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Date May 18, 1973

THE EFFECTS OF ELECTRIC CURRENTS ON ORTHODONTIC MOVEMENT *IN VIVO*

by

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Submitted in partial fulfillment of the requirements

for the Degree of Master of Science

Department of Orthodontics

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THE EFFECTS OF ELECTRIC CURRENTS ON
ORTHODONTIC MOVEMENT IN VIVO

Abstract

by

DENNIS CHARLES BEESON

From a variety of experiments to date, it seems that a controlling mechanism for bone remodeling may be related to stress induced electric currents or fields. During orthodontic tooth movement, the bone around the moving tooth is known to remodel. A relationship between orthodontic movement and bioelectric currents is easy to infer but, as yet, has no benefit of any support from the literature. Accordingly, the purpose of the present investigation is to examine the relationship between an externally applied current and the rate of bone remodeling associated with orthodontic tooth movement.

The effects of a 10 μA current on the amount of tooth movement was measured in vivo. Each of twelve cats was prepared with a sectional tooth moving apparatus and a miniaturized constant-current power source. Platinum-iridium electrodes were implanted in the alveolar bone on either side of the teeth to be moved. The experimental treatments consisted of 1) a current flowing with the cathode mesial to the anode, 2) a current with the polarity reversed, and 3) a control with no current flowing. Radiographic and direct intra-oral measurements were taken weekly for five weeks

to determine the amount of tooth movement. The effects of the treatments were examined via a balanced incomplete block design and the appropriate analysis of variance.

The results of this investigation did not show a statistically significant among-treatment difference. In the present experiment, it could not be demonstrated that a 10 μA current passed around a moving tooth had an observable effect on the extent of tooth movement.

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INTRODUCTION

Unlike many tissues, bone retains the capacity to remodel, resorb, and regenerate. This ability serves to adapt the structure of bone to the mechanical demands placed upon it, a relationship which has been widely recognized since Wolff's classic work in 1892.

There are many factors that influence the regulation of bone growth, but the actual local control mechanism is, as yet, undefined. Systemic control is generally thought to involve hormones, nutrition, oxygen concentration, enzymes, temperature, and the like. Bone must also be subjected to local and regional control, since not all bones grow at the same rate and direction. Enlow (1968) summarized these local controlling factors as 1) genetic predisposition, 2) stress (pressure-tension), 3) tissue and cell induction, 4) selective cell responses to stimuli, 5) the functional matrices (as proposed by Moss, 1962), and 6) bioelectric factors. The first five of these factors are descriptive of the end result of local growth mechanisms, but they do not explain how the mechanism actually operates on a cellular or molecular level. In contrast, consideration of bioelectric phenomena has generated more basic hypotheses concerning the actual control mechanism.

As Bassett (1971) has stated, "the stimulus for bone formation and destruction appears to be largely electrical in nature." According to the contemporary workers, functional pressures

on bone are thought to be transduced into electrical energy by the bone itself, the resulting piezoelectricity acting as a signal to which osteoblasts and, perhaps, osteoclasts can respond. This response would be controlled in a negative feedback system with electricity as the mediator.

With the results of current research, it seems likely that manipulation of these yet-unknown control mechanisms may result in a clinically useful tool in the fields of orthopedics and orthodontics. It will be the purpose of this investigation to explore a procedure to control bone remodeling. By applying an electrical current to areas which are normally active in both bone growth and resorption, this investigation will seek to characterize the input-output relationship while treating the actual control mechanism as a black box. It is hoped that the data gained from this investigation will add a few pieces to the puzzle so that eventually the exact transfer function for the response of bone to external forces can be identified.

REVIEW OF THE LITERATURE

The Electrical Response of Bone

Piezoelectric effects in bone were first investigated by Fukada and Yasuda (1957). They established that bone does exhibit stress-induced electric potentials. Bassett and Becker (1962) found that stressed bone specimens generate an electric potential whose polarity is dependent on the direction of the bending.

Cochran et al. (1967) studied the potentials produced in a moist bovine mandible. The teeth were axially loaded by a pneumatic plunger applying up to 10 Kg via the tooth and periodontal ligament to the supporting bone. The voltage, ranging from 0.5 to 5 millivolts (mV), was proportional to the load and decayed to zero if the loading was sustained. It was concluded that electric potentials would be produced during normal mastication and that these potentials could play a role in the normal maintenance of the periodontal structures.

Gillooly et al. (1968) refined further Cochran's design to record more accurately potentials in mandibular bone of dogs. These potentials were produced in response to tipping forces of 1-2 Kg applied to the crown of a tooth. Surface and "inset" electrodes were applied to the bone and recordings were made as the tooth was tipped. It was concluded that areas of bone toward which the force was directed become more positively charged in the cribriform plate

However, the hydroxyapatite in bone prevents access of water to all parts of the collagen fibers. They concluded that collagen in bone would continue to have piezoelectric properties even if the bone itself were fully hydrated.

The Origin of Stress-Induced Potentials

The exact origin of these electric potentials has not been verified. Many organic and inorganic substances which lack a center of symmetry can possess piezoelectric properties. Fukada and Yasuda (1957) discovered that collagen itself can develop an electric charge when deformed. This led to the conclusion, later substantiated by Shamos and Lavine (1964, 1965, 1967) and Williams and Berletz (1971), that collagen is the primary source of these potentials. Christiansen et al. (1961) generated potentials by bending a rod of potassium hyaluronate. This opened the possibility that hyaluronic acid in bone could be the source of these potentials. Hydroxyapatite has not been shown to have piezoelectric properties, but Mackay and Sinha (1967) described piezoelectric activity in Whitlockite [$Ca_3(PO_4)_2$].

Becker et al. (1964), Becker and Bachman (1965), and Becker (1965) suggested that a solid state phenomenon exists between collagen, an n-type material (electron donor), and apatite, a p-type material (electron receiver). This collagen-apatite interface could act as a semi-conducting p-n junction when bone is subjected to mechanical stress. Bassett (1965) showed that this junction is the probable source of observed stress-induced potentials in bone.

area and more negatively charged on the external surface of the cortical plate. The area of relative positivity corresponded with the area of pressure, while the negatively charged area corresponded to areas under tension. From these data, Gillooly's group theorized that negatively charged areas would show bone deposition and that positively charged areas would undergo resorption. They suggested that these stress-induced potentials would be present even if the load values were reduced to more accepted orthodontic levels, and could be recorded if the sensitivity of the apparatus were improved.

Most of these observations were made on dry bone; Cochran et al. (1968), however, designed their experiments to include moist bone, in vitro, and under physiologic stresses, in vivo. Currents were recorded from feline tibiae that had been subjected to forces which simulated walking activity. The amplitude of the stress-induced potentials recorded in moist bone corresponded closely to the rate of deformation. Cochran suggested that this current is neutralized by ionic charge carriers. If the deforming force was too slow or if charge leakage was too great, as in moist decalcified bone, a voltage could not be recorded. If the rate of the deforming force was sufficiently high, stress-generated potentials could be recorded. This, Cochran maintained, leaves open the possibility that charge displacement is present, and that a bidirectional current exists. As a result, a second current of opposite polarity was produced when the load was discontinued.

Anderson and Eriksson (1970) concluded that pure collagen would not have piezoelectric properties if it were fully hydrated.

Pyroelectricity of bone (Athenstaedt, 1970) and ferroelectricity of RNA (Stanford and Lorey, 1968) have been listed as possible sources of electrical energy. In addition, potentials can be created when charged molecules flow past sites of a fixed charge. As in blood vessels, streaming potentials can be found in bone when extracellular fluid moves (Anderson and Eriksson, 1970). Also charge potentials are created by nerves, muscles, and cells themselves. At present, the origin of significant electric potentials, and not their presence, is the subject of active investigation.

Bioelectric Phenomena

Friedenberg and Brighton (1966) and Friedenberg, Dyer, and Brighton (1971) measured spontaneous bioelectric potentials that exist in bone independent of any stresses. These potentials were found to exist *in vivo* and to persist for a few hours in freshly removed bone. It was found that the diaphysis carries a positive charge relative to the epiphysis or metaphysis. Friedenberg and Smith (1969) showed that the normal electrical pattern is changed by the creation of a fracture. In this case, the entire bone becomes more electro-negative, with the greatest increase occurring at the fracture site. Becker (1961) concluded that negativity is related to tissue growth. Friedenberg, Dyer, and Brighton (1971), however, speculated that this phenomenon could be explained by many factors, including:

1) an increase in vascularity, in which red blood cells and the endothelium are negatively charged

2) a higher protein to mineral ratio

3) an increase in cellular content

4) pH changes in the healing bone

5) a different ionic concentration caused by tissue metabolism.

Friedenberg and Brighton (1966) reported that these potentials are the summation of many metabolic and physiologic sources. Whatever the origin, they believed that these potentials are influenced, among other factors, by disease, injury, mechanical stress, metabolic state, and depth of anesthesia.

Swanson and Lafferty (1972) reported that conductivity of electrical currents in bone depends primarily on the mineral content of the bone. Conductivity of rat bone was decreased after immobilization and was increased with age. It was found that stress-induced electrical fields were of shorter duration in mature bone. From these studies, they concluded that conductivity changes may influence bone growth. Although never tested, they theorized that the rate of healing in demineralized bone would be faster than in normal bone, especially when an electric field is being applied.

Bioelectric phenomena have been studied in many other tissues besides bone. Other than the obvious example of electrical activity in nerves, electric fields have been linked with cellular migration (Ben-Or et al., 1960), amphibian-limb regeneration (Becker, 1961), cellular dedifferentiation of amphibian red cells (Becker and Murray, 1967), regression of malignant tumors in mice (Humphrey and Seal, 1959), initiation of blood coagulation (Sawyer et al., 1961), and decalcification of tooth structure (Parker, 1969).

With these studies in mind, the bioelectric effects seen in bone were related to a control system of bone remodeling. Experiments were then conducted to characterize the effects that an artificially induced direct current would have on osteogenesis.

Electrically-Induced Bone Formation

Yasuda, Noguchi, and Sata (1955) were the first to report the formation of a bony callus on a femur after a three-week stimulation of under 100 microamperes (μA). If the current was raised above 1 milliamp (mA), bone destruction took place. Becker *et al.* (1964) observed that a 0.2-1 μA current caused tropocollagen in saline to precipitate a band of collagen at right angles to the electric field. They explained this by suggesting that charged molecules could by means of electrophoresis align themselves in the presence of a current *in vitro*, and similarly *in vivo*.

Bassett *et al.* (1964) implanted in the femurs of twelve dogs platinum-iridium electrodes connected via a series resistor to a 1.4 volt battery. Three different resistors were selected, so as to deliver 1, 10, and 100 μA, respectively. The 1 μA configuration produced no differences in bone formation compared to the controls; however, the 10 μA and 100 μA packs produced new bone around the cathode in fourteen days. Tissue resistance initially reduced the current to 0.8, 8.0, and 80 μA, respectively. Within twenty minutes, electrode and tissue polarization had further reduced the current to 0.7, 2.0, and 3.5 μA, respectively. Bassett realized that passage of an artificial current through instressed bone is probably

not equivalent to stress-induced potentials. Yet he concluded that osteogenic processes are affected in some way by low level currents and that new bone is deposited primarily in regions of relative electro-negativity.

Other researchers have had difficulty matching Bassett's success. Minkin et al. (1968) concluded that a 70 μA current may induce bone growth if the electrodes are implanted in the distal femoral epiphysis of a rabbit. The increased deposition, however, was not significantly different from that caused by the implantation of sham electrodes. O'Connor and associates (1969) tried to duplicate Bassett's experimental design as closely as possible. Their results generally confirmed Bassett's. In 7 out of 12 cases, more bone was around the cathode; in 2 cases, however, less bone was found near the cathode.

The difficulty in assessing the extent of bone growth around the electrodes prompted Hambury et al. (1971) to develop a method of measurement based on strontium-85 uptake, a measure of the amount of calcium hydroxyapatite deposited. Rabbit femurs were subjected to a 36 μA implant which quickly polarized to 3 μA. They could get no consistent evidence in support of a difference in bone formation between the cathode and anode.

Crelin and Dueker (1970) used mice femurs fitted with electrodes 5 mm apart and driven by packs delivering 100 μA before implantation. No mention was made of the current level after polarization. The results indicate that the amount of bone formation around the electrodes never exceeded, and sometimes was less than,

the bone formed around non-conducting sham electrodes. These results would then seem to substantiate Minkin's investigation.

Friedenberg and Kohanim (1968) tried to determine if the length of long bones could be influenced by an electrical current. Using young rabbits, they implanted stainless steel electrodes approximately 2 cm apart in two different configurations. The electrode placement for one group was centered across the epiphyseal line. The second group had one electrode in the diaphysis and one in the metaphysis. The current in both groups initially ranged from 6 to 13.5 μA and gradually decreased to a range of less than 2 to 5 μA. In neither group did these currents affect the overall length of rabbit tibiae. However, areas surrounding the positive electrode generally underwent tissue destruction, including intravascular damage and tissue coagulation. Lysis of red blood cells was seen beyond this area of destruction. Bone destruction around the anode was more prevalent in the metaphysis but was also seen in the epiphysis in the first group. In the second group, bone destruction around the anode could be observed radiographically in 45% of the cases and histologically in 80% of the cases. In both groups, bone formation occurred around the cathode in approximately 45% of the cases. In these, there was minimal formation of new medullary trabeculae and only 20% could be detected radiographically. There was no significant increase in vascularity around the anode.

Because of the seemingly wide variation in the response of bone to small electric currents, Lavine, Lustrin, and Shamos (1969) and later Lavine et al. (1971) designed experiments to elucidate

the response of bone located in the path of an electric current. In this paradigm, the possible effects of a foreign body reaction to the electrodes would not be confounded with the response elicited by the current. Using the femur of rabbits, Lavine placed platinum electrodes 7.5 mm to either side of a hole which was drilled to produce an experimental defect. The current ranged from 2 to 4 μA for periods of from one to three weeks. The results indicated that direct current may enhance the normal healing rate of the "experimental defect" by a factor of two. Lavine concluded that the application of electrical currents hastens the normal calcification process. Although there are many factors responsible for bone healing, Lavine suggested that perhaps a more rapid orientation of fibers and dissociation of bound calcium would be effected by such a current.

Concurrently, Friedenberg and associates (1970) studied the bone response around electrodes driven by a constant-current source. This device, comprised of a battery, two field-effect transistors, and a resistor, was designed to supply a constant current regardless of changes in resistance. In previous investigations, as tissue and electrode resistance increased, the current delivered to the bone decreased. Using the femurs of rabbits, Friedenberg and coworkers implanted constant-current devices and stainless steel electrodes. Bone and cartilage formation, fibrous proliferation, and tissue destruction were observed at both the anode and cathode. The intensity of the reaction appeared to be a function of the current density. Bone production was most often seen at the cathode

between 5 and 20 μA. Significant tissue destruction was seen at all currents above 20 μA, especially at the anode.

Using the same constant-current device set at 10 μA, Friedenberg, Roberts, Didizian, and Brighton (1971) reported that they could stimulate the rate of healing of a fractured rabbit fibula if the cathode was placed directly in the fracture site. Subsequently, (Friedenberg, Harlow, and Brighton, 1971) their findings were applied to the treatment of a fracture non-union in the medial malleolus of a fifty-one-year-old woman. Conventional attempts to achieve bony union had failed. A stainless steel cathode was implanted in the fracture, and a 10 μA current was passed for nine weeks. The anode was an aluminum grid placed on the surface of the skin. Union was achieved, an event which Friedenberg attributed to the electrical stimulation, inasmuch as the fracture had given no evidence of healing during the preceding year.

Lavine et al. (1972) administered approximately the same therapy to a fourteen-year-old boy who had a congenital pseudo-arthrosis of the tibia and for whom conventional attempts at bony union had failed. A 3.9 μA direct current was delivered via platinum electrodes positioned 1.9 cm on either side of the defect. A histologic examination showed osteogenesis and collagen formation in the nonunion after the passage of current for 125 days. Lavine inferred that the electrical potentials acted to direct osteogenesis and remodeling of bone through an, as yet, unknown mechanism.

Levy (1971) and Levy and Rubin (1972) reported that they

had induced osteogenesis using a pulsed monophasic DC source. Levy implanted pulsed circuits, DC circuits, and sham circuits, each having platinum-iridium electrodes with a 3 cm separation, into the medullary cavities of femurs and ribs of dogs. The frequency, duration, amplitude, and total exposure were varied. Regression equations were used to determine how significant each variable was in altering the osteogenic response. The firing rate and the total time of implantation were the two most significant parameters (correlation coefficient not stated). The average increase in bone area from all the pulsed stimulations was 43%, while the average increase for the DC stimulations was 17%. Sham experiments produced an increase of 3%. It should be noted that the range for peak output was from 0.2 to 2.5 mA with all DC stimulators set at 0.5 mA (500 μA). This was not within the range previously determined to be optimal by Friedenberg. With the pulsed stimulators, the most active region of osteogenesis was located in the region between the electrodes, with no preferential growth occurring at a specific electrode.

The use of electric and magnetic fields can influence bone formation. McElhaney, Stalnaker, and Bullard (1968) have presented an hypothesis to explain this phenomenon. In a piezoelectric material, an electric field will produce a strain deformation. If bone is piezoelectric, the electric field would cause the bone to deform. To present evidence supporting this hypothesis, they investigated the effect of artificially induced electric fields on the bone loss normally caused by immobilization (Kazarian and Von Gierke,

1969). Various fields were created by externally placed electrode plates on the skin surface of rats, which seemed to reduce the amount of bone weight loss normally seen by immobilization.

Bassett and Herrmann (1968) subjected cultures of fibroblasts to pulsed and continuous DC fields. Cultures grown under the continuous DC field showed a 20% increase in DNA and tritiated hydroxyproline as compared to controls. The uptake of labeled hydroxyproline was used as a measure of collagen synthesis during the fourteen day treatment. Cultures subjected to the pulsed DC fields demonstrated a 20% increase in DNA and a 100% increase in hydroxyproline. This indicated that there was a faster rate of collagen synthesis using the pulsed electric field. Norton and Moore (1972) cultured rat parietal bone in an electric field created by a grid system which was capable of delivering up to 700 volts. Unidirectional pulsed fields were found to alter the normal growth patterns: bone grown in the field had disoriented trabeculae and had a faster metabolic rate, although labeled thymidine studies indicated that the field had little effect on cellular DNA manufacture. New bone matrix was deposited on negatively charged surfaces in culture. This was seen nearest the positive grid because this grid attracted a negative potential on the bone surface closest to it.

Alveolar Bone and Tooth Movement

The results of the experiments to date seem to indicate that the "trigger" for bone remodeling is either a current-induced or a

field-related event. Cochran et al. (1967) and Gillooly et al. (1968) have demonstrated an electric potential in alveolar bone as a result of forces placed upon the teeth. Utley (1968) summarized the numerous studies of bone in response to tooth movement, but the question of how mechanical forces are transduced into cellular responses remains unanswered.

DeAngelis (1970) used the various piezoelectric data to suggest how bone might respond to stress transmitted from a tooth undergoing orthodontic movement. Using rats labeled with tritiated proline, DeAngelis examined the areas of newly deposited bone matrix around the moving tooth and in the marrow cavity. The bone on the tension side was labeled with tritiated proline, while that on the pressure side was not. Within the marrow spaces, the bone surfaces closest to the moving tooth were labeled on the pressure side and unlabeled on the tension side. Daprano (1971) and DeAngelis agreed that since the alveolus might easily be distorted by the pressures of tooth movement (Baumrind, 1969), a resultant stress pattern could alter the local electric environment because of the piezoelectric nature of bone. This alteration in the electric environment would then act to regulate the differentiation of bone cells and subsequent alveolar bone changes characteristically seen during tooth migration.

Since there is evidence that electric currents are associated with the functional remodeling of bone, and since remodeling is known to occur during orthodontic movement, it is tempting, therefore, to infer that tooth movement may be, at least

in part, associated with bioelectric currents. The purpose of the present investigation is to characterize the relationship between certain electric currents and tooth movement.

Since the present investigation measures the amount of tooth movement, it will be necessary to know how a tooth normally moves under orthodontic forces. Burstone (1962), among others, described the characteristic phases of tooth movement when a relatively constant force was applied to a tooth as: 1) the initial phase, 2) the lag phase, and 3) the post-lag phase. Burstone found that during the initial phase, there existed a period of rapid tooth movement. This rapid rate was attributed to compression of the periodontal membrane. As the membrane was compressed further, areas of devitalization occurred in the regions of maximum stress. The lag phase was characterized by a reduced rate of tooth movement which Burstone attributed to the presence of the devitalized tissues impeding the movement of the tooth. The lag phase was followed by the post-lag phase during which time tooth movement proceeded again. Burstone related the removal of these devitalized areas by osteoclasts to the increased rate of tooth movement normally seen in this final phase.

METHODS AND MATERIALS

General Description

Twelve male cats with complete permanent dentitions were employed. The lower first premolars were extracted in order to permit mesial orthodontic movement of the lower second premolars by specially designed sectional appliances. Platinum-iridium electrodes were implanted in the alveolar bone mesial and distal to the second premolars. The electrodes were attached to coiled stainless steel leads which were covered with a non-conductive tubing. The percutaneous leads exited the nape of the neck and were connected to a battery pack and a constant-current circuit which was immobilized by a leather harness. The circuit was calibrated (Friedenberg et al., 1970) to deliver a constant 10 μA current. The amount of tooth movement was measured both directly and from radiographs at weekly intervals for five weeks. A histologic survey was done at the end of the fifth week. Statistical analysis of the various treatment effects was carried out by way of a balanced incomplete block analysis of variance.

Experimental Design

The present study tested the effects of three treatments on the rate of tooth movement. In statistical terms, the mandible of each cat constituted two plots--the left and right quadrants. Obviously, therefore, only two of the three treatments could be

assigned to any one cat, and identical treatments could never be found in the same cat. Pairs of treatments were assigned randomly (Table 1), subject to the restriction that each treatment appear a total of eight times. A further discussion of the treatment assignments and statistical analysis employed in the present study is found at the conclusion of Methods and Materials (Data Reduction).

The three treatments, A, B, and C, can be described as follows: treatment A consisted of implanting the anode distal to the root of the second premolar and the cathode near the canine (Figure 1); treatment B employed the same configuration, but the polarity was reversed; and in treatment C electrodes were implanted as before, but no current passed.

Tooth Movement Apparatus

The sectional arch , presented in Plates I and II, was fabricated using a one centimeter length of .007 x .036" open stainless steel coil anchored in place by a .022" stainless steel wire which bridged between the canine and the first molar. The distal end of each sectional arch terminated in a right angle bend which fit into a notch cut in the molar. The other end encircled the gingival third of the canine. A small hole was made in the mesial cusp tip of the molar, and .010" ligature wire was used to fasten the .022" anchor wire to the molar. After etching the molar and canine with 55% phosphoric acid for one minute, the appliance was cemented to the teeth using Sevriton (Claudius Ash, Inc., Niagara Falls, New York) with a brush-on technique (Nagel, 1972).

TABLE 1

TREATMENT ASSIGNMENTS

Cat	Quadrant	
	Right	Left
6	C	B
7	A	B
12	C	A
8	C	A
1	C	B
2	A	B
4	B	A
11	A	C
5	B	A
10	B	C
3	A	C
9	B	C

Treatment: A--Anode distal, cathode mesial
B--Cathode distal, anode mesial
C--No current

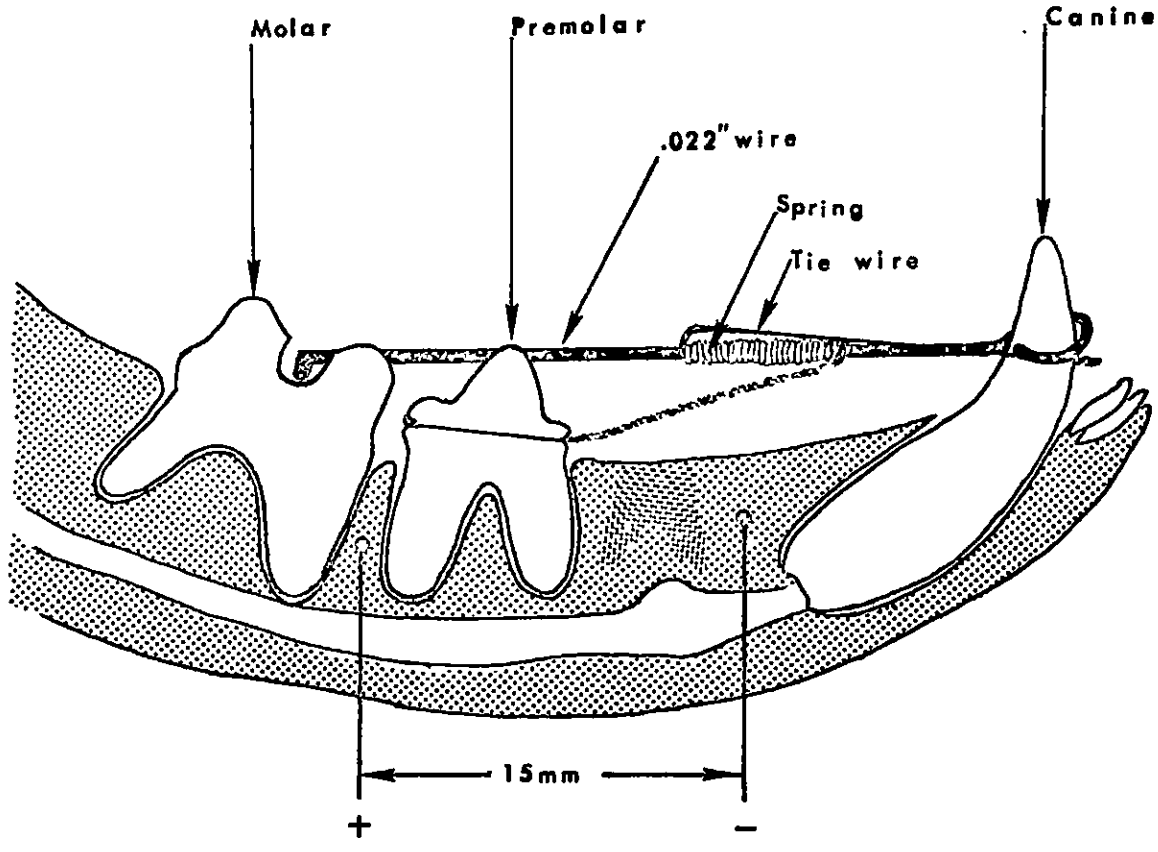


Figure 1.--Electrode placement for treatment A (right side)

The second premolar was notched with a small round bur around the gingival margin in order to hold a .010" ligature tie. This wire connected to the mesial portion of the open coil spring. The spring was fully compressed by a ligature tie from the distal of the coil spring to the cuspid and was activated weekly to approximately 6 ounces. The cusp tip of the maxillary premolar was flattened in order to avoid any occlusal interferences.

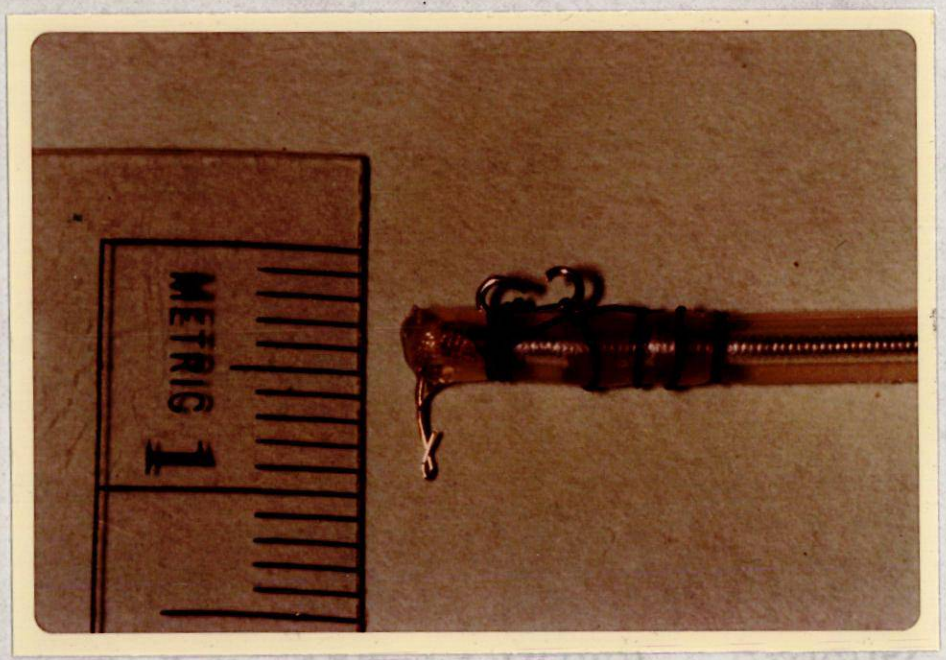
The .022" anchor wire ran parallel to the lingual surfaces of the lower teeth. Two shallow notches (15 mm apart) were made in the .022" wire for the purpose of determining, subsequently, the amount of magnification in the radiographs.

Electrodes and Leads

The electrodes, as seen in Plate III, were made from .010" Teflon-coated platinum-iridium (90:10) wire (Medwire Corp., Mount Vernon, New York). A small piece of this wire was attached to a lead wire by using stainless steel solder. Each lead (Medtronic, Inc., Minneapolis, Minnesota) was eight inches long and was made of a helical coil of stainless steel wire covered with an insulated tubing. The electrodes were made following the steps outlined in Figure 2. Silk suture (3-0) was tied around the insulation at the level of the small drops of acrylic in order to insure an immoveable connection between the insulation and the helical lead wire. This same suture was used to tie in a small wire to be used as an anchor point for the lead.

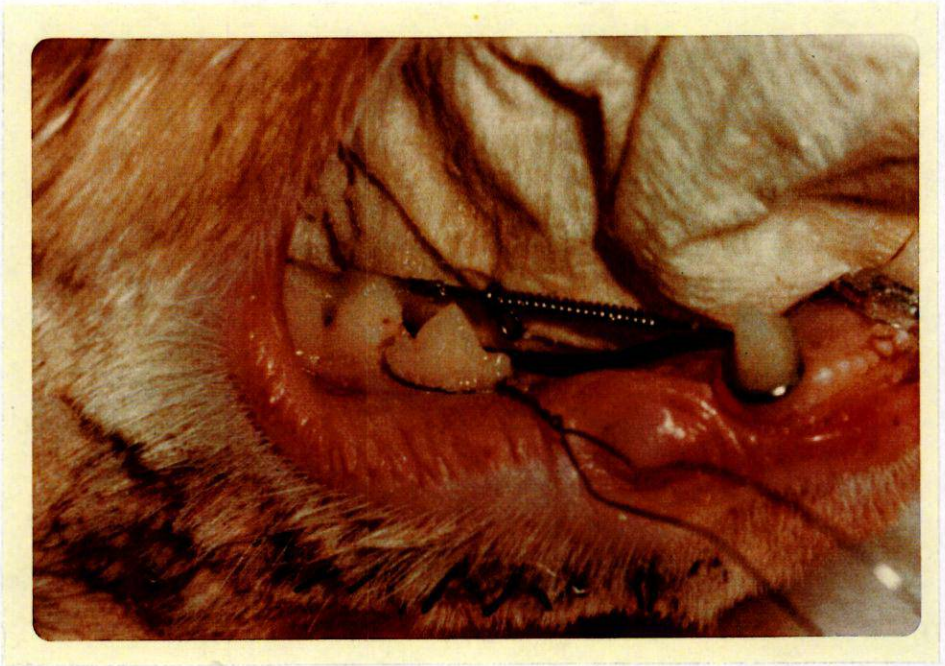
A right angle bend was placed in the electrode at the end

PLATE III



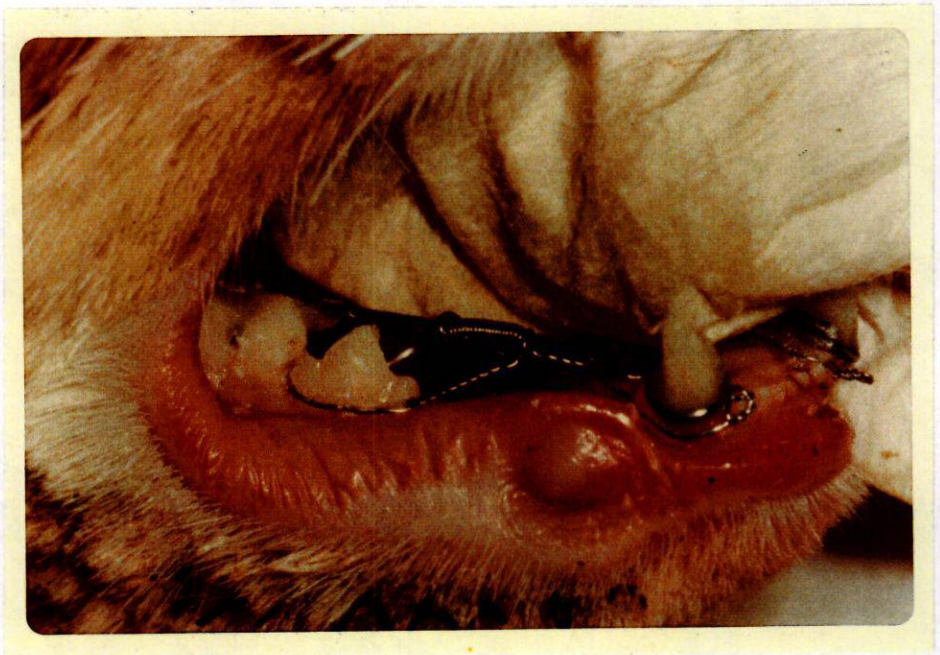
ELECTRODE AND LEAD

PLATE I



TOOTH-MOVING APPARATUS

PLATE II



TOOTH-MOVING APPARATUS--ACTIVATED

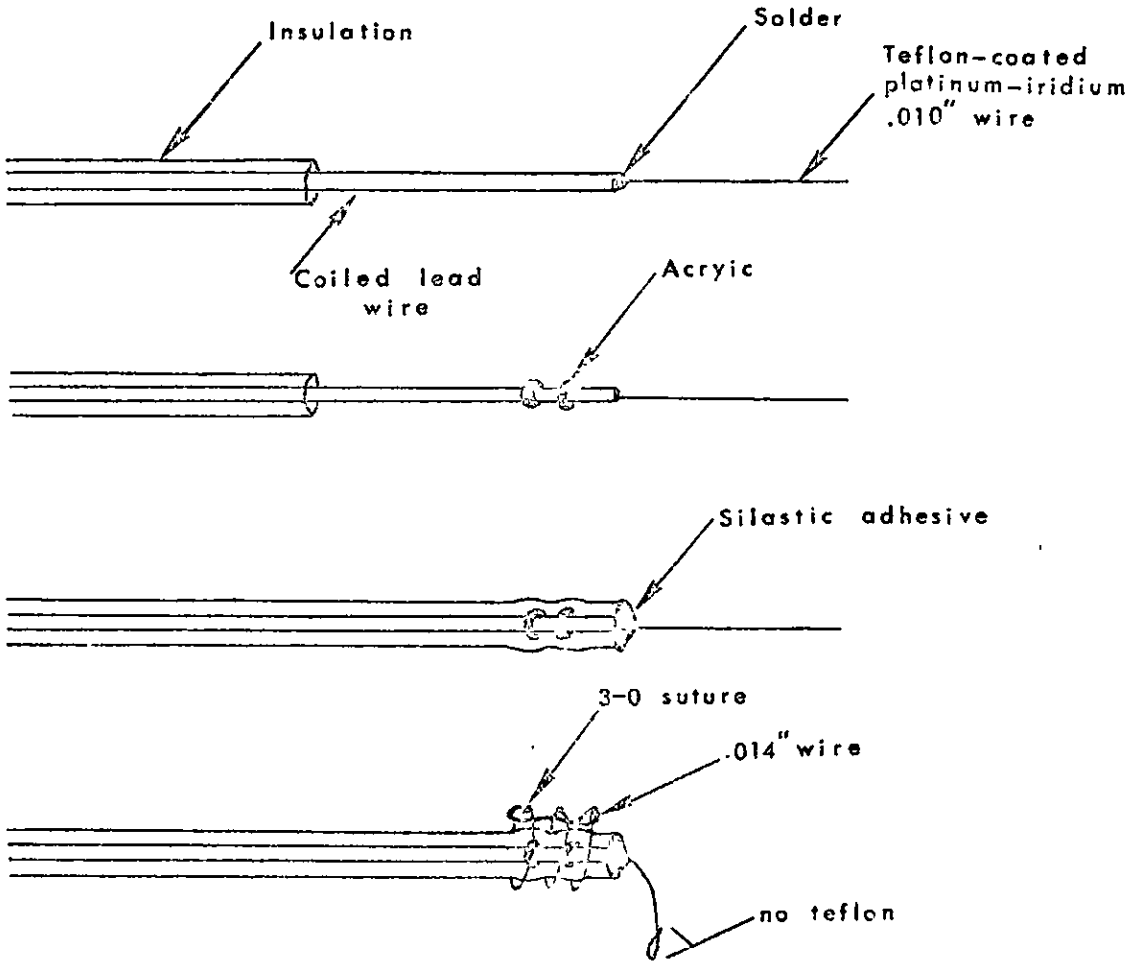


Figure 2.--Construction of electrode

of the insulation tubing. The electrode was cut at 6 mm, and the Teflon coating was stripped from the terminal 2 mm. The last 2 mm were bent into a crushed loop so that the overall length of the electrode was 4.5 mm.

Interface Fabrication

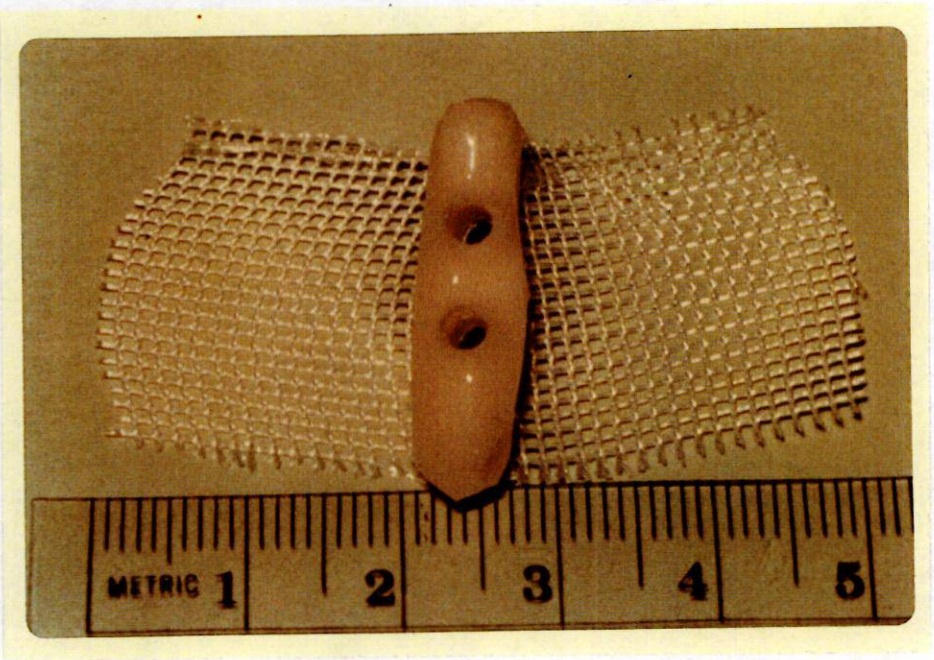
The leads extended percutaneously from the mandible to the back of the neck caudal to inion. They penetrated the skin through an interface made of dacron mesh and Silastic (Plate IV). Each interface was constructed by folding a piece of dacron cloth in half and placing metal rods, the same diameter as the lead wire, through the mesh. Silastic 382 (Dow Corning, Midland, Michigan) was applied to the mesh to form a cylinder of Silastic at the fold. Removal of the metal rods left holes for the lead wires (Figure 3).

Surgical Implantation of Electrodes, Leads, and Interface

The cat was anesthetized with sodium pentobarbital (35 mg/kg). After routine shaving and cleansing, a two centimeter incision was made in the midline of the back of the neck caudal to inion. Another incision was made over the inferior border of the body of the mandible. This incision was made from the molar region to the mental foramen. The periosteum was reflected in this region. A blunt probe was inserted subcutaneously and passed to the incision on the back of the neck. This probe was then used to thread the leads from the mandible to the neck.

Two divergent holes (0.7 mm) were drilled between the

PLATE IV



INTERFACE

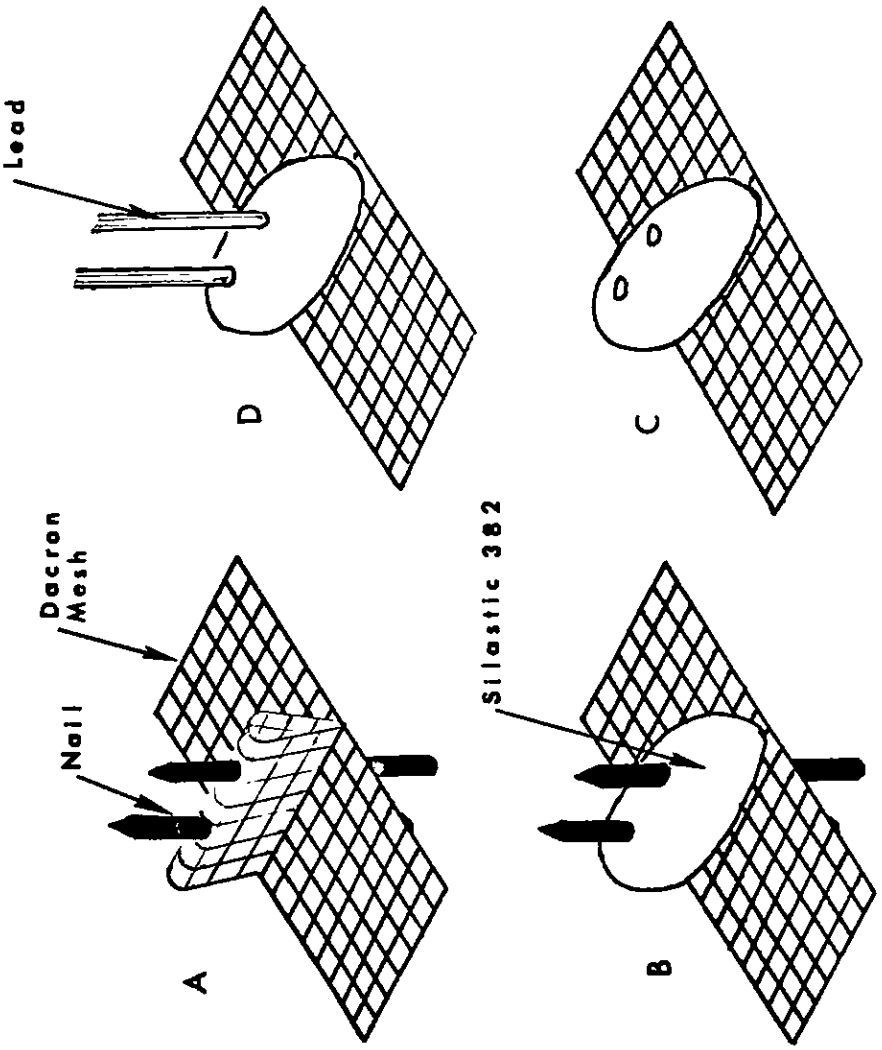


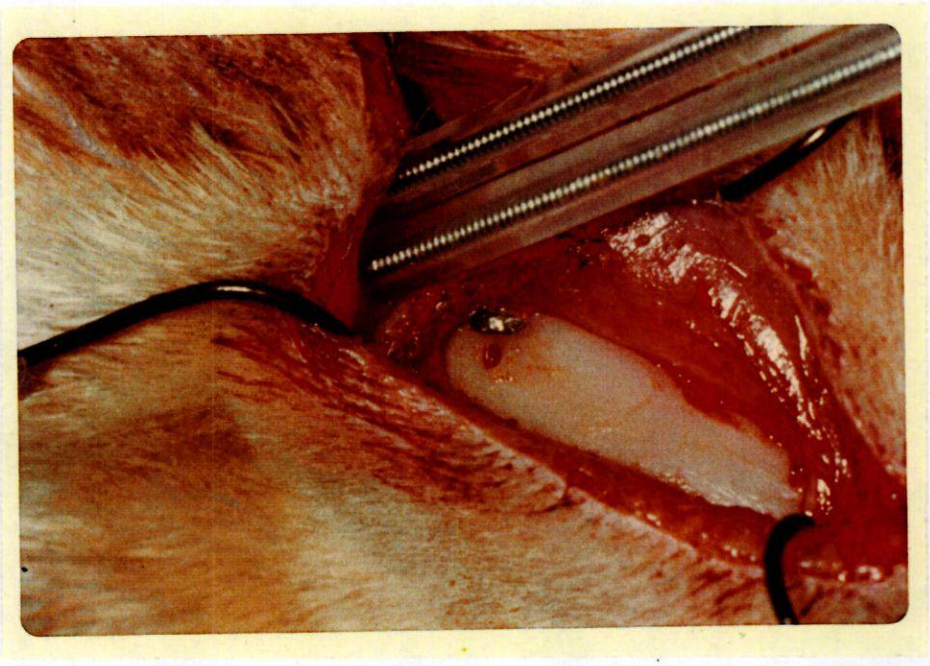
Figure 3.--Construction of interface

second premolar and molar roots and distal to the mental foramen, and tight-fitting platinum-iridium pins were driven into each hole so as to leave about 2 mm exposed (Plate V). These pins were used as anchors to secure the electrodes. Another hole, 0.5 mm in diameter, was drilled between the second premolar and the molar roots slightly superior to the first hole. The "distal electrode" was placed in this hole and fastened with suture to the 0.7 mm pin (Plates VI and VII). The hole for the "mesial electrode" was drilled near the canine root at a standardized distance of 15 mm from the distal electrode. All holes extended through the buccal cortical bone and into the cancellous bone, but never deep enough to penetrate the lingual cortical plate.

After both electrodes were fastened with suture to the anchor pins, a fast setting cranioplastic acrylic (L. D. Caulk, Milford, Delaware) was used to cover and to attach both electrodes securely to the pins (Plate VIII). After the acrylic had cured, this area was washed with saline and the incision was closed by interrupted 3-0 silk suture (Plate IX).

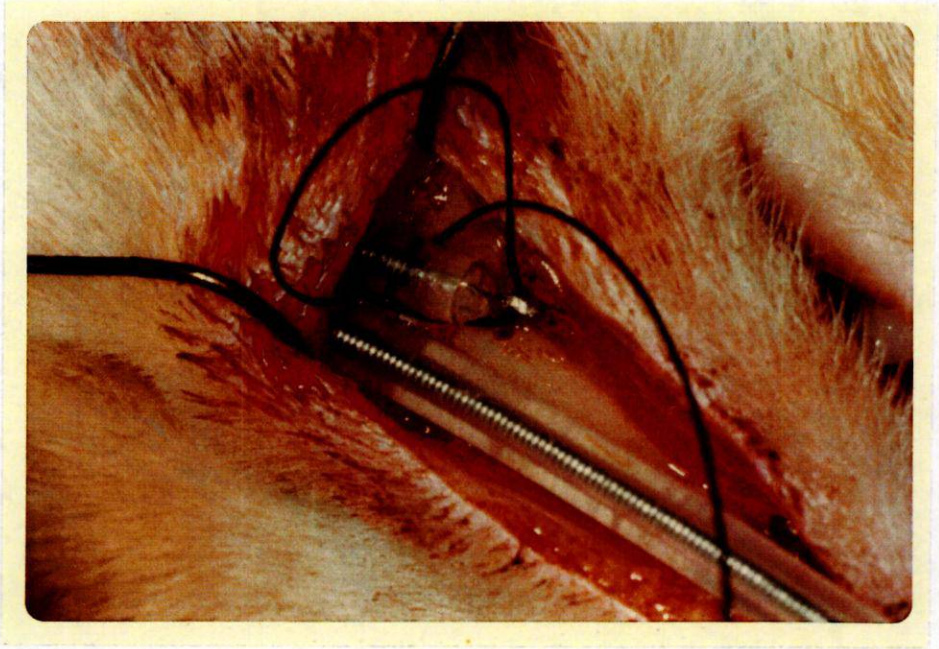
The leads were threaded through the interface which was then inserted into the incision on the back of the neck while the dacron flaps were spread laterally under the dermis. After healing was complete, the mesh produced an excellent mechanical lock (Gertler et al., 1971). In addition, sutures were placed through the cylinder of Silastic and were secured to the adjacent skin. The lead wires were sealed to the interface with an abundant amount of Silastic Medical Grade A Adhesive (Dow Corning, Midland,

PLATE V



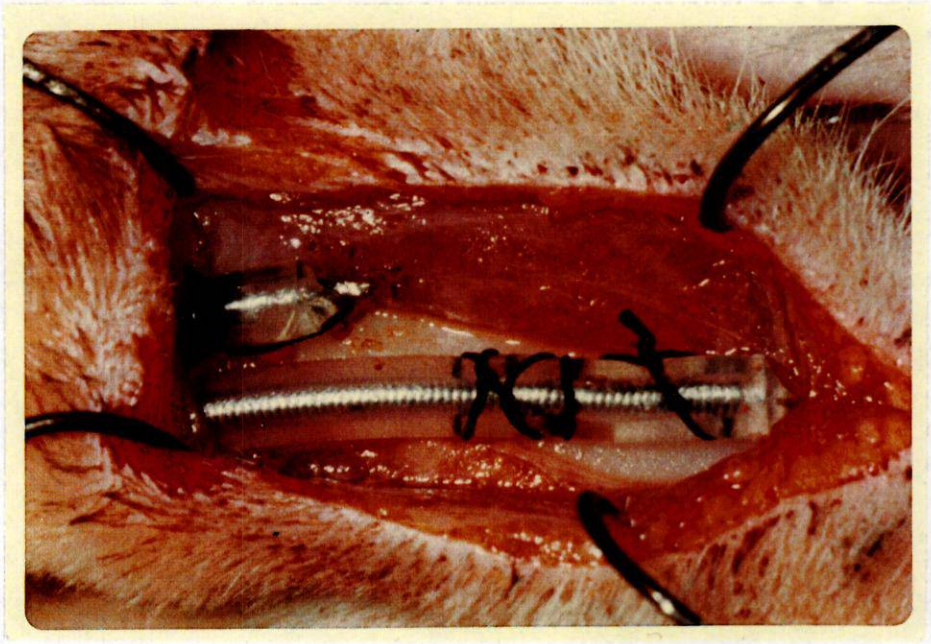
SURGICAL PROCEDURE--ANCHOR PIN IN PLACE

PLATE VI



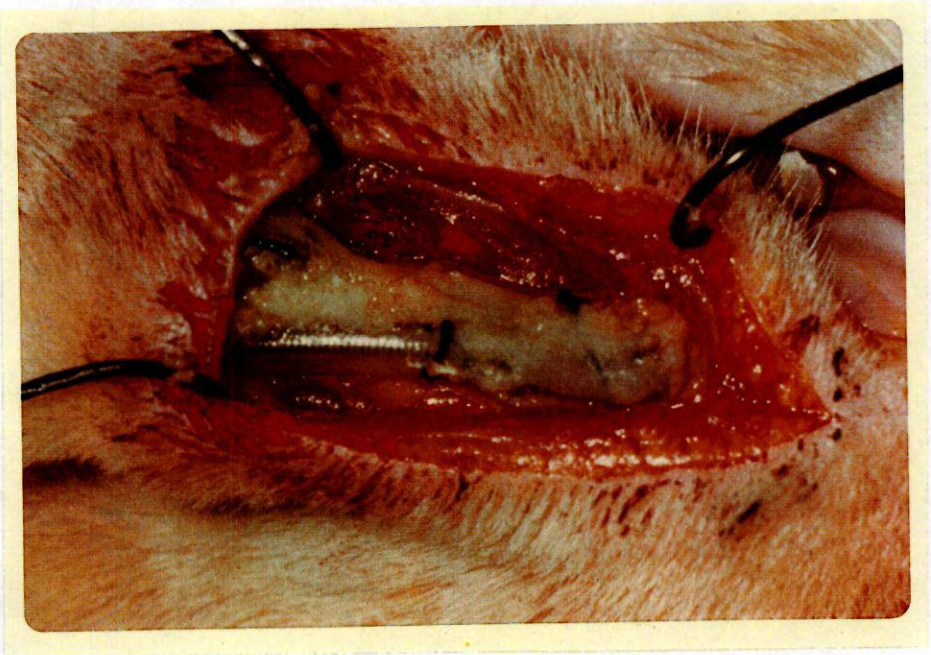
SURGICAL PROCEDURE--ELECTRODES BEING ATTACHED

PLATE VII



SURGICAL PROCEDURE--ELECTRODES ATTACHED

PLATE VIII



SURGICAL PROCEDURE--ACRYLIC COVERING ELECTRODES

PLATE IX



SURGICAL PROCEDURE--CLOSURE

Michigan) (Plate X).

Power Unit

Each unit contained a 7 volt mercury battery (Union Carbide Corp., New York, New York) and was designed to deliver a constant current (Figure 4). Once the variable resistor was set so that the circuit delivered 10 μA, the circuit continued to deliver the same current in the face of slight variations in output resistance. Each circuit was encased in a plastic mini-box which was attached to a leather animal harness (Plate XI).

Each power unit was checked prior to, and at termination of, the experiment. Measurements of the voltage drop across the electrodes and across the measuring resistor were made weekly during the experiment. Adjustments in the variable resistor were made if necessary in order to keep the amperage centered at 10 μA.

Cephalostat

A head holding device was designed to permit reliable repositioning of the mandible for serial roentgenographic measurements. Accordingly, it was necessary to ensure that the source-film distance (123 cm) and object-film distance (≈ 6.5 cm) were kept constant for a given animal (Plate XII).

The head of the cat was held secure by two orbital rods and a palatal bar (Plate XIII). The hard palate, the orbital rims, and the incisors were used as landmarks to continually reposition the head in the cephalostat. The cat's head was turned 20 degrees from the mid-saggital plane so that the alveolar ridge was parallel to

PLATE X



BATTERY PACK AND ELECTRODES IN PLACE

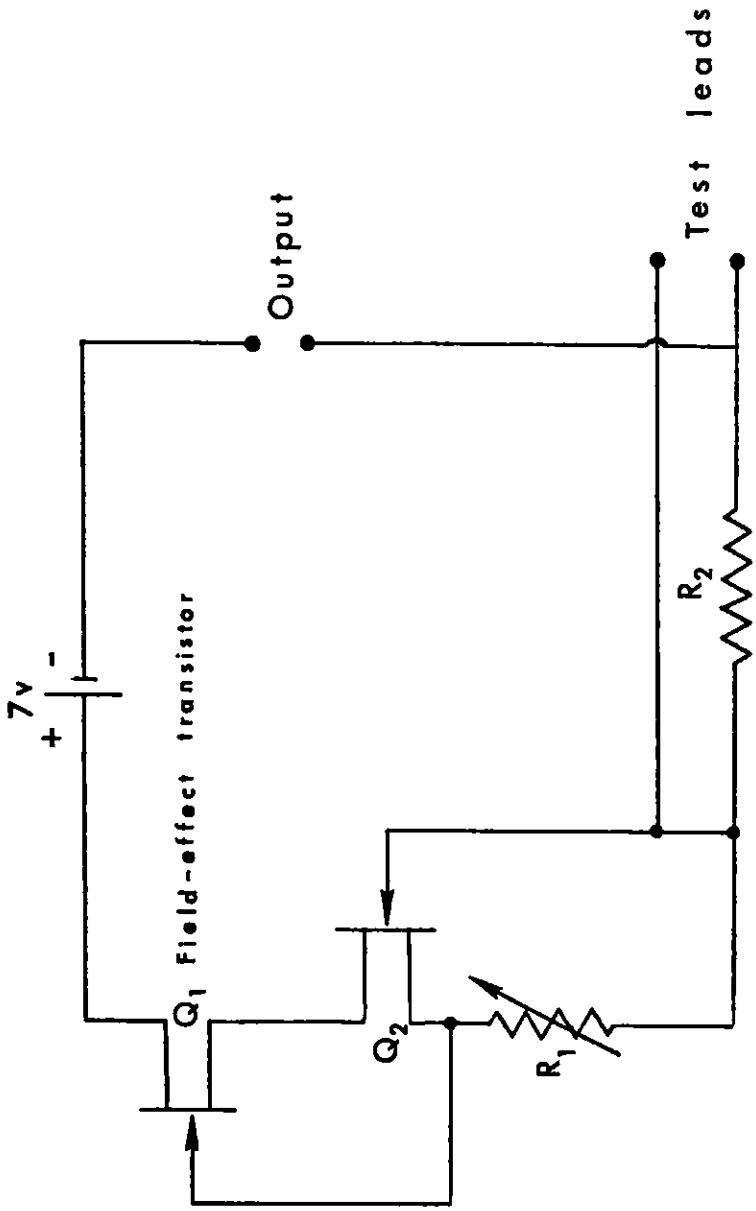
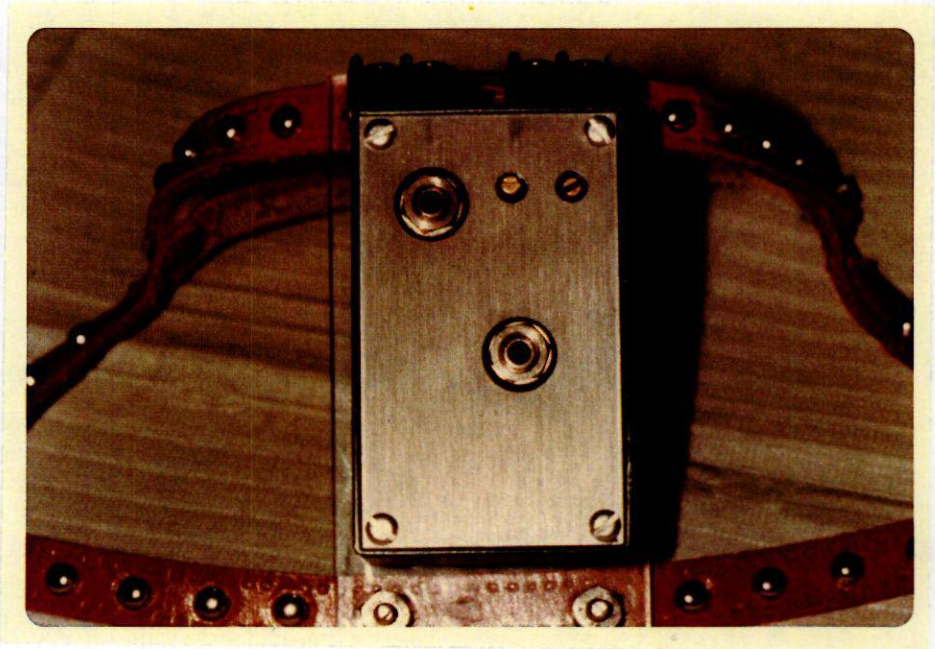


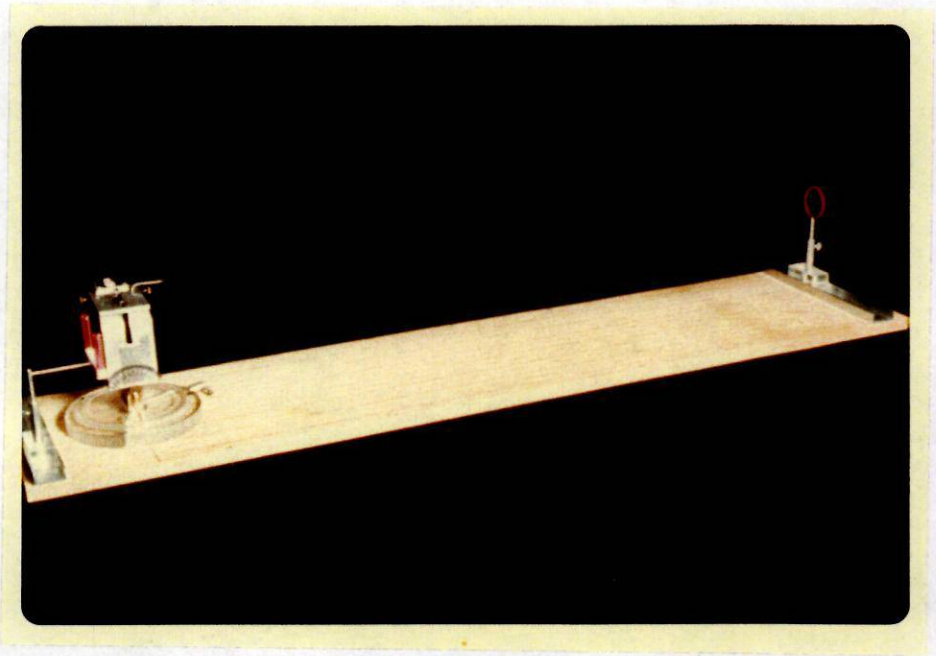
Figure 4.--Diagram of circuit (from Friedenberg et al. 1970)

PLATE XI



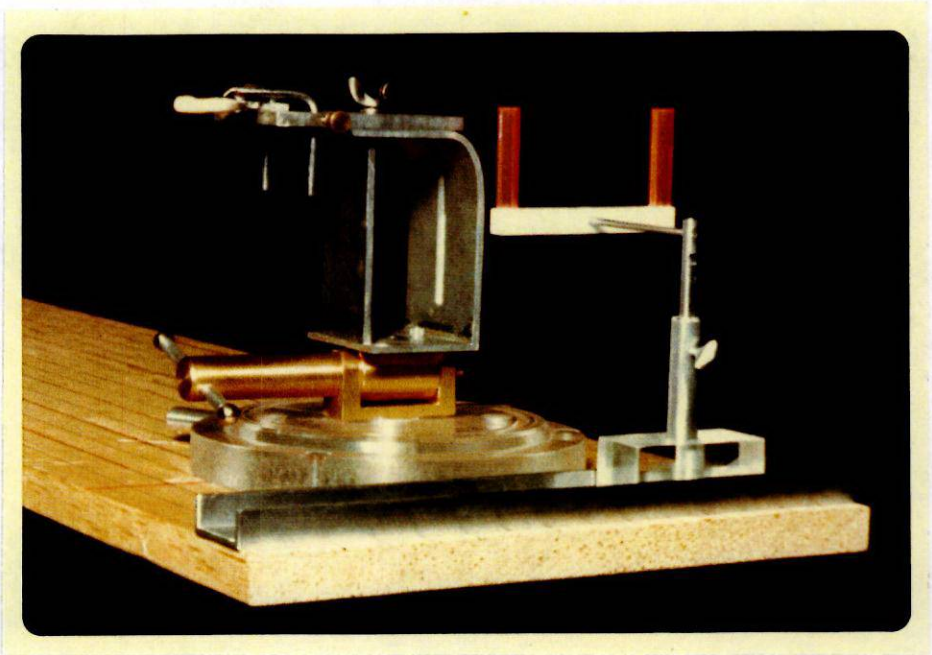
BATTERY PACK AND LEATHER HARNESS

PLATE XII



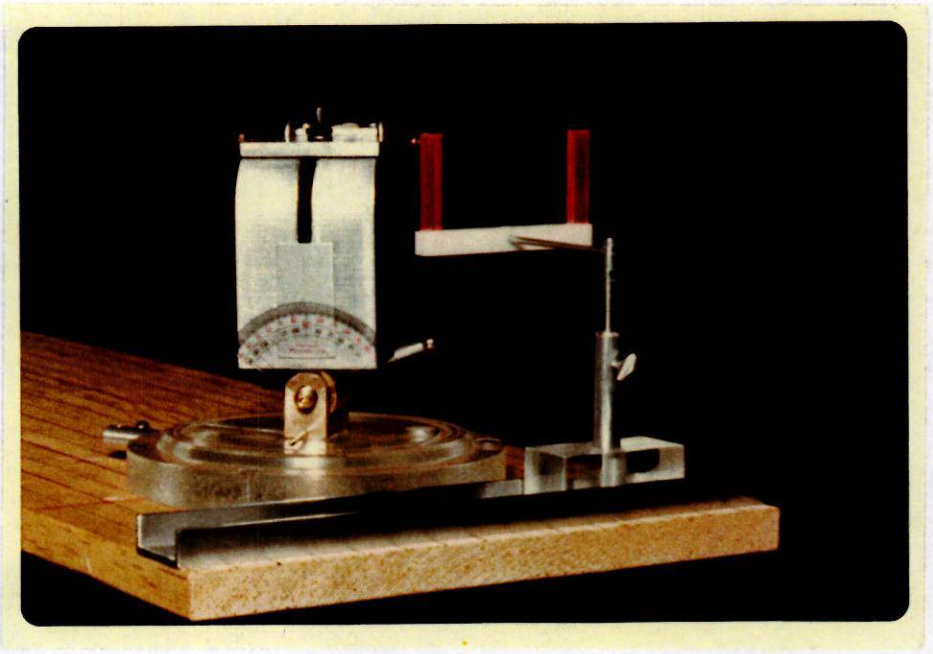
CEPHALOSTAT

PLATE XIII



CEPHALOSTAT

PLATE IV



CEPHALOSTAT

the film and was rotated 10 degrees so that the teeth closest to the film would be lower (Plate XIV). Both the film and the dental ridge were perpendicular to the central ray of the x-ray beam. An exposure of 4 seconds at 90 KVP and 15 mA proved adequate.

Measurements of Data

The amount of movement of the second premolar was determined in two ways. A direct intra-oral measurement was taken from the notch on the molar to the notch on the premolar. The notches were made with a small bur close to the gingival margin and centered on the tooth mesial-distally. This was a recording of the linear crown movement in a tipping fashion (Figure 5).

The use of cephalometric x-rays provided the second method of recording tooth movement. A measurement was taken from the mesial root of the premolar (Figure 6). In each case, it was taken slightly below the cemento-enamel junction at the crest of the interseptal bone. In most cases, this distance was perpendicular to the long axis of the interseptal bone. This approximated, to a degree, bodily movement, rather than tipping movement, since it was taken closer to the center of rotation (Figure 7). The average amount of magnification in the roentgenographs was calculated from images of the notches in the sectional wire and all measurements were adjusted appropriately.

Both sets of measurements represented the total amount of tooth movement in five weeks time.

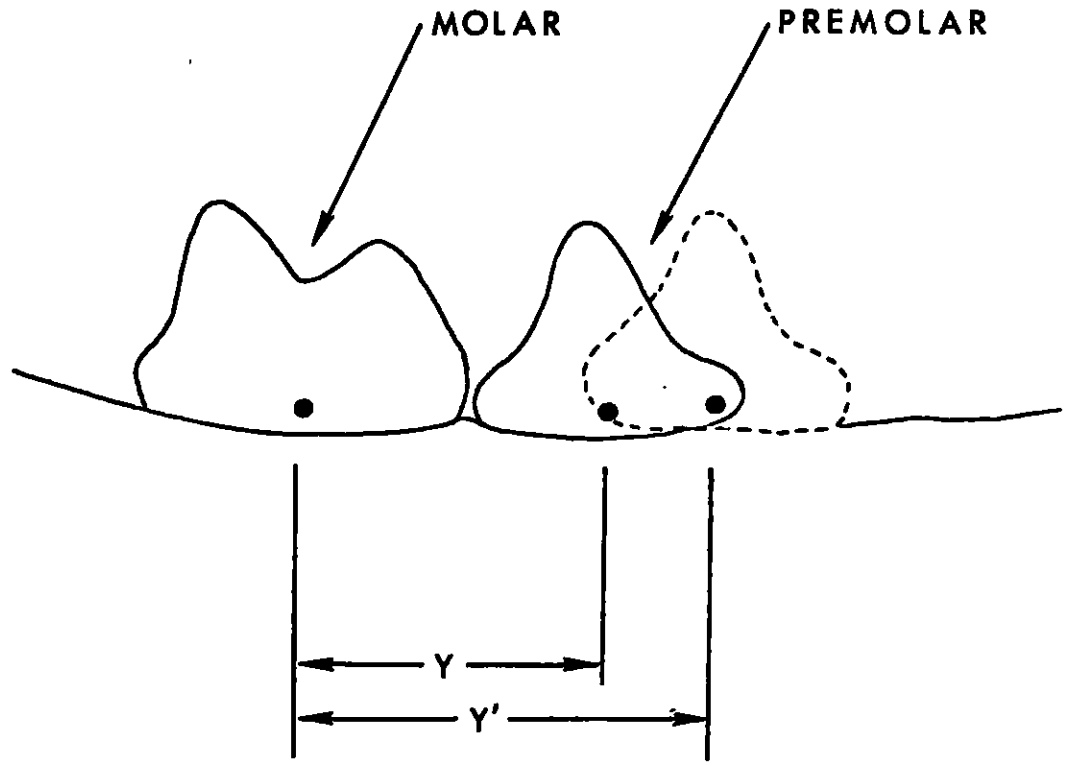


Figure 5. Intra-oral recording landmarks
(Right Side)

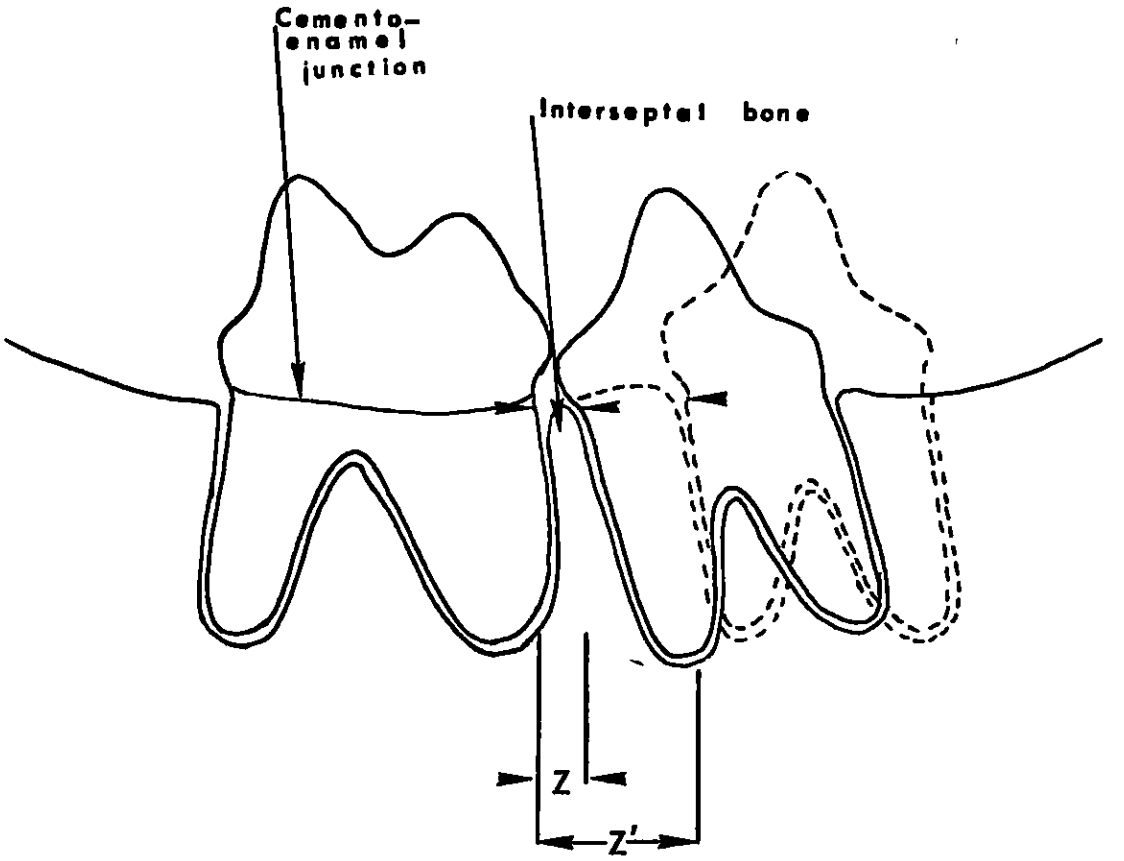


Figure 6.--Radiographic recording landmarks

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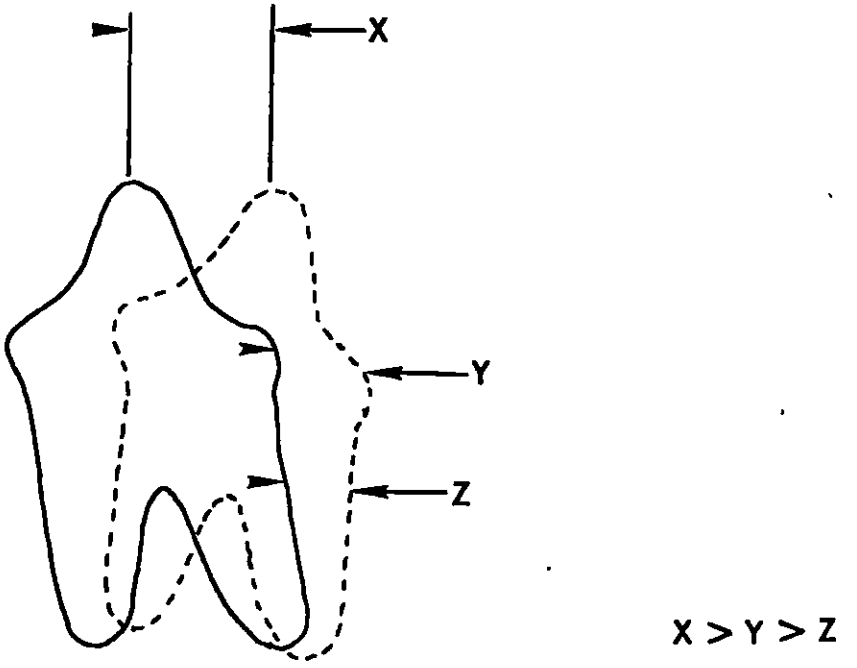


Figure 7.--Inherent discrepancy in measurement techniques

Data Reduction

Since each block had two plots, all three treatments could not be performed on the same animal at one time. Accordingly, the investigation was cast in the form of a balanced incomplete block design, as may be seen in Cochran and Cox (1957). The basic design in this situation consists of three treatment pairs (AB, AC, BC) assigned randomly to three cats. To increase the power, this paradigm was repeated four times so that the entire experiment consisted of twelve blocks and three treatments; replications and repetitions were not kept separate.

To test for treatment differences, an analysis of variance was performed on the cumulative amount of tooth movement at the end of five weeks.

Formulae and symbols used in the balanced incomplete analysis of variance are presented in Appendix I.

RESULTS

The results of this investigation are presented in three categories: 1) intra-oral measurements, 2) radiographic measurements, and 3) general histologic survey.

Intra-oral Measurements

The amount of crown movement occurring at the end of each week is presented in Tables 2 through 4 and depicted in Figures 8 and 9. Generally, there was an initial phase of rapid tooth movement followed immediately by a phase characterized by a decreased rate of tooth movement (the "initial" and "lag" phases, respectively). After this lag phase, the rate of tooth movement generally increased slowly for the remaining weeks.

Comparative Description

Although individual contrasts are not justified, it should be noted that premolars closer to the cathode (treatment B) had a delayed initial phase and took twice as long to begin the lag phase. Teeth closer to the anode (treatment A) had, on the average, a rapid initial phase and a less apparent lag phase. The mean distance moved in five weeks was the greatest with treatment A.

Analysis of Variance

The results of the analysis of variance of the intra-oral

TABLE 2

INTRA-ORAL MEASUREMENTS
TREATMENT A--ANODE DISTAL
(millimeters)

	Weeks					
Cat	1	2	3	4	5	Total
2	1.47	1.50	1.25	1.94	.41	6.57
3	.51	.08	.21	.08	.18	1.06
4	.34	.30	-.01	.06	.37	1.06
5	.74	.23	1.05	.76	.64	3.42
7	.34	1.02	.50	.95	1.13	3.94
8	.58	.16	.03	.47	.75	1.99
11	1.08	1.27	1.24	.72	1.43	5.74
12	.84	.74	1.21	.51	.80	4.10
Total	5.90	5.30	5.48	5.49	5.71	27.88
$\bar{X}$*	.74	.66	.68	.69	.71	3.48

*Rounded where necessary to the nearest hundredth

TABLE 3

INTRA-ORAL MEASUREMENTS
TREATMENT B--CATHODE DISTAL
(millimeters)

	Weeks					
Cat	1	2	3	4	5	Total
1	-.03	.75	-.07	.57	.57	1.79
2	.78	1.55	.37	.60	1.27	4.55
4	.15	.27	.14	-.04	.05	.57
5	.37	.76	.96	.70	.53	3.32
6	.64	.41	.73	1.38	.86	4.02
7	.16	.52	.11	.75	1.88	3.42
9	.46	.43	.76	.99	.93	3.57
10	.27	1.01	.95	1.04	1.37	4.64
Total	2.80	5.70	3.95	5.99	7.46	25.88
$\bar{X}^*$	.35	.71	.49	.75	.93	3.23

*Rounded where necessary to the nearest hundredth

TABLE 4

INTRA-ORAL MEASUREMENTS
TREATMENT C--CONTROL
(millimeters)

	Weeks					
Cat	1	2	3	4	5	Total
1	.95	.10	.51	.21	1.06	2.83
3	.33	.04	.15	.18	.20	.90
6	.53	.09	1.05	.47	.60	2.74
8	.85	.17	.24	.78	.61	2.65
9	.71	.69	.13	.20	.73	2.46
10	.65	.47	.55	.40	1.06	3.13
11	1.90	.88	.82	1.02	1.28	5.90
12	.43	.72	.96	1.22	.43	3.76
Total	6.35	3.16	4.41	4.48	5.97	24.37
$\bar{X}^*$	.79	.40	.55	.56	.75	3.05

*Rounded where necessary to the nearest hundredth

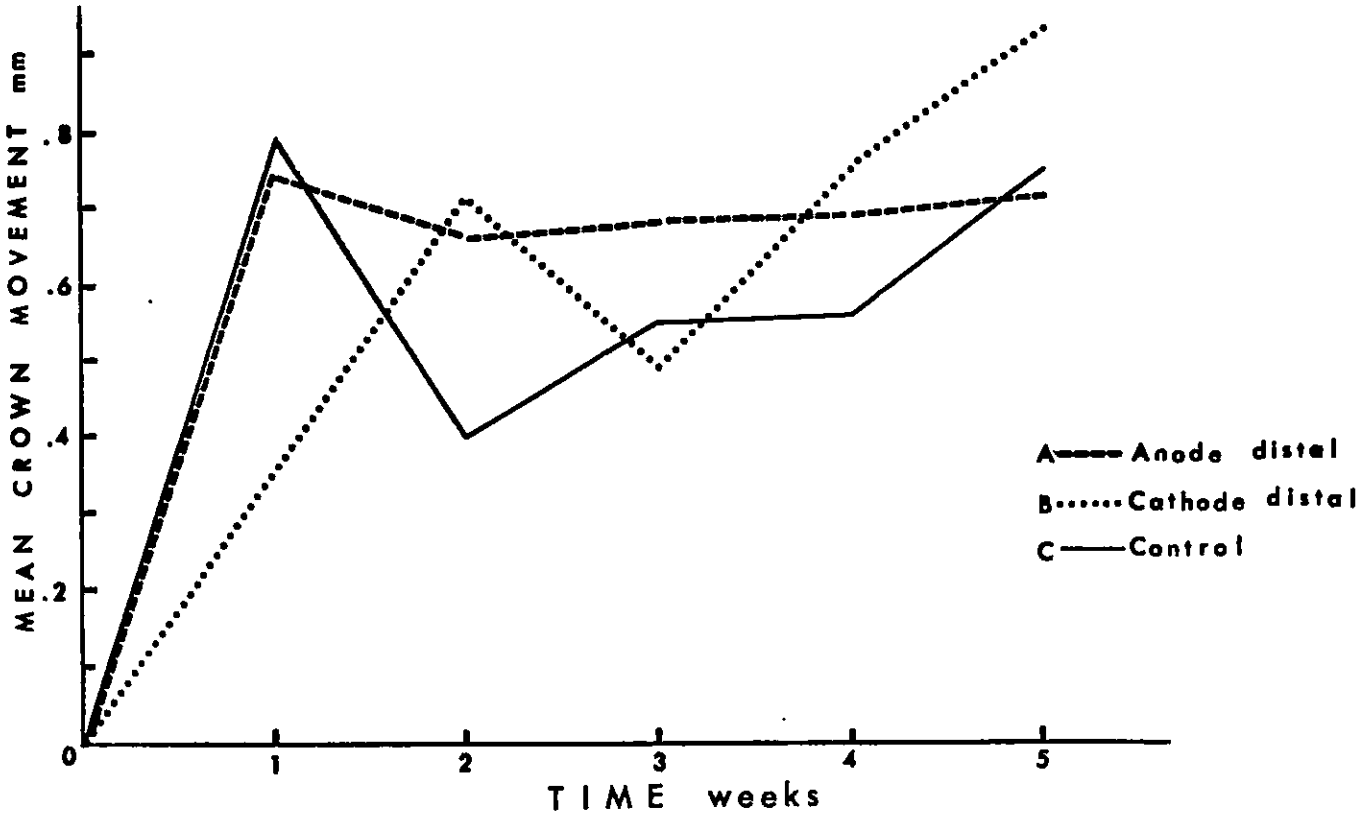


Figure 8.--Average weekly tooth movement intra-oral measurements

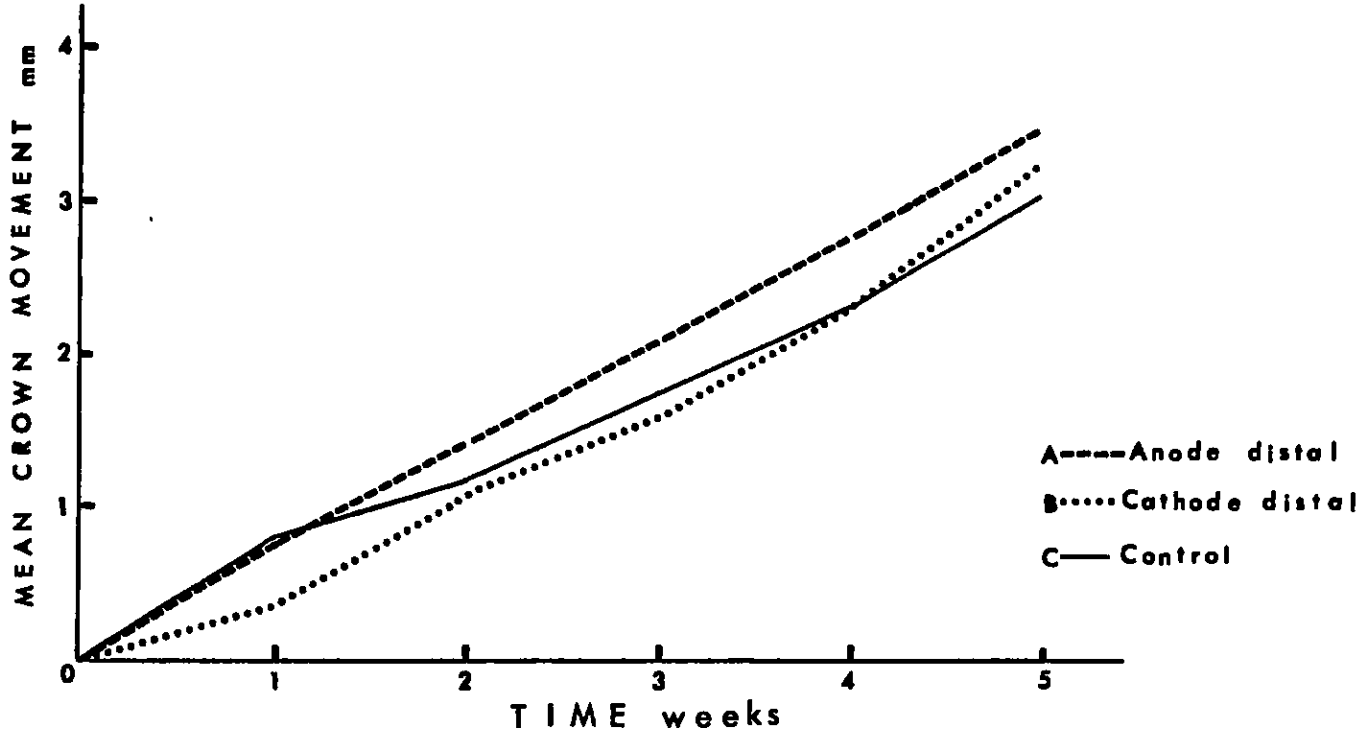


Figure 9.--Average weekly cumulative movement intra-oral measurements

data are listed on Table 5. The null hypothesis could not be rejected.

Radiographic Measurements

The amount of tooth movement occurring in each weekly period is summarized on Tables 6 through 8; the means are Figures 10 and 11. Because of the tipping, the root movement was less than the crown movement. The characteristic initial and lag phases were not readily detected in the average root movement. The rate of root movement generally increased throughout the course of the experiment.

Comparative Description

Although detailed comparisons among treatments are, again, not justified, it should be noted that apparent differences could be visualized graphically at three weeks, but not at five weeks.

Analysis of Variance

The results of the analysis of variance for the radiographic measurements are listed in Table 9. Because the null hypothesis could not be rejected, no treatment comparisons were attempted.

Histologic Survey

Mandibles were fixed in 10% neutral formalin, decalcified for ten days in 90% formic acid, sectioned at 10 μ, and stained with H and E using routine histologic procedures. Each section was oriented so as to bisect the tooth and at the same time

TABLE 5

ANALYSIS OF VARIANCE: INTRA-ORAL DATA

Source		df	SSQ	MSQ
Treatments	Adjusted	2	.601	. .
	Unadjusted		.775	. .
Blocks	Adjusted	11	51.642	4.695
	Unadjusted		51.817	. .
Error		10	5.117	.512
Total		23	57.534	. .

VARIANCE RATIO

Source	df	MSQ	F
Adjusted treatment total per unit	2	.399	.60
Effective error	10	.659	

$F(2,10).95 = 4.10$

TABLE 6

RADIOGRAPHIC MEASUREMENTS
TREATMENT A--ANODE DISTAL
(millimeters)

Cat	Weeks					Total
	1	2	3	4	5	
2	.59	.40	.56	1.25	1.80	5.60
3	.38	.56	.22	.07	.01	1.24
4	.05	.18	.07	.02	-.03	.29
5	.44	.04	.25	.58	.08	1.39
7	.41	.22	.63	.53	.79	2.50
8	.29	.19	.16	.32	.40	1.36
11	.40	1.09	1.37	.05	.93	3.84
12	.29	.31	1.79	-.44	.60	2.55
Total	2.85	2.99	5.05	2.38	4.58	18.77
$\bar{X}$*	.36	.37	.63	.30	.57	2.35

*Rounded where necessary to the nearest hundredth

TABLE 7

RADIOGRAPHIC MEASUREMENTS
TREATMENT B--CATHODE DISTAL
(millimeters)

	Weeks					
Cat	1	2	3	4	5	Total
1	.01	.16	.12	.18	.39	.86
2	.09	.82	.85	.86	.57	3.19
4	.22	.21	.14	-.16	.28	.69
5	.02	.45	.15	.04	.84	1.50
6	.43	.45	.03	.37	.21	1.49
7	.52	.17	.27	.42	1.11	2.49
9	.09	.07	.10	.01	.70	.97
10	.02	.73	.25	.60	.57	2.17
Total	1.40	3.06	1.91	2.32	4.67	13.36
$\bar{X}$*	.18	.38	.24	.29	.58	1.67

*Rounded where necessary to the nearest hundredth

TABLE 8

RADIOGRAPHIC MEASUREMENTS
TREATMENT C--CONTROL
(millimeters)

	Weeks					
Cat	1	2	3	4	5	Total
1	.53	.09	.30	.12	.95	1.99
3	.23	.55	.08	.00	.18	1.04
6	.29	.22	.51	.05	.62	1.69
8	.04	.18	.17	.38	.46	1.23
9	.10	.25	.22	.09	.34	1.00
10	.01	.39	.07	.64	.42	1.53
11	.19	.28	.91	.64	1.40	3.42
12	.07	.27	.54	.92	.26	2.06
Total	1.46	2.23	2.80	2.84	4.63	13.96
$\bar{X}^*$	.18	.28	.35	.36	.58	1.74

*Rounded where necessary to the nearest hundredth

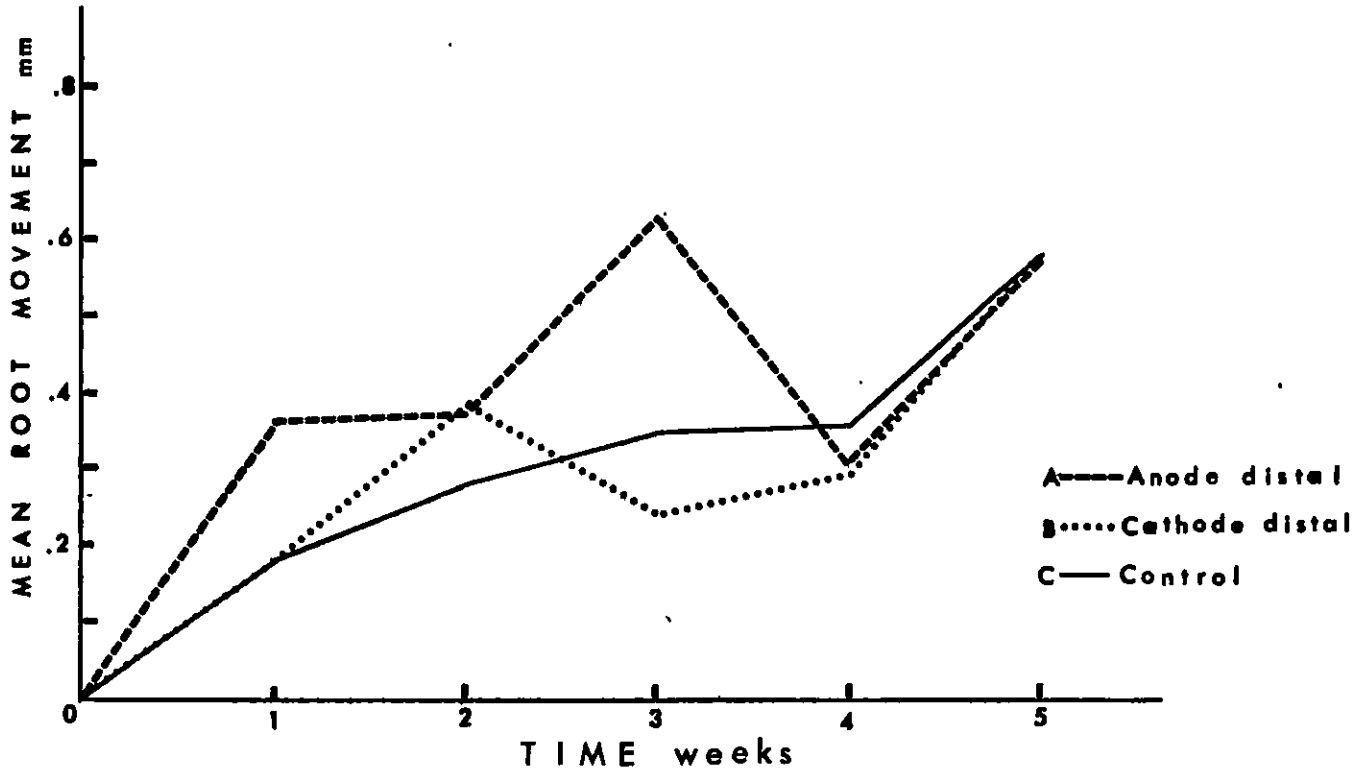


Figure 10.--Average weekly tooth movement radiographic measurements

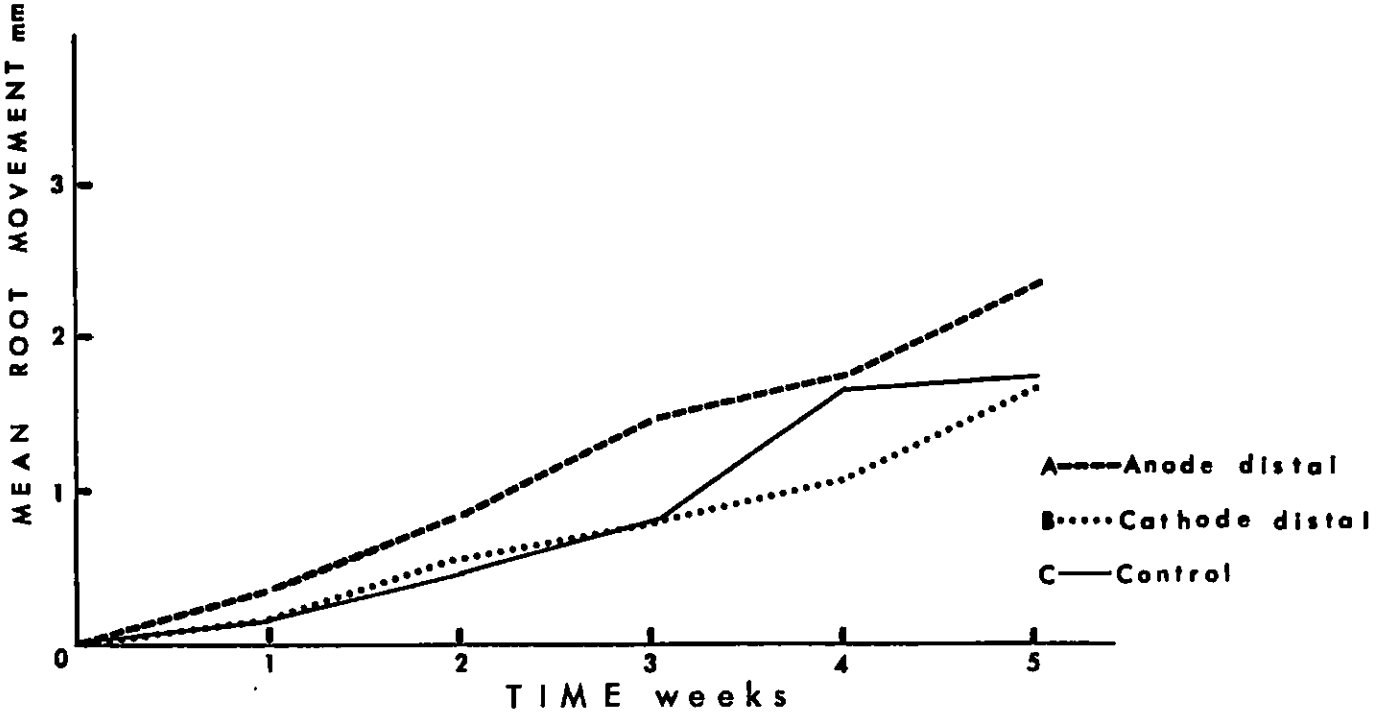


Figure 11.--Average weekly cumulative movement radiographic measurements

TABLE 9

ANALYSIS OF VARIANCE: RADIOGRAPHIC DATA

Source		df	SSQ	MSQ
Treatments	Adjusted	2	.713	. .
	Unadjusted		2.198	. .
Blocks	Adjusted	11	26.577	2.416
	Unadjusted		28.062	. .
Error		10	3.378	.338
Total		23	32.153	. .

VARIANCE RATIO

Source	df	MSQ	F
Adjusted treatment total per unit	2	.556	1.29
Effective error	10	.431	

$F(2,10).95 = 4.10$

parallel the body of the mandible. There was no attempt to quantify the results.

Controls

Most first premolars had been extracted at least three weeks prior to the initial experimental surgery. At the termination of the experiment, the extraction sites had filled in with organized connective tissue. Some osteoid was apparent and trabeculae had started to form. The pulps of most molars were either hyperemic or necrotic indicating that there had been severe trauma, probably resulting from the heat produced while drilling the hole in the crowns.

Only a few controls had obvious inflammatory cells around the electrode sites. There was some osteoclastic activity and remodeling of bone adjacent to the holes drilled for the posts and electrodes. A fibroblastic lining was usually present directly surrounding the electrodes and posts.

Most surfaces of bone mesial to the moving premolar showed the characteristic resorption of bone and compression of the periodontal ligament; the distal surfaces showed osteoblastic activity, especially proximal to the crown. There was generalized remodeling on most surfaces adjacent to the premolar.

Areas Near Anode

In many instances, the area around the anode was infiltrated with inflammatory cells. Micro-abscesses often occurred in this region, as well as a generalized area of hydropic degeneration.

Irregular margins of bone were indicative of osteoclastic activity and bone resorption. Many areas directly adjacent to the electrode were necrotic or fibrotic.

The bone surfaces surrounding the moving premolar appeared the same as those of the controls. On occasion, fewer trabeculae were observed around premolars closer to the anode (treatment A).

Areas Near Cathode

An inflammatory infiltrate could usually be seen in areas near a cathode, but to a lesser degree than around an anode. The areas of degeneration near the electrodes were usually walled off with fibroblasts. Bone destruction seemed to take place to a lesser degree around the cathode, as compared to the anode. Osteoblasts and trabeculae were generally more apparent. There was, however, no single characteristic which was uniformly correlated with any particular treatment.

In one case (#6L) there was a rapidly growing exophytic and pedunculated growth which contained many well organized trabeculae and abundant osteoblasts.

DISCUSSION

General

When an investigation does not show statistically significant results, a discussion of how and why this may have happened is in order. In the present experiment, there was a wide range of results. Some cats had teeth that moved very slowly regardless of the treatment. Utley (1968) has concluded that each cat has its own individual rate of tooth movement. This individuality in cats had a more important role in the rate of tooth movement than did the amount of force applied to the tooth. Hermanson (1972) concurred that the rate of tooth movement was correlated to the individual characteristic of each cat. The large amount of variance seen in the "blocks" (Tables 5 and 9) substantiates this finding. If the differences in cats were related to age, a future study might well be advised to use litter mates or animals with standardized ages.

The orthodontic appliance was designed to deliver a relatively constant force of six ounces. Each section of open coil spring was the same length and had the same number of turns. In addition, all springs were calibrated weekly. If, however, one tooth did move faster than the one on the other side, one spring would be compressed to a lesser degree than the other. This inequality would last until the next weekly spring calibration. In a one week period, this discrepancy of spring compression never exceeded 1.34 mm. This is the equivalent of about one

ounce in force. Boester (1972) could not demonstrate any significant difference in the rate of tooth movement between the five and eleven ounce force levels in humans, but the relationship in cats, though probably similar, has never been characterized.

The average overall movement of the crown was 3.26 mm, and movement of the root averaged 1.92 mm. The small size of these measurements maximizes the impact of any measurement error that might be present. In addition, variability of spring forces, surgical trauma, infection, friction, occlusion, and the small number of experimental units could overshadow any effects of the treatments. By using only twelve animals, the power of the present experiment may not have been sufficient to detect subtle treatment differences.

Moreover, there must have been some variability in electrode placement and, perhaps more importantly, current pathways. The current flowed from one electrode to the other, but there was no way to determine if all premolars saw the same charge density. The more movement that occurred, the further the tooth was from the distal electrode and accordingly, a smaller charge density would exist in the bone near the tooth. This might explain why the data were more significant ($P < .15$) at three weeks than at five weeks ($P < .40$). At three weeks, the rate of tooth movement was the fastest when the tooth was closer to the anode (treatment A) and slowest when closer to the cathode (treatment B). Throughout the entire experiment, the average total movement was the greatest for the teeth subjected to treatment A.

If this experiment be viewed as a pilot study, future experiments of this genre should be designed to eliminate the variability of charge densities. This could be done if the tooth, rather than an implanted electrode, were to carry the current through the adjacent bone. No matter where the tooth-electrode moved, it would still have the same relative charge density. Possibly a more feasible solution would be to utilize pulsed DC electrical stimulation. In this case, osteogenesis is stimulated between the two electrodes and not preferentially around a specific electrode (Levy and Rubin, 1972). Accordingly, the variability associated with the proximity of a tooth to a certain electrode need not play as important a role as it may have in the present investigation. Also the use of pulsed DC currents, in the parameters set as most favorable by Levy, may have a greater cellular response in bone than non-pulsed direct currents.

Polarization

The resistance at the electrode and in the bone changes as a function of time, degree of polarization, and metabolic state of the bone. In theory, this variability of resistance due to polarization can be divided into three categories (Feder, 1963): 1) polarization at the electrode surface, 2) polarization due to an ionic gradient built up near the electrode-solution interface, and 3) polarization in the electrode itself caused by temperature change, impurities, and other variables.

The circuit (Figure 4), designed by Friedenberg et al. (1970)

and used in the present investigation, biased the field-effect transistors in such a way as to maintain a relatively constant current even if the effective tissue resistance did change slightly (Zucker, 1969). After the electrodes had been implanted and the circuit had been connected for more than twenty minutes, the variable resistor was calibrated so that a 10 μA current was delivered between the electrodes. If there was an increase in tissue resistance, there would also be an increase in voltage. The voltage across the electrodes gave an indication of the effective tissue resistance. At the end of the five week period, the resistance ranged from 180,000 to 324,000 ohms with the average of 234,000 ohms.

Figure 12 shows the degree of stability of the constant-current device as the tissue resistance varied. This circuit was preset to deliver 10 μA with the tissue resistance of 234,000 ohms. The circuits were checked weekly and minor adjustments were made if necessary. Figure 13 indicates the average weekly voltages recorded across the electrodes. The average voltage increased during the first week and then stabilized for the remaining four weeks. On the average, the increase in polarization reached a plateau which corresponded to the 2.6 volt reading.

Possible Mechanisms of Bioelectric Control

It is tempting to think of the limitless possibilities offered for electric stimulation in orthodontic and orthopedic applications. However, before the clinician jumps on the

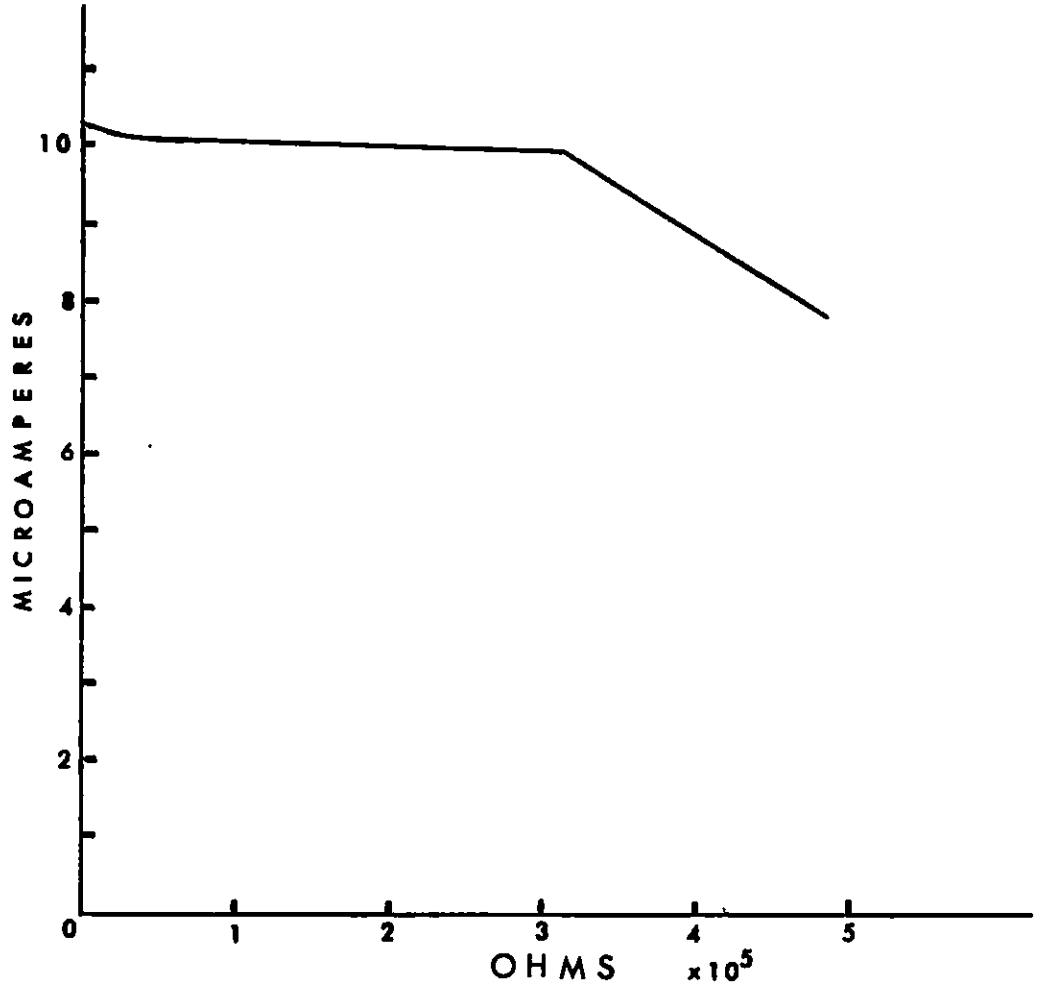


Figure 12.--Constant-current output characteristics (set for 10 μA at 234,000 ohms)

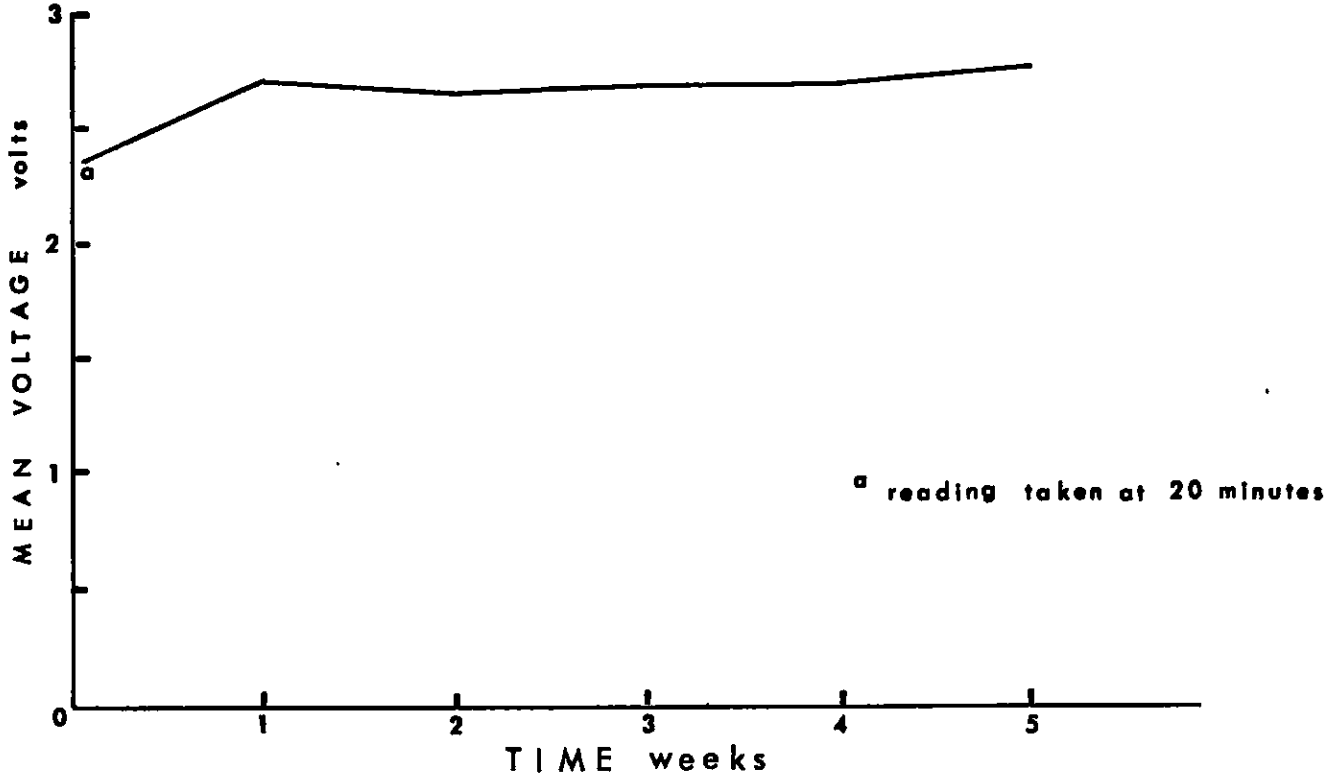


Figure 13.--Average weekly voltage

"bioelectric bandwagon," a considerable amount of data need be gathered before knowing for sure in which direction to leap. No study has been performed specifically to measure any short-term toxic effects. In addition, beyond the fact that passing a current in bone induces a tissue response, not much is known for sure as to how or why this happens. In the present investigation, the input-output relationship was observed with no attempt to identify the specific mechanism by which electric signals might control a specific cellular response in bone. However, numerous principles have been discussed as to how this might occur. A discussion of some of these principles, although not a direct part of this experiment, is presented in Appendix II.

SUMMARY AND CONCLUSIONS

From a variety of experiments to date, it seems that a controlling mechanism for bone remodeling may be related to stress induced electric currents or fields. During orthodontic tooth movement, the bone around the moving tooth is known to remodel. A relationship between orthodontic movement and bioelectric currents is easy to infer but, as yet, has no benefit of any support from the literature. Accordingly, the purpose of the present investigation is to examine the relationship between an externally applied current and the rate of bone remodeling associated with orthodontic tooth movement.

The effects of a 10 μA current on the amount of tooth movement was measured in vivo. Each of twelve cats was prepared with a sectional tooth moving apparatus and a miniaturized constant-current power source. Platinum-iridium electrodes were implanted in the alveolar bone on either side of the teeth to be moved. The experimental treatments consisted of 1) a current flowing with the cathode mesial to the anode, 2) a current with the polarity reversed, and 3) a control with no current flowing. Radiographic and direct intra-oral measurements were taken weekly for five weeks to determine the amount of tooth movement. The effects of the treatments were examined via a balanced incomplete block design and the appropriate

analysis of variance.

The results of this investigation did not show a statistically significant among-treatment difference. In the present experiment, it could not be demonstrated that a 10 μA current passed around a moving tooth had an observable effect on the extent of tooth movement.

APPENDIX I

Balanced Incomplete Block Analysis Of Variance

t= treatments	=3	
K= number of units per block	=2	given: tr=Kb
r= number of replications	=8	
b= number of blocks	=12	

G= Σx_i

T= Σx_a, Σx_b, Σx_c

BT= block totals

B= block totals of all blocks in which treatment occurred

Q= KT-B

W= T-2B+G

E_b= adjusted block MSQ

E_e= intrablock error MSQ

$$\mu = \frac{(b-1)(E_b-E_e)}{t(K-1)(b-1)E_b + (t-K)(b-t)E_e}$$

AT MSQ= adjusted treatment total per unit MSQ = $\dfrac{\dfrac{\Sigma(T+\mu W)^2}{r} - \dfrac{(\Sigma T+\mu W)^2}{tr}}{t-1}$

EE MSQ= effective error MSQ = $E_e[1+(t-K)\mu]$

$$F = \frac{\text{AT MSQ}}{\text{EE MSQ}} \qquad @\ df = t-1 \qquad @\ df = tr-t-b+1$$

SOURCE	df	SSQ
Blocks adjusted	b-1	Blocks(unadj)+Treat(adj)-Treat(unadj)
Blocks unadjusted	b-1	$\frac{\Sigma BT^2}{K} - \frac{(\Sigma BT)^2}{tr}$
Treatments adjusted	t-1	$\frac{(t-1)(\Sigma Q^2)}{K(tr)(K-1)}$
Treatments unadjusted	t-1	$\frac{\Sigma T^2}{r} - \frac{G^2}{tr}$
Intrablock error	tr-t-b-1	Total-Blocks(adj)-Treat(unadj)
Total	tr-1	$\Sigma(x_i)^2 - \frac{G^2}{tr}$

Intra-oral Measurements μ= .2884

	T	B	Q	W	T+μW
A	27.88	52.95	2.81	.11	27.91
B	25.88	52.03	-0.27	-.05	25.87
C	24.37	51.28	-2.54	-.06	24.35
	78.13	156.26	0	0	78.13

Radiographic Measurements μ= .2762

	T	B	Q	W	T+μW
A	18.77	34.39	3.15	-3.92	17.68
B	13.36	29.35	-2.63	.75	13.57
C	13.96	28.44	- .52	3.17	14.84
	46.09	92.18	0	0	46.09

APPENDIX II

Possible Mechanisms of Bioelectric Control

Since functional forces play an important role in shaping the skeleton, bone must have the ability to respond to a changing mechanical stress. Mechanical energy may be transduced to a form recognizable by bone cells in at least two ways.

Firstly, cells may be affected by the mechanical pressures directly. Frost (1964) theorized that hydraulic and hydrostatic forces can act directly on a cell in order to alter the cell's functional capacities. Nutbourne (1968) showed that hydrostatic pressures affect sodium transport across a cellular membrane. Osteoblasts on the surface of bone, however, would in many instances be outside the regions subjected to stresses.

A second possibility is that mechanical energy is converted to an electrical event which would, in turn, act to control the cell's capability as a bone producing agent. Since it has been demonstrated that bone does create electrical potentials in response to stress, this theory of electrical control is at least assuasive.

Electric currents and electrostatic fields can influence the course of fracture healing. The pH of an area can be changed when an externally applied current of a certain polarity is superimposed on a biologic system. At the anode, acidic conditions are present: lysosomal enzymes and acid phosphates are more abundant in this area (Bassett, 1971). Moreover, calcium salts

and collagen are less insoluble under acidic conditions (Jahn, 1966), a finding which agrees with reports that bone resorption occurs nearer the anode (Friedenberg and Kohanim, 1968, and Friedenberg, Andrews, Smolenski, Pearl, and Brighton, 1970). Likewise, alkaline conditions are created nearer the cathode. Insoluble calcium salts and osteoblasts with alkaline phosphatase would more likely be in this area (Bassett, 1971). This finding is consistent with the data that show osteogenesis occurs at the cathode.

Since ionic migration is known to occur in the presence of magnetic or electrostatic fields, and that ions are important in enzyme synthesis in a cell, it has been suggested that electric fields could alter the rate of enzyme synthesis and enzyme-substrate reactions (Bassett, 1971). Trypsin and other enzymes were found to be affected by a magnetic field (Haberditzl, 1967). Numerous cell functions could be modified by a change in the electric environment. It remains to be seen if these changes in cell and enzyme function are the triggering agents in osteogenesis.

Calcium ion concentrations can be altered with electric, and its resulting pH, changes. Loewenstein (1967) found that inter-cellular membrane connections (so-called "tight junctions") were sensitive to calcium ion changes. These junctions between cells are normally in close approximation when a low calcium ion concentration exists and tend to separate in high calcium concentrations. Junctional control could act as a means to

communicate within a colony of cells and might possibly explain why an undifferentiated cell can become specialized (Becker and Murray, 1967). Calcium ion and pH are known to alter the permeability of a cell membrane (Stephens, 1969). Mitochondria are also sensitive to calcium ion changes and electrostatic charges (Lehninger, 1969).

A pulsed electric signal may affect the degree of nutrition of an osteocyte by pumping charged metabolites into the area (Bassett, 1965). Also, the nutritional needs of a cell could be regulated by the electric charge on the cell membrane (Bassett, 1971). Thus, an osteoblast, in the absence of electrical stimulation, would not get adequate nutrition and would slow down its cellular metabolism and bone production. In addition, nutritional supply to cells is increased by more vascularity and proximity to red blood cells. Both could be influenced to some extent by the electrical activity in the area, since they both have their own electrostatic charges.

There are therefore numerous explanations of how the bone cell may be affected by an electric current. Bassett concluded:

> From the data now available, the stimulus for bone formation and destruction appears to be largely electrical in nature. It is clear that bone converts mechanical energy to an electric signal, and changes in the electric environment of mesenchymal cells may control, to a large degree, their mitotic and functional activity.

SELECTED BIBLIOGRAPHY

Anderson, J. C. and Eriksson, C. 1970. Piezoelectric properties in dry and wet bone. Nature, 227: 491-492.

Athenstaedt, H. 1970. Permanent longitudinal electric polarization and pyroelectric behaviour of collagenous structures and nervous tissue in man and other vertebrates. Nature, 228: 830-834.

Bassett, C. A. L. and Becker, R. O. 1962. Generation of electric potentials by bone in response to mechanical stress. Science, 137: 1063-1064.

Bassett, C. A. L., Pawluk, R. J., and Becker, R. O. 1964. Effects of electric currents on bone in vivo. Nature, 204: 652-654.

Bassett, C. A. L. 1965. Electric effects in bone. Sci. Am., 213: 18-25.

Bassett, C. A. L. and Herrmann, I. 1968. The effect of electrostatic fields on macromolecular synthesis by fibroblasts in vitro. J. Cell Biol., 39: 9a.

Bassett, C. A. L. 1971. Biophysical principles affecting bone structure. In The Biochemistry and Physiology of Bone, vol. III. 2nd Edition. Edited by G. H. Bourne. Academic Press Inc., New York, pp. 1-76.

Baumrind, S. 1969. A reconsideration of the propriety of the "pressure-tension" hypothesis. Am. J. Orthod., 55: 12-22.

Becker, R. O. 1961. The bioelectric factors in amphibian-limb regeneration. J. Bone Joint Surg., 43-A: 643-656.

Becker, R. O., Bassett, C. A. L., and Bachman, C. H. 1964. Bioelectric factors controlling bone structure. In Bone Biodynamics. Edited by H. M. Frost. Little, Brown, Boston, pp. 209-232.

Becker, R. O. 1965. The electronic solid state properties of bone. J. Bone Joint Surg., 47-A: 1101.

Becker, R. O. and Bachman, C. H. 1965. Bioelectric effects in tissue--Letters to the Editor. Clin. Orthop., 43: 251-253.

Becker, R. O. and Murray, D. G. 1967. A method for producing cellular dedifferentiation by means of very small electrical currents. Trans. N.Y. Acad. Sci., 29: 606-615.

Ben-Or, S., Eisenberg, S., and Doljanski, F. 1960. Electrophoretic mobilities of normal and regenerating liver cells. Nature, 188: 1200-1201.

Boester, C. H. 1972. An investigation of the concepts of differential and optimal force in canine retraction. M.S. Thesis, Case Western Reserve University, Cleveland.

Burstone, C. J. 1962. The biomechanics of tooth movement. In Vistas in Orthodontics. Chapter 5. Edited by B. S. Kraus and R. A. Riedel. Lea and Febiger, Philadelphia.

Christiansen, J. A., Jensen, C. E., and Vilstrup, T. 1961. Displacement potentials and bending of rod-like polyelectrolytes. Nature, 191: 484-485.

Cochran, G. V. B., Pawluk, R. J., and Bassett, C. A. L. 1967. Stress generated electric potentials in the mandible and teeth. Arch. Oral Biol., 12: 917-920.

Cochran, G. V. B., Pawluk, R. J., and Bassett, C. A. L. 1968. Electromechanical characteristics of bone under physiologic moisture conditions. Clin. Orthop., 58: 249-270.

Cochran, W. G. and Cox, G. M. 1957. Experimental Designs. 2nd Edition. John Wiley and Sons, Inc., New York, pp. 439-537.

Crelin, E. S. and Dueker, D. K. 1970. The response of the femur to trauma, a foreign body, and a direct electrical current in mice. Yale J. Biol. Med., 43: 71-75.

Daprano, A. A. 1971. Canine retraction in healed and recent extraction sites. M.S. Thesis, Case Western Reserve University, Cleveland.

DeAngelis, V. 1970. Observations on the response of alveolar bone to orthodontic force. Am. J. Orthod., 58: 284-294.

Enlow, D. H. 1968. Wolff's law and the factor of architectonic circumstance. Am. J. Orthod., 54: 803-822.

Feder, W. 1963. On secondary currents and electrode polarization. Perspect. Biol. Med., 6: 424-442.

Friedenberg, Z. B. and Brighton, C. T. 1966. Bioelectric potentials in bone. J. Bone Joint Surg., 48-A: 915-923.

Friedenberg, Z. B. and Kohanim, M. 1968. The effect of direct current on bone. Surg., Gynecol., and Obstet., 127: 97-107.

Friedenberg, Z. B. and Smith, H. G. 1969. Electrical potentials in intact and fractured tibia. Clin. Orthop., 63: 222-225.

Friedenberg, Z. B., Andrews, E. T., Smolenski, B. I., Burton, W. P., and Brighton, C. T. 1970. Bone reaction to varying amounts of direct current. Surg., Gynecol., and Obstet., 131: 894-899.

Friedenberg, Z. B., Dyer, R. H., and Brighton, C. T. 1971. Electro-osteograms of long bones of immature rabbits. J. Dent. Res., 50: 635-639.

Friedenberg, Z. B., Harlow, M. C., and Brighton, C. T. 1971. Healing of nonunion of the medial malleolus by means of direct current: a case report. J. Trauma, 11: 883-885.

Friedenberg, Z. B., Roberts, P. G., Jr., Didizian, N. H., and Brighton, C. T. 1971. Stimulation of fracture healing by direct current in the rabbit fibula. J. Bone Joint Surg., 53-A: 1400-1408.

Frost, H. M. 1964. The Laws of Bone Structure. Charles C Thomas, Springfield, Illinois.

Fukada, E. and Yasuda, I. 1957. On the piezoelectric effect of bone. J. Physiol. Soc. Japan, 12: 1158-1162.

Gertler, R. A., Adler, A. G., and Mortimer, J. T. 1971. An interface for passing lead wires through the skin of laboratory animals. I.E.E.E. Trans. Biomed. Eng., 18: 72-73.

Gillooly, C. J., Hasley, R. T., Mathews, J. R., and Jewett, D. L. 1968. Electric potentials recorded from mandibular alveolar bone as a result of forces applied to the tooth. Am. J. Orthod., 54: 649-654.

Haberditzl, W. 1967. Enzyme activity in high magnetic fields. Nature, 213: 72.

Hambury, H. J., Watson, J., Sivyer, A., and Ashley, D. J. B. 1971. Effect of microamp electrical currents on bone in vivo and its measurement using strontium-85 uptake. Nature, 231: 190-192.

Hermanson, P. C. 1972. Alveolar bone remodeling incident to tooth movement. Angle Orthod., 42: 107-115.

Humphrey, C. E. and Seal, E. H. 1959. Biophysical approach toward tumor regression in mice. Science, 130: 388-389.

Jahn, T. L. 1966. Contraction of protoplasm II theory: anodal vs. cathodal in relation to calcium. J. Cell Physiol., 68: 135-148.

Kazarian, L. E. and Von Gierke, H. E. 1969. Bone loss as a result of immobilization and chelation. Clin. Orthop., 65: 67-75.

Lavine, L. S., Lustrin, I., and Shamos, M. H. 1969. Experimental model for studying the effect of electrical current on bone in vivo. Nature, 224: 1112-1113.

Lavine, L. S., Lustrin, I., Shamos, M. H., and Moss, M. L. 1971. The influence of electric current on bone regeneration in vivo. Acta Orthop. Scand., 42: 305-314.

Lavine, L. S., Lustrin, I., Shamos, M. H., Renaldi, R. A., and Liboff, A. R. 1972. Electric enhancement of bone healing. Science, 175: 1118-1121.

Lehninger, A. L. 1969. Acid-base changes in mitochondria and medium during energy-dependent and energy-independent binding of CA. Ann. N.Y. Acad. Sci., 147: 816-823.

Levy, D. D. 1971. Induced osteogenesis by electrical stimulation. Ph.D. Dissertation, Polytechnic Institute of Brooklyn, Brooklyn, New York.

Levy, D. D. and Rubin, B. 1972. Inducing bone growth in vivo by pulse stimulation. Clin. Orthop., 88: 218-222.

Loewenstein, W. R. 1967. Permeability of membrane junctions. Ann. N.Y. Acad. Sci., 137: 441-472.

McElhaney, J. H., Stalnaker, R., and Bullard, R. 1968. Electric fields and bone loss of disuse. J. Biomech., 1: 47-52.

Mackay, A. L. and Sinha, D. P. 1967. The piezoelectric activity of Whitlockite. J. Phys. Chem. Solids, 28: 1337-1338.

Minkin, C., Poulton, B. R., and Hoover, W. H. 1968. The effect of direct current on bone. Clin. Orthop., 57: 303-309.

Moss, M. L. 1962. The functional matrix. In Vistas in Orthodontics. Edited by B. S. Kraus and R. A. Riedel. Lea and Febiger, Philadelphia.

Nagel, N. J. 1972. The enamel etch resin restoration. Dent. Dig., 78: 402-405.

Norton, L. A. and Moore, R. R. 1972. Bone growth in organ culture modified by an electric field. J. Dent. Res., 51: 1492-1499.

Nutbourne, D. M. 1968. The effect of small hydrostatic pressure gradients on the rate of active sodium transport across isolated living frog-skin membranes. J. Physiol., 195: 1-17.

O'Connor, B. T., Charlton, H. M., Currey, J. D., Kirby, D. R. S., and Woods, C. 1969. Effects of electric current on bone in vivo. Nature, 222: 162-163.

Parker, R. B. 1969. Bioelectric phenomena in dental decay. J. Dent. Res., 48: 795-798.

Sawyer, P. N., Dennis, C., and Wesolowski, S. A. 1961. Electrical hemostasis in uncontrollable bleeding states. Ann. Surg., 154: 556-562.

Shamos, M. H. and Lavine, L. S. 1964. Physical bases for bioelectric effects in mineralized tissues. Clin. Orthop., 35: 177-188.

Shamos, M. H. and Lavine, L. S. 1965. Bioelectric effects in tissue--Letters to the Editor. Clin. Orthop., 43: 254-255.

Shamos, M. H. and Lavine, L. S. 1967. Piezoelectricity as a fundamental property of biological tissues. Nature, 213: 267-269.

Stanford, A. L. and Lorey. R. A. 1968. Evidence of ferroelectricity in RNA. Nature, 219: 1250-1251.

Stephens, W. G. S. 1969. Hydrogen ion and the activation of electrically excitable membranes. Nature, 224: 547-549.

Swanson, G. T. and Lafferty, J. F. 1972. Electrical properties of bone as a function of age, immobilization and vibration. J. Biomech., 5: 261-266.

Utley, R. K. 1968. The activity of alveolar bone incident to orthodontic tooth movement as studied by oxytetracycline-induced fluorescence. Am. J. Orthod., 54: 167-201.

Williams, W. S. and Perletz, L. 1971. P-n junctions and the piezoelectric response of bone. Nature New Biol., 233: 58-59.

Wolff, J. 1892. Das Gesetz der Transformation der Knocken. Hirschwald, Berlin.

Yasuda, I., Noguchi, K., and Sata, T. 1955. Dynamic callus and electric callus. J. Bone Joint Surg., 37-A: 1292.

Zucker, M. H. 1969. Electronic Circuits for the Behavioral and Biomedical Sciences. W. H. Freeman and Co., San Francisco, pp. 1-18.

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