentation has the advantage of avoiding the use of adhesives (i.e., dental acrylic) and allows the brain potential to be detected from a well-defined anatomical location without interference from associated structures. The attachments are sufficiently strong to allow the animal to be suspended from the central EEG connector at the time of necropsy.

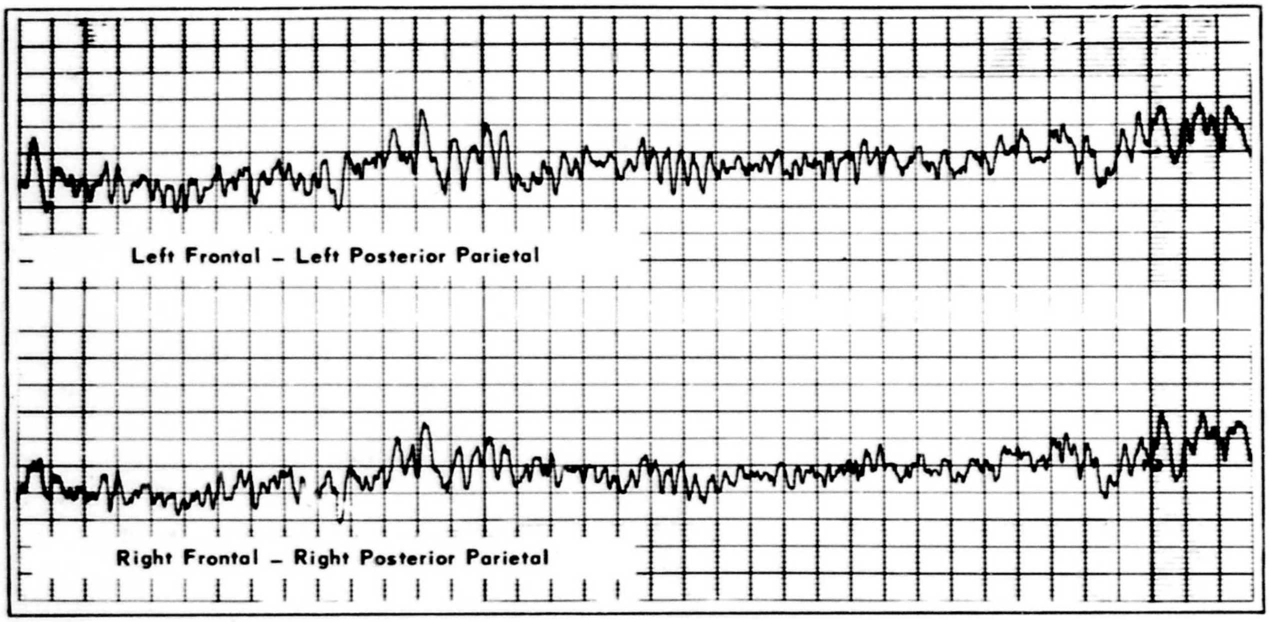

Figure 8. Electroencephalogram recorded at 20 mm/sec

V. SUMMARY

Procedures and instrumentation for recording the ECG, body temperature, and EEG of the moderately restrained monkey have been presented. These methods have been tested in both preirradiated and postirradiated subjects for periods of one month. The instrumentation has been successful in producing signals capable of being transported, via hard wire and booster amplifiers, for distances in excess of 200 feet. No appreciable performance decrement or deterioration of physiological data has been observed in the animals implanted in this manner, except for the tissue reactions produced by the silicone compound used to protect the thermistors. A gamma-neutron radiation pulse of 5000 rads has not had any significant effect on the instrumentation which has been described.

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