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THE EFFECT OF SURGICAL RESECTION OF THE SUPERIOR CERVICAL GANGLION AND THE INFERIOR ALVEOLAR NERVE ON ORTHODONTIC TOOTH MOVEMENT

by

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THE EFFECT OF SURGICAL RESECTION OF THE SUPERIOR CERVICAL GANGLION AND THE INFERIOR ALVEOLAR NERVE ON ORTHODONTIC TOOTH MOVEMENT

Abstract

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A review of the literature makes it clear that many factors influence the various types of tooth movement. Past studies treated active eruption, passive eruption, drift, and orthodontic tooth movement as separate entities, which were examined on an individual basis. In this study, the premise was made that all types of tooth movement, whether physiologic or therapeutic, are variations of a single process involving common basic cellular mechanisms and components. As a consequence, the multitude of factors reported to influence individual types of tooth movement (e.g., vascularity, hormones, piezoelectricity, fluid dynamics, cellular contractility, diet, neurologic innervation), were theorized to also influence other types of tooth movement. In addition, the basic factors or influences of tooth movement mentioned above were theorized to be interrelated and controlled during normal physiologic conditions by some overriding primary mechanism. It was suggested that this primary mechanism involves the neurophysiologic component of the PDM.

To test the hypothesis that tooth movement is controlled by, or at least involves nerve transmission, the superior cervical ganglion and a segment of the ipsilateral inferior alveolar nerve were surgically resected from one side of eight cats. Mandibular first premolars were extracted, and bilateral second premolars were protracted by reciprocal forces. The rate and amount of tooth movement on each side of the mandible were determined by direct intra-oral and by cephalometric measurements, with the aid of amalgam tooth markers and tantalum bony implants. Procion vital dyes were also used to aid in the microscopic analysis of the bony changes.

Teeth were moved for a period of nine weeks or until therapeutic exfoliation occurred. At the termination of the study, all animals were examined for nerve regeneration, and appropriate tissue samples were taken for histologic preparation. These tissue samples were of two types: (1) tissue suspected to be of inferior alveolar nerve origin, and (2) tooth, PDM and surrounding bone which had been biologically stained <u>in vitro</u>. The latter tissue sections were not available for examination in time to be included herein.

The results of this study may be summarized as follows:

1. A new approach to the investigation of possible PDM mediated influences on orthodontic tooth movement has been developed that utilizes unilateral sympathetic and somatic denervation of the mandible.

2. Three out of five surviving animals showed substantially different rates of tooth movement for the control and experimental sides; two out of these three showed an increase in the rate of tooth movement on the denervated side over the control side by a factor of 2:1 or greater, and one animal showed the opposite trend.

3. These results are compared with past studies which showed an increase in incisor eruption rate following PDM denervation, and with studies that demonstrated the presence of mechanisms by which nerves might control tooth movement (e.g., myofibroblastic model), but no definite correlation could be made.

4. Regeneration of resected nerve tissue occurred at a rapid rate and was complete in most animals before the termination of the study. This is in contrast to the findings of Aldskorgius and Arvidsson (1978), Grant and Arvidsson (1975), and Westrum et al. (1976), which showed retrograde neural degeneration and nerve cell death following peripheral nerve transection.

5. A new finding is reported in which a right/left side anatomical dimorphism of the relative positions of superior cervical ganglion and the nodose ganglion of the vagus nerve exists (Figure 2).

6. On the basis of these results, tooth movement appears to be a multifactorially influenced process; if neurologic transmission is a primary controlling factor in tooth movement, then alternate mechanisms may exist which tend to compensate for the loss of this primary component.

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DEDICATED

TO

My wife, Janice, for
her love and patience.

and

My mother, for her love,
guidance and generosity.

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INTRODUCTION

Many theories exist concerning the enabling and causative factors of the various types of tooth movement. Normal tooth development, muscular influence, cellular proliferation, vascularity, fluid dynamics, hormones, piezo-electricity and dietary influence are some examples of the mechanisms explored by such theories. To date, however, the above theories fail to answer many of the major questions or to explain known facts regarding tooth movement and the accompanying soft and hard tissue remodeling.

Research of the physiology of bone growth and remodeling is evolving from a descriptive phase into a mechanistic phase in which the controlling agents or processes involved are being studied. The basic problem still remains: what specific cells, tissues, or biological substances are responsible for the initiation and direction of movements of organs and parts of organs during growth and development or as a result of therapy.

The intention of this experimental study is to test a hypothesis which suggests that the series of physiologic events which occurs in the periodontal membrance (PDM) of a therapeutically moving tooth have a neurological link, and that if this link is broken (i.e., denervation of the PDM), the tooth movement would be affected in some way. This will be attempted by unilateral surgical resection of the superior cervical ganglion and the inferior alveolar nerve, after

which bilateral orthodontic appliances will be fitted onto certain teeth. Right and left mandibular premolar teeth will then be protracted, with equal orthodontic forces being applied to the control side and to the partially denervated treatment side. Direct intraoral and cephaloradiographic measurements, using implant markers and vital dyes, will be used to assess the respective rates and amounts of tooth movement.

REVIEW OF THE LITERATURE

Physiologic tooth movements (eruption, rotations, tipping, horizontal and vertical drift) occur naturally in every individual. Therapeutic tooth movement is the result of an extrinsic and man-made force application to a tooth. To integrate present knowledge with regard to each, the following review is divided into three major parts: the neuroanatomy of the PDM, a histologic description of PDM and bony remodeling, and the possible causes and mechanisms for such remodeling, with special attention given to neurophysiologic mechanisms.

Neuroanatomy of the PDM

The early reports on the innervation of the PDM remain classic works today. In a series of studies by Lewinsky and Stewart (1936, 1937, 1938), the course of nerves and the types of nerve endings were reported from sectional examination of cat PDM tissue. They described innervation from two sources, the first being from the apical region, running gingivally, and the second from the lateral cortical plate, which then divides and courses apically and gingivally. Two types of nerve fibers were also described. Coarse or thick fibers were found in the peripheral portion of the PDM, which terminated in specialized "terminal knob-like" end organs. These end organs were postulated to function in tactile and pressure reception. Finer

fibers, found in the deeper portions of the PDM, have many arborizations, no end organs, and were speculated to function in pain reception.

The nerve endings in the PDM were perhaps first described by Berkelbach Van Der Sprenkel in 1936, based on examination of mouse tissue. He reported three types of endings: small end-rings on collagenous fibrils close to the alveolar wall, representing an individual locus of innervation (i.e., not from a plexus); terminal reticula surrounding connective tissue nuclei; and axons which lose their sheath, combine into a reticulum and individually penetrate into the layer of cementoblasts.

The course and innervation of the PDM was also examined in human tissue by Bernick (1952), who reported three categories of nerve supply: branches given from the dental nerve just before it enters the tooth, interalveolar branches from spetal medullary bone, and interradicular branches around molars. In 1957, Bernick examined the PDM of monkeys and found two types of nerve endings. Non-medullated fibers were said to unite, and then arborize into fine filaments which terminate in approximation to stroma cells, cementoblasts and cementum. The second type, a medullated ending in the connective tissue stroma near the lower third of the roots, was described as having elongated spindle-like terminals. Similar results in a more detailed study were reported by Corpron et al. (1974).

More recent and comprehensive studies of the PDM receptor mechanism in humans are best exemplified in a series of reports by

Griffin and Harris (1974, 1974), Harris and Griffin (1974, 1974) and Harris (1975). They classify receptors as: (1) simple mechanoreceptors from single or paired myelinated fibers (i.e., end-knobs, Lewinsky and Stewart, 1936, 1937, 1938); (2) compound and complex end-rings; and (3) the neural complex, composed of myelinated free nerve endings.

The compound receptor is said to be extremely sensitive to tension changes and resembles stretch receptors in skeletal muscle, in which different endings pursue a spiral course around adjacent myelinated nerve fibers and collagen fibrils. Muscle spindles have annulo-spiral endings, where afferent fibers spiral around intrafusal muscle fibers. In a muscle and in the PDM, stretching of these tension sensitive fibers similarly excite the receptors (Griffin and Harris, 1974). The complex mechanoreceptor consists of encapsulated nerve fibers and end-rings, exposed and lacunar endings, and a metarteriole. These receptors also are claimed to be tension sensitive (Harris and Griffin, 1974).

Corbin (1940) and Corbin and Harrison (1940) investigated the mesencephalic nucleus of the fifth cranial nerve in cats, and found it to supply sensory fibers to the superior and inferior alveolar nerves, as well as sensory and motor fibers to the nerves of mastication. They found no evidence of autonomic fibers arising from or passing through the mesencephalic nucleus.

More recently, Jerge (1963) and Sakada (1974) found the PDM to be innervated by pseudounipolar sensory neurons of the semi-lunar ganglion and by nerves from the mesencephalic nucleus of the fifth cranial nerve.

Evidence supporting the view that many of the nerves supplying the PDM originate from the mesencephalic nucleus is also supplied by Byers and Holland (1977). They ruled out the Gasserian ganglion as a primary supplier of nerve fibers to the PDM in rats by autoradiographical mapping of the PDM after labeling Gasserian ganglionic fibers with tritiated-L-proline.

There is some debate as to whether or not the inferior alveolar nerve contains any sympathetic innervation of the teeth and PDM in cats, Christensen (1940) found that the superior cervical ganglion gives off two main unmyelinated nerves which course cephalically along the common carotid, external carotid and external maxillary arteries. At that point, a nerve plexus forms and follows the internal maxillary artery, where it gives off nerve branches, located in the adventitia or in the adjacent connective tissue, that follow the inferior alveolar artery and tributaries. Some fibers are then reportedly incorporated into the inferior alveolar nerve, either peripherally or very deep within the nerve mass. Bishop and Dorman (1963), severed the inferior alveolar nerve in dogs and found some resultant vasodilation of the mandibular area; electrical stimulation of the cut distal nerve trunk produced some vasoconstriction.

From the above studies, it can be concluded that sympathetic innervation to the PDM, at least in cats, originates entirely from the superior cervical ganglion. It also appears that the inferior alveolar nerve, as well as other somatic nerves in the face, do contain some, albeit few, sympathetic fibers. In other words,

sympathetic fibers course adjacent to vessels and somatic nerves, and are also incorporated into somatic nerve masses.

Remodeling of the Periodontium

A tooth moving through bone as a result of application of an orthodontic force presumably includes the following sequential events: a force is applied to a tooth; compression of the PDM occurs on the pressure side with resultant ischemia and hyalinization; osteoclastic activity takes place on the pressure side (frontal or undermining resorption); stretching of the PDM on the tension side results in realignment of alveolar trabeculae (transitional bone, Oppenheim, 1911); a relocation of the entire PDM occurs via sliding of the collagen fibers in conjunction with collagen synthesis and degradation; and finally, osteoblastic activity proceeds on the tension side, producing osteoid, which is then calcified (Goldman and Gianelly, 1972; Graber, 1972; Moyers, 1950). Of course, this presumed series of physiological events is actually a continuous process resulting from a force application and a so-called "bioplastic deformation" (Storey, 1973).

Primary tooth resorption, permanent tooth elongation, increase in alveolar height, bodily translation of the tooth occlusally, and other processes associated with eruption are well documented (Moyers, 1973). Ness (1964), reported three types of eruption, classified by rate. They are:

1. Slow: 1-10 u/day, for continued eruption.
2. Medium: 10-100 u/day, associated with the eruption of limited growing teeth.

3. Fast: 100-1,000 u/day, associated with the eruption of continuously growing teeth.

Obviously, tissue of the PDM has a potentially tremendous turn-over rate, for the PDM must of necessity remodel to accomplish eruption. However, a well accepted description of the microscopic events associated with PDM remodeling during tooth movement is lacking in the literature.

The existence of an intermediate-plexus of periodontal fibers midway between tooth and bone in the PDM was postulated by Sicher in 1923. The re-linkage of collagen fibers within this plexus was theorized to be the basic mode for PDM remodeling during eruption, a theory which persisted for many decades. However, Ramos and Hunt (1967) labeled the PDM collagen of guinea pig molars with H^3-proline and found no specificity for the intermediate plexus, with the H^3-proline being uniformly distributed throughout the width of the PDM. They described the movement of the PDM fibers occlusally with the erupting tooth, finding that as the fibers moved past the bony crest, they became non-functional and lysed, while new fibers quickly formed across the entire width of the PDM in a continuous process. In a similar experiment, tritiated glycine was demonstrated to be incorporated uniformly into the entire PDM of rabbits (Thomas, 1967), suggesting that distinct zones within the PDM do not exist. In addition, Edwards (1968) concluded, from a review of the literature, that the intermediate plexus does not exist.

The pendulum swung back when Kraw and Enlow (1967)

described in minute detail the relocation of the PDM during physiologic tooth movement in rats. Using polychrome stain to differentiate precollagenous from collagenous fibrils, and tetracycline for labeling bone changes, they acknowledged the presence of an intermediate zone in the PDM, either as a discrete "zone" or diffusely distributed throughout the ligament (Enlow, 1975). This zone is said to be the site of a progressive shortening of fibers adjacent to resorptive areas. On the tension side, this intermediate zone presumably moves with the tooth, continuously re-linking new inner and outer zones. In 1973, Beertsen administered H^3-proline to mice and found three zones of the PDM. The dental and middle zones were found to move coronally with the erupting tooth, while the alveolar zone remained static. Between the middle and alveolar zones, Beertsen described an area of low cell-population density that is a proposed site of tissue shear (i.e., tearing of PDM fibers).

Inherent in the multiple zone PDM concept are the other concepts of "slippage", "re-linkage", and collagen turn-over. The cellular basis for such events has only recently been provided by Ten Cate et al. (1976). They have stated that the fibroblast is capable of simultaneous collagen synthesis and degradation and that this double function of the fibroblast is the physiological basis for PDM remodeling during tooth movement.

Mechanisms of Tooth Movement

In 1941, Massler and Schour listed seven possible mechanisms

for tooth eruption. They are:

1. Root elongation.
2. Pulpal constriction.
3. Cellular proliferation.
4. Resorption of the alveolar crest.
5. Pressure from muscular action.
6. Growth of the PDM tissue.
7. Vascularity changes.

It has been shown by the works of Herzberg and Schour (1941), Massler and Schour (1941) and Berkovitz and Thomas (1969) that the first four mechanisms listed to not significantly affect tooth movement, and that muscular action does not influence tooth eruption. However, muscular action has been assumed by many to play a role in other physiologic tooth movements, such as mesial drift and post-orthodontic relapse.

After eruption has been accomplished, the migration of teeth is most commonly referred to as mesial drift, which is said to be the result of the mesial component of force. It has been demonstrated by Moss and Picton (1967) that molars and incisors generally migrate mesially, if allowed, however, cuspids tend to remain stationary and bicuspids tend to drift distally, if allowed. Which types of tooth drift are components of normal growth and development or the result of compensations to muscular function, and which are iatrogenic or pathological in nature, have not yet been determined.

Muscular action is directly or indirectly involved in the rationale for many of the theories of orthodontic relapse. The bulk of the literature directed to the problem is heavily concentrated on clinical observations which involve mechanical or spatial relationships, such as: tooth-to-tooth (occlusion), tooth-to-apical base, teeth-to-basal bone, functional muscle balance, and tipped versus bodily moved teeth. Good reviews of the above theories are provided by Huckaba (1952), Reitan (1960) and Reidel (1960).

The question arises: does the PDM contain the cellular or mechanistic basis responsible for tooth movement? Massler and Schour (1941) felt that it did not. They said:

> This theory is invalidated by histologic examination of the direction of periodontal fibers during tooth eruption, which shows that the periodontal fibers are being pulled by the tooth and do not themselves pull upon the tooth.

Ness (1957) also refuted the concept of the PDM housing the eruptive forces. When the roots of rabbit incisors were transected, eruption was decreased. It has been subsequently well established however, that the PDM is the tissue directly responsible for tooth movement. Berkovitz and Thomas (1969) also transected the roots of rabbit incisors, but demonstrated opposite results from Ness (1957) and stated opposite conclusions. Before this study, Thomas (1967) postulated that the synthesis and catabolism of collagen results in the shrinkage of periodontal fibers and hence, the eruption of teeth. He demonstrated that radioactive glycine labels disappear from PDM fibers in five to seven days, and that corticosteroid therapy

decreases the eruption rate in rabbits. In addition, Litton (1974) found that an ascorbic acid deficient diet caused a complete cessation of osteogenesis and a disorganization of the PDM of orthodontically moved teeth in guinea pigs. Collagen synthesis is needed for orthodontic tooth movement and is thus a limiting factor.

Goldman and Gianelly (1972) selected two of the most likely alternatives representing a possible triggering mechanism for bony remodeling to be intraligament pressure and piezo-electricity. It has been demonstrated by Reitan (1959) that stretched PDM fibers do not rearrange to an unstrained condition until approximately 28 days after tooth movement, and the stretched gingival fibers persist up to 232 days post-treatment. Intraligament pressure obviously exists, but it must in turn activate another process and therefore, logically cannot be the final answer. Additional evidence against intraligament collagen tension assuming a key role is supplied by Gowgiel (1961), Grant et al. (1970), and Grant and Bernick (1972), in which irradiation produced rootless teeth continue to erupt, and teeth with immature PDM's, incapable of organized collagen tension, also erupt. Piezo-electricity however, is a more promising consideration.

Electric potentials were found to exist around areas of bony deformation in amphibian long bones (Bassett and Becker, 1962). In addition, the observation was made that the polarity was dependent on the direction of the deformation (i.e., compression caused a negative potential), and that the amplitude was dependent on the magnitude of the deformation. However, Besson et al. (1973), in experimental studies with cats using artifically applied electrical

currents, were unable to substantiate this phenomenon as being applicable to orthodontic tooth movement and associated bony changes.

As early as 1900, Constant proposed tissue pressure or hydrostatic pressure to be the eruptive force. Main and Adams (1966) attempted to determine if blood pressure was responsible for the association between vascularity and eruption. Guanethidine and Hydrolazine administered to rats reduced systemic blood pressure by twenty percent, but did not affect the eruption rate of the incisors.

There are three fluids of concern: vascular, interstitial, and intracellular. Bien (1966) felt that these fluids are responsible for the physiological response to intrusive forces on teeth. He supported this theory on the basis of the non-linearity of the PDM response to applied forces. Bryer (1957) also gave support to the influence of fluid dynamics and after various surgical procedures on rats, stated:

> ... The eruptive force of the incisor is derived predominantly from the tissue tension within the pulp and periodontal tissues and that this tension is dependent upon the dynamics of the blood circulation.

However, in an earlier study, Reitan (1954) removed the pulp of human teeth with no effect on orthodontic tooth movement, and concluded that the fluid dynamics of the dental pulp do not play a significant role.

Various types of tooth movement and bony remodeling have been related to blood supply by numerous researchers (Massler and Schour, 1941; Castelli and Dempster, 1965; Khouw and Goldhaber, 1970; Moyers and Bauer, 1950). They concluded that vascularity to and within the

remodeling area is the major determining factor of tooth movement.

On the other hand, however, Taylor and Butcher (1951) found that the eruption rate of rat incisors was not affected by altered vascularity produced by sympathectomy or interruption of the carotid artery. A similar study with rabbits resulted in the same lack of effect on eruption, even though osteoclastic activity was shown to have a direct relationship to vascular changes (Miller, 1957).

Hormones have long been suspected of influencing tooth movement, especially eruption. Schour and Van Dyke (1931) were perhaps the first to investigate hormonal influence on eruption rates. They found that hypophysectomy decreased eruption rate, but that growth hormone injections did not increase eruption rate. In a series of reports in 1954, Baume et al. found eruption to be influenced by hormone injections following thyroidectomy and hypophysectomy (Table 1). They concluded that the eruption of teeth is presided over by growth hormone and thyroxine.

Hormonal influence was studied by Gianelly and Schour in 1969, and they demonstrated that tooth movement was more rapid in rats injected with parathyroid hormone. As it is well established that parathyroid hormone has a resorptive effect on bone (Guyton, 1971), a possible influence on tooth movement by this hormone is understandable, in view of known bone physiology. The problem with this theory is that parathyroid hormone levels have not been shown to be higher, either locally or systemically, in individuals with rapidly moving teeth.

Table 1

Results of Hormonal Studies

by Baume *et al.* (1954)

Treatment	Eruption Rate
Thyroidectomy only	45% decrease from normal
Thyroidectomy + growth hormone	10% increase over thyroidectomy animal
Thyroidectomy + thyroxine	27% increase over thyroidectomy animal
Thyroidectomy + growth Hormone + thyroxine	almost normal
Hypophysectomy only	50 to 70% decrease from normal
Hypophysectomy + growth hormone	no change from hypophysectomy animal
Hypophysectomy + thyroxine	36% increase over hypophysectomy animal
Hypophysectomy + growth hormone + thyroxine	almost normal

It is interesting to note that neurohormones have also been reported to affect eruption rate. Sturman (1957) noticed that an adrenergic blocking agent, priscoline, along with numerous other substances, produced an increase in rat incisor eruption rate. An excellent review of hormonal influence on eruption is provided by Ten Cate (1969).

Neurological Mechanism

Reitan (1954) and Heuttner and Young (1955), having removed the pulps of teeth from humans and monkeys, respectively, found no difference in the rate of orthodontic tooth movement between vital and devitalized teeth. It is probable that this information, coupled with the belief that the PDM is purely a sensory organ, has resulted in a lack of research interest in PDM neurophysiology as it relates to orthodontic tooth movement.

Neurological influence on eruption rate has been investigated, but with confusing and conflicting results. A significant increase in the eruption rate of teeth after the resection of the superior sympathetic ganglion and/or the inferior alveolar nerve, has been demonstrated in a variety of animals by numerous investigators (King, 1936; Edwards and Kitchen, 1938; Taylor and Butcher, 1951; Miller, 1957; Brown et al., 1961; Rehak, 1963). Unfortunately, the majority of these experiments were conducted on rats with fully occluding incisors. In fact, the most often cited explanation for the results was the loss of sensation and proprioception, which resulted in

greater attrition and even fracturing of the operated side incisor, and then an increase in eruption rate. In no case was there any consideration given to possible cross innervation between incisors.

In a more recent study, Tornick et al. (1972) found that denervation of the PDM of rats (i.e., resection of the inferior alveolar nerve and superior sympathetic ganglion), had no effect on eruption. Resection of the inferior alveolar nerve in monkeys has been shown to have no effect on the development of the teeth (Butcher and Taylor, 1951). In spite of altered PDM physiology resulting from denervation, such as dilatation of vessels and a decrease in the PDM cholinesterase (Avery et al., 1971), the effect on eruption rate appears inconclusive at this time.

A Myofibroblastic Model

In the past decade, much attention has been given to the microstructure and function of contractile cells in areas previously thought to be devoid of non-vascular muscle tissue. In the 1950's, the commonly accepted explanation for wound contraction, that of collagen synthesis and subsequent shrinkage, was first suspect. Abercrombie et al. (1956) observed that the wounds of scrobutic (ascorbic acid deficient) guinea pigs contracted normally, in spite of the lack of new collagen synthesis. Additional evidence against the collagen shrinkage theory of wound contraction was supplied by Majno (1958). Observing that transplanted rat-tails which normally shrink, fail to do so with hydrocortisone therapy, Majno postulated

the presence of a contractile apparatus.

In spite of the above information, it was not until the early 1970's that this line of research was resumed. In 1971, Abercrombie et al. successfully isolated specialized fibroblasts in vitro from chick heart embryo tissue. These specialized fibroblasts were reported to have longitudinally arranged microfilaments and microtubules similar to those of smooth muscle cells. In this same study, the locomotion of these fibroblasts via cell extension to form new adhesions with neighboring cells, and by contraction of cell filaments, was described.

Majno et al. (1971) demonstrated that granulation tissue contains cells that behave similarly to smooth muscle cells in the presence of specific agents, such as 5-hydroxytryptamine. Electron-microscopic examination of the same tissue type by Gabbiani et al. (1971) revealed that these cells contain a fibrillar system, nuclear deformations and surface differentiations typical of smooth muscle.

After a more comprehensive study of this specialized fibroblast by Gabbiani and associates (1972), the term myofibroblast was coined. From examination of granulation tissue, electron microscopy revealed the presence of cells structurally typical of smooth muscle. Furthermore, pharmacologic experimentation demonstrated that smooth muscle stimulants, such as 5-hydroxytryptamine, angiotensin, vasopressin, norepinephrine, bradykinin and epinephrine, induced wound contraction. Smooth muscle relaxants, such as papaverine, were likewise found to cause relaxation of the wound. In the same study,

immunofluorescent labeling with human anti-smooth muscle serum successfully tagged the myofibroblasts present throughout the wound. This type of fluorescent labeling of myofibroblasts was also successfully done by Herschel et al. (1971) and again by Gabbiani et al. in 1973.

In a study of human granulation tissue, Ryan and co-workers (1974) concluded that "these modified fibroblasts, or 'myofibroblasts,' are responsible for the contraction of granulation tissue." They made this conclusion from their own results, which were:

1. Myofibroblasts contain massive bundles of intracytoplasmic microfilaments.
2. The cytoplasm of these modified fibroblasts show immunofluorescent staining with human anti-smooth muscle serum.
3. The nuclei have indentations and folds which are common to contractile cells.
4. There are cell-to-cell and cell-to-stroma connections which allow for the transmission of tension to adjacent cells and tissue.
5. Strips of granulation tissue contract or relax, in vitro, according to the pharmacologic agent administered.

The most complete microscopic description of the myofibroblast is supplied by Azuma et al. (1975), from electron microscopic examination of the rat periodontal membrane, sutures and periosteum. They observed that these cells contain dense bodies and numerous bundles of long intracytoplasmic microfilaments parallel to the cellular long axis. Microfilaments measuring 20-70 Å in diameter, on the average, were cited in the cytoplasmic processes.

Microtubules averaging approximately 230 Å in diameter, were scattered throughout. Smooth muscle-like caveolae were found just under the cell surfaces. Intercellular connections of the macula adherens, nexus, and various other types were frequently observed, as well as hemidesomosome-like complexes. Gabbiani and Badonnel (1976), however, have described these connections as being gap or tight junctions.

This contractile apparatus has been reported to exist in a wide variety and multitude of tissues and pathological conditions, some of which are renumerated in Table 2. A more complete list is supplied by Guber and Rudolph (1978).

In the last studies listed in Table 2, it is reported that the contraction of the testicular capsule is evoked by adrenergic nerve transmission to myofibroblasts. This is highly significant to this investigation because it is the first to directly link the contraction of tissue found to contain myofibroblasts with neurologic transmission.

Most directly related to this study however, is the role of the myofibroblast in the PDM, as it relates to various tooth movements. The traditional model for a tooth moving through bone was described above. In brief, it is generally assumed that a force applied to a tooth physically moves that tooth, while a series of physiological processes occur around it, allowing the tooth to translate. One possible basis for a hypothesis that links orthodontic tooth movement to neurophysiologically influences processes and cells is supplied by Azuma et al. (1975). They postulate a model for tooth movement, skeletal displacement at sutures and periosteal migration

Table 2

Places and Conditions that

Myofibroblasts are Found

1. Degenerating and cirrhotic livers (Bhathal, 1972; Gabbiani and Ryan, 1974).

2. The theca externa of rat ovarian follicles, which suggest a role in ovulation (O'Shea, 1970).

3. Epidermal cancer cells, thus supplying an explanation for cancer cell motility (Maleck and Lentz, 1974).

4. Interstitial cells of pulmonary alveolar septa, which suggest a role in autoregulation of the ventilation/perfusion ratio (Kapanci et al., 1974).

5. The cell walls of ganglia of the wrist (Ghadially and Mahto, 1971).

6. Dupuytrere's Disease, which is a progressive contraction of one or more digits (Gabbiani and Majno, 1972).

7. Aortic endothelial layers, thus possibly playing a role in hypertension (Gabbiani et al., 1975).

8. Curcumscribed fibromatosis (Feiner and Daye, 1976).

9. The adrenal gland capsule (Bressler, 1973).

10. Tissues surrounding silicone mammary protheses, in trachea and larynx granulation tissue following intubation, and in carpal tunnel syndrome (Gabbiani and Badonnel, 1976).

11. The capsules of rat testes (Gorgas and Bock, 1974; Bell and McLean, 1973).

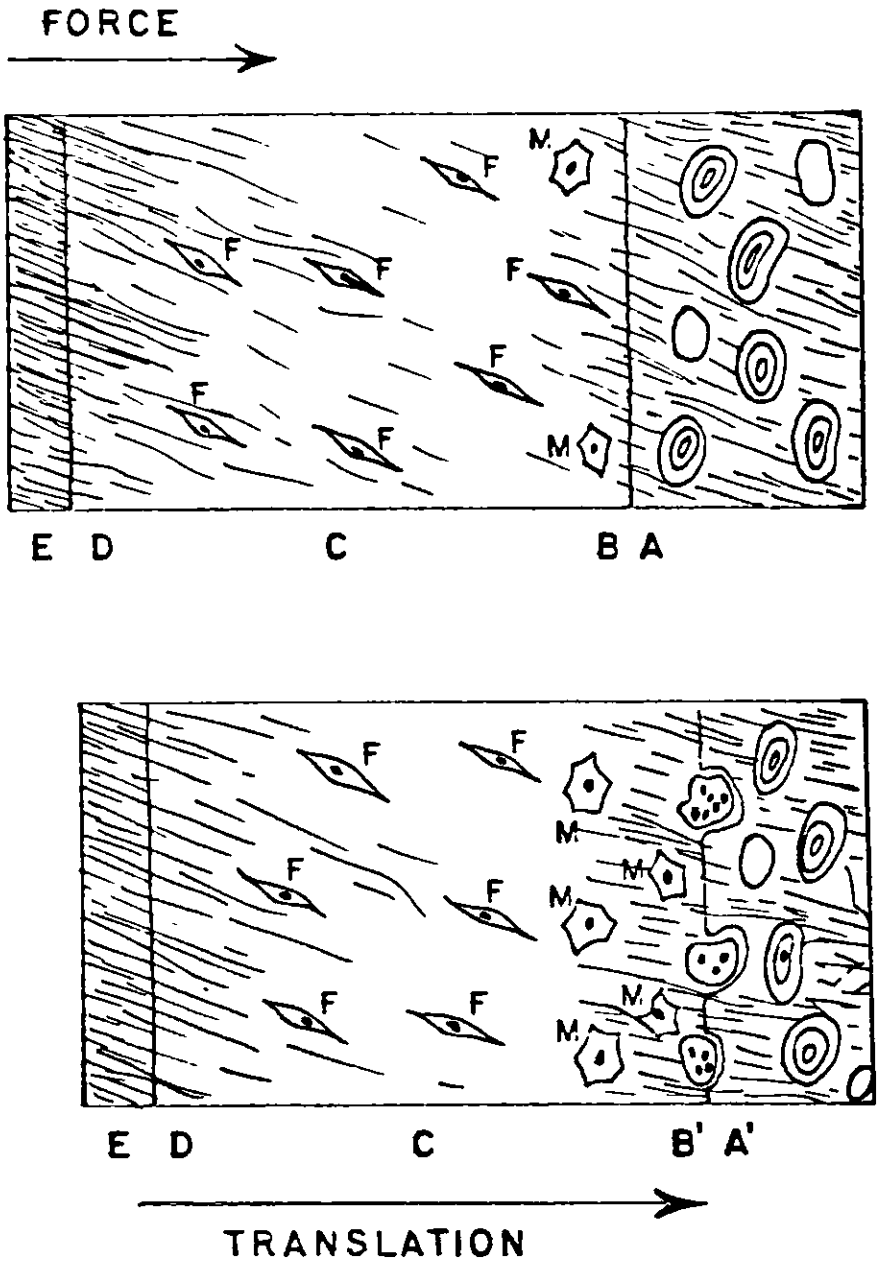
that assigns the myofibroblast as the basis for the forces that produce such movements.

Azuma and co-workers state that of all the areas of the human PDM (inner, outer and linkage zones; resorptove and depository sides), the outer zone (i.e., the closest to the alveolar bone) of the resorptive side contain the highest concentration of myofibroblasts. The culmination of information presented above led these investigators to a hypothesis similar to the one which follows.

A force application to a tooth causes an inflammatory reaction in the PDM, which then results in a widening of the PDM and osteoclastic activity on the pressure side. As this occurs, bony matrix fibers are uncovered or released to become available to serve as new PDM fibers. Simultaneously, fibroblasts modulate into myofibroblasts (how, it is now known), especially in the outer zone, and produce a contractions that are transmitted to the collagenous fibers. Whether myofibroblasts are derived from true fibroblasts, from multipotential stem cells or from some other cell type is also not presently known. The tooth is then literally pulled through the "moving" PDM space. Subsequent collagen synthesis and degradation (in the linkage zone, when present as such) allows for fiber shortening and re-linkage with new outer zone fibers. Of course, a reverse process would occur on the tension side, to be followed by osteoclastic activity. These events are diagramatically represented in Figure 1.

Figure 1.--Diagrammatic representation of myofibroblastic model of tooth movement (modified diagram from Azuma et al. 1975).

A alveolar bone
B outer zone of PDM
C linkage zone of PDM
D inner zone of PDM
E cementum
A' new alveolar wall
B' new outer zone of PDM
F collagen producing and destroying fibroblast
M myofibroblast


FORCE
F
M
E D
C
B A
E D
C
B' A'
TRANSLATION

The processes of eruption, tooth drift and post-orthodontic relapse are included in this hypothesis, with minor variations where vertical displacement occurs. To date, the force stimulus has been unknown for such tooth movements.

It is fundamental to this study that the myofibroblast has been established to be structurally and functionally "smooth muscle-like", for smooth muscle action is a result of autonomic neural transmission. If the nerve supply to a smooth muscle were interrupted, that muscle would not function normally. Hence, if the nerve supply to the myofibroblast is interrupted, one might also expect its function to be impaired.

The rationale for this study includes the premise that all types of tooth movement, be it physiologic (eruption, drift, post-orthodontic relapse) or therapeutic, are variations of a single event with common basic cellular mechanisms. Having made this assumption, it can be acknowledged that the forces responsible for tooth movement are unknown. Consequently, the examination of any cells, tissue organs, or physiological events suspected of influencing tooth movement is justified. With this in mind, the literature reviewed above becomes significant in the following points: (1) possible mechanisms and forces responsible for tooth movement not related to the PDM neurophysiology have been extensively investigated; (2) none of these same mechanisms or forces, based on scientific investigation, can be said conclusively to be responsible for the initiation or direction of tooth movement; (3) the

neurophysiology of the PDM as it relates to tooth movement has not been extensively investigated; and (4) those studies that have focused on the PDM neurophysiology have produced some promising results. To briefly restate some examples: the PDM was reported by Griffin and Harris (1974) to contain nerve receptor mechanisms similar to the skeletal muscle stretch receptor, and Azuma et al. (1975) have demonstrated the presence of smooth muscle-like cells, called myofibroblasts, within the PDM. Gorgas and Bock (1974) have shown that myofibroblasts in rat testes respond to adrenergic stimulation by causing a contraction of the capsule. In addition, resection of the superior cervical ganglion and the ipsilateral inferior alveolar nerve of rats was shown to cause an increase in incisor eruption rate of the operated side (King, 1936; Edwards and Kitchen, 1938; Taylor and Butcher, 1951; Miller, 1957; Brown et al., 1961; Rehak, 1963).

It has been frequently pointed out here that many of the reported theories for tooth movement have been lacking because they fail to identify any initiating agents or actions for the subsequent events. However, in view of the above information, it is now possible to hypothesize that orthodontic tooth movement, as well as other types, is a neurophysiologically initiated and directed process.

STATEMENT OF THESIS

In recent years there has been considerable attention given to the description and examination of a specialized, "smooth muscle-like cell", called a myofibroblast, that has been found in a wide variety of tissues, including the human periodontal membrane. As a result of such examination, the myofibroblast has been postulated to be the basis for cellular tissue and organ motility. Tooth movement is one example.

The assumption that any "smooth muscle-like cell" would presumably have, directly or indirectly, neurological innervation, has led to this investigation. A hypothesis is thus formulated which contends that tooth movement (physiologic or therapeutic) is a neurophysiologic initiated and directed process.

To test this hypothesis, the PDM of cats have been partially denervated by resection of the superior cervical ganglion and the ipsilateral inferior alveolar nerve, followed by bilateral orthodontic tooth movement. Although smooth muscle is autonomically innervated, the inferior alveolar nerve was also resected because it probably contains some, albeit few, sympathetic fibers, and for the benefit of denervating the PDM as completely as possible. The relative rates, total distance moved and degree of tipping of the treated and non-treated side teeth were determined by direct intraoral and indirect cephalometric measurements, with the aid of amalgam markers in teeth and tantalum implant markers in the corpus of

the mandible. Vital bone stains were also used to microscopically identify regions of new bone deposition.

This preliminary investigation is intended to determine, simply, whether or not denervation of the PDM may appear to have some effect (acceleration or retardation) on the rates of experimentally-moved teeth in laboratory animals. Because of the constraint on the number of large-sized animals that could be utilized, meaningful statistical evaluation of results are not possible. The results of the study, rather, are intended to supply suggestive data that may form the basis for new avenues of research.

MATERIALS AND METHODS

Sample

Eight, young adult male cats with complete permanent dentitions and ranging in weight from 2.7 Kg to 4.3 Kg were utilized in this experimental study. This animal model was chosen because:

1. the animal is of adequate size to allow for the reliable surgical resection of certain nerves without the aid of unusual instrumentation;
2. the dentition of the cat is similar to that of the human (e.g., diphydont, thecodont, heterodont);
3. the dentition of the cat allows for separate unilateral orthodontic tooth movements without concern for cross-innervation of the nerves of the mandible (e.g., incisors of rodents);
4. the size of the animal is adequately suited to the construction and manipulation of orthodontic appliances;
5. the cat is readily available and is easy to work with;
6. the hormonal variation of the male cat is less than the female cat (Crouch, 1969).

Experimental Design

The superior cervical ganglion and the inferior alveolar nerve of the ipsilateral side were unilaterally resected and the mandibular second premolar teeth were bilaterally protracted in

all eight cats. The surgical procedures performed were divided equally between right and left sides, with each animal randomly assigned to receive either a right or a left side operation. Teeth were moved for a period of nine weeks or until exfoliation was imminent.

A single variant, two sample, paired data design exists, with the surgically treated sides serving as the experimental sample, and the surgically non-treated sides serving as the control. The variant is the rate of tooth movement (Table 3).

Experimental Procedure

Upon receipt, each cat was weighed, checked for condition of general health, age (i.e., scars, injuries, gingival recession, tooth abrasion and attrition, etc.), sex, and the presence of all permanent teeth in good condition. A two week period of isolation was selected to ensure that the animal's health was stable before treatment was instituted.

Nerve Resection

Anesthesia

The cats were premedicated with acepromazine maleate (2 mg/Kg) injected intramuscularly. General anesthesia was obtained with sodium pentobarbital (60 mg/ml) injected into the femoral vein at a dose individually titrated for each animal (2.5 to 3.5 cc). The cats were then intubated (#12 endo-tracheal tube) to protect the airway from laryngospasm and surgical manipulation.

Table 3

Treatment Assignments

Cat	Stain	Sham	Side	
			Right	Left
0506	yes	no	experimental	control
0517	yes	no	control	experimental
0520	no	no	control	experimental
0524	no	no	control	experimental
0534	yes	yes	experimental	control
0535	yes	no	control	experimental
0536	no	yes	experimental	control
0537	no	yes	experimental	control

Surgical Procedure

Aseptic techniques were used in all surgical procedures. The surgical site was shaved, scrubed with a betadine surgical scrub solution and draped. A single midline incision was made ventrally from the anterior border of the mandible (i.e., symphysis) to the inferior level of the neck. The skin and fascia were retracted.

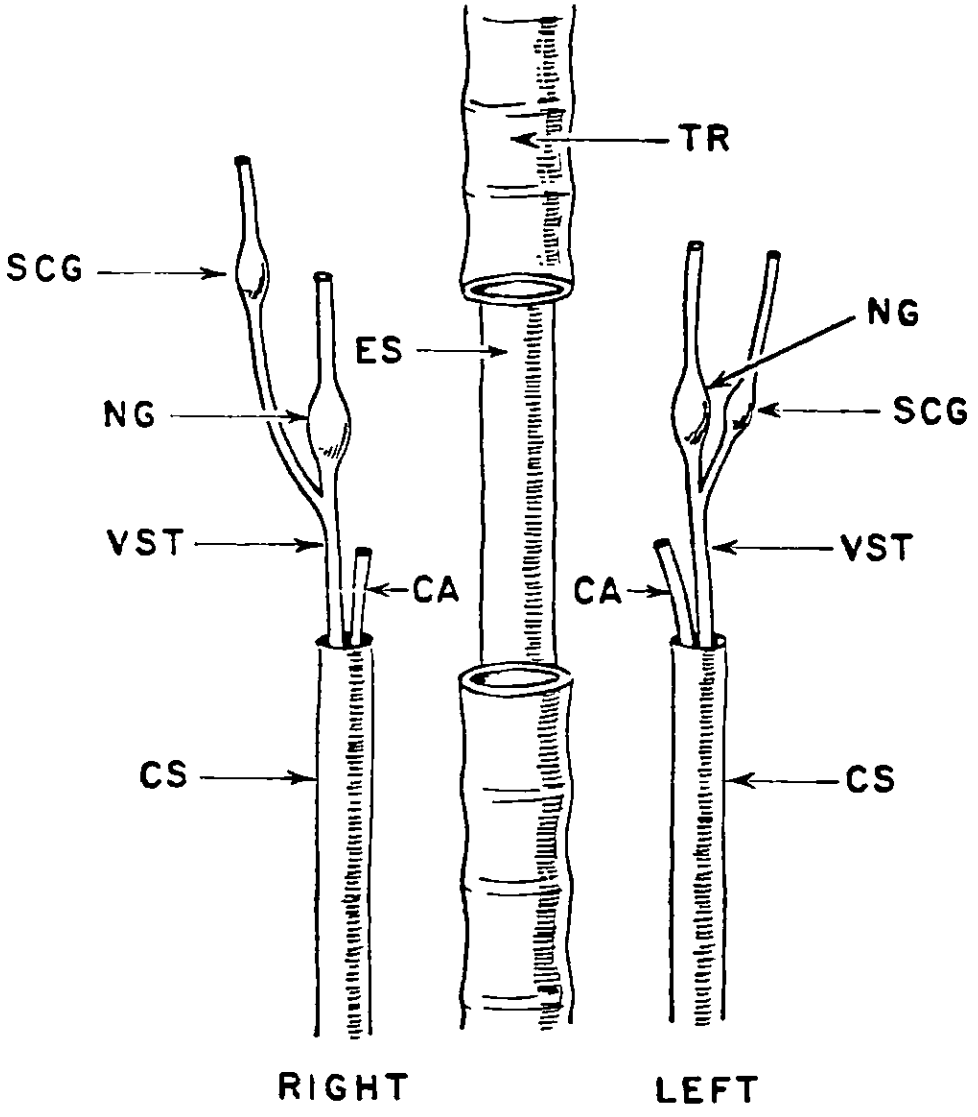
Superior Cervical Ganglion

Access to the deeper portion of the neck was obtained by blunt dissection through the fascial plane lateral to the sternohyoideus muscle and medial to the sternothyroideus muscle. All sizable vessels were ligated to ensure a dry surgical field. The carotid sheath, which is found immediately lateral to the esophogus, was opened to separate the carotid artery from the vasosympathetic trunk; the latter was dissected superiorly to a large ganglion. At this point, a right and left dimorphism was observed in all the animals used. On the left side, the large ganglion mentioned above was actually two ganglia. The larger nodose ganglion of the vagus nerve was positioned medially, and the smaller superior cervical sympathetic ganglion laterally. On the right side, the first ganglion observed when tracing the nerve trunk superiorly, was the larger nodose ganglion, and the smaller superior cervical ganglion was found approximately 5 mm further superior (Figure 2).

In either case, the sympathetic nerve was severed proximally

Figure 2.—Diagrammatic representation of the right and left side anatomical dimorphism of the nodose and superior sympathetic ganglia.

TR trachea
ES esophogus
CS carotid sheath
CA carotid artery
VST vagosympathetic trunk
SCG superior sympathetic ganglion
NG nodose ganglion


TR
SCG
ES
NG
NG
SCG
VST
VST
CA
CA
CS
CS
RIGHT
LEFT

to its ganglion, dissected distally to its joining with the vagus nerve, and again severed at this point. The carotid artery and vagus nerve were left intact. Ethicon 3-0 silk sutures (Ethicon, Johnston & Johnston) were placed to close deeper fascial planes.

Inferior Alveolar Nerve

Utilizing the same cutaneous opening just described, access to the medial surface of the mandible was then obtained by reflecting the masseter muscle from the inferior border of the mandible, starting at the anterior margin of the muscle and working posteriorly. Again, all sizable vessels were ligated. The anterior portion of the medial pterygoid muscle was also reflected in such a manner that the inferior alveolar nerve and artery could be seen entering the mandibular canal. A 10 to 15 mm section of the nerve was then carefully resected, so as not to damage the inferior alveolar artery. Muscles were then repositioned and loosely sutured in place with Ethicon 3-0 silk sutures. The entire surgical site was then closed with several layers of silk sutures to close fascial planes, and with Vetafil light synthetic sutures (W. A. Butler Co.) to close the skin. A plastic protective dressing (Spray-band, Schuco Co.) was used over the incision after cleansing with 75% alcohol.

Sham surgery. To simulate the surgical manipulation of the muscles of mastication in the process of resecting the inferior alveolar nerve, a sham operation was performed on the

opposite (control) side of the mandible in three of the eight animals. It was not done on all eight cats because of the excessive length of the surgery for the initial animals. The exact same procedure was followed for the sham, except that the nerve was not resected.

Postoperative Care

Postoperatively, the animals were returned to their cages where they were given 150,000 units of a long acting penicillin (Longicil, Fort Dodge, Fort Dodge, Ind.). This antibiotic was administered at three day intervals for the remainder of the study. For approximately one week postoperatively, the cats were given daily alternating doses (100 cc) of 9% saline and glucose (5% dextrose, 0.2% saline), administered subcutaneously.

A semi-soft diet of CD cat food (Hills Co.) was fed to the cats for two weeks postoperatively, afterwhich a normal hard diet of Purina Cat Chow (Ralston Purina Co.) was given until the appliances were inserted.

Tooth Extractions and Implant Insertions

Approximately one month was allowed for animal recovery from the first surgery and for nerve degeneration to occur. At this time, the animals were sedated with an intramuscular injection of Ketamine hydrochloride (100 mg/ml) and promazine hydrochloride (7.5 mg/ml), (Ketaset Plus, Bristol Lab., Syracuse, N.Y.), 1 to 2

cc as needed. The mandibular right and left premolar teeth were extracted (cat dental formula: 3.1.3.1./3.1.2.1.). It was necessary to bisect these two-rooted teeth in order to remove them without fracturing the fragile roots.

In order to create radiographic landmarks, small amalgam markers were placed into cavities prepared with a 33½ inverted cone burr in the buccal groove of the mandibular right and left second premolar and molar teeth. In addition, two tantalum implant markers were driven into each side of the mandible from an intraoral approach with the aid of a mallet and a Bjork implanter. The implants were placed at the depth of the buccal vestibule, one in the anterior portion of the body of the mandible, and one in the posterior (Figures 3 and 4, Plate II).

Tooth Moving Appliance

A mandibular stabilizing base arch was fabricated directly on the sedated animals using .022 inch stainless steel wire, which when inserted, bridged molar-to-cuspid-to-cuspid-to-molar. Troughs were cut around the cervix of the mandibular second premolars, through which .010 inch dead soft stainless steel wires were ligated, and terminated in hooks on the mesial surface.

In a separate procedure, the base arch was directly bonded to the molar and cuspid teeth of the sedated animal using Concise direct bonding agent (3M Co.), and the maxillary premolars were ground out of occlusion with the mandibular teeth to prevent

Figure 3.--Lateral view of mandible, teeth, metallic markers and tooth moving appliance.

MAM molar amalgam marker
DB direct bond
PAM premolar amalgam marker
LH ligature hook
BA .022 inch base arch
EL elastic
Ca canine
SP second premolar
Mo molar
TI tantalum implant
ES extraction site

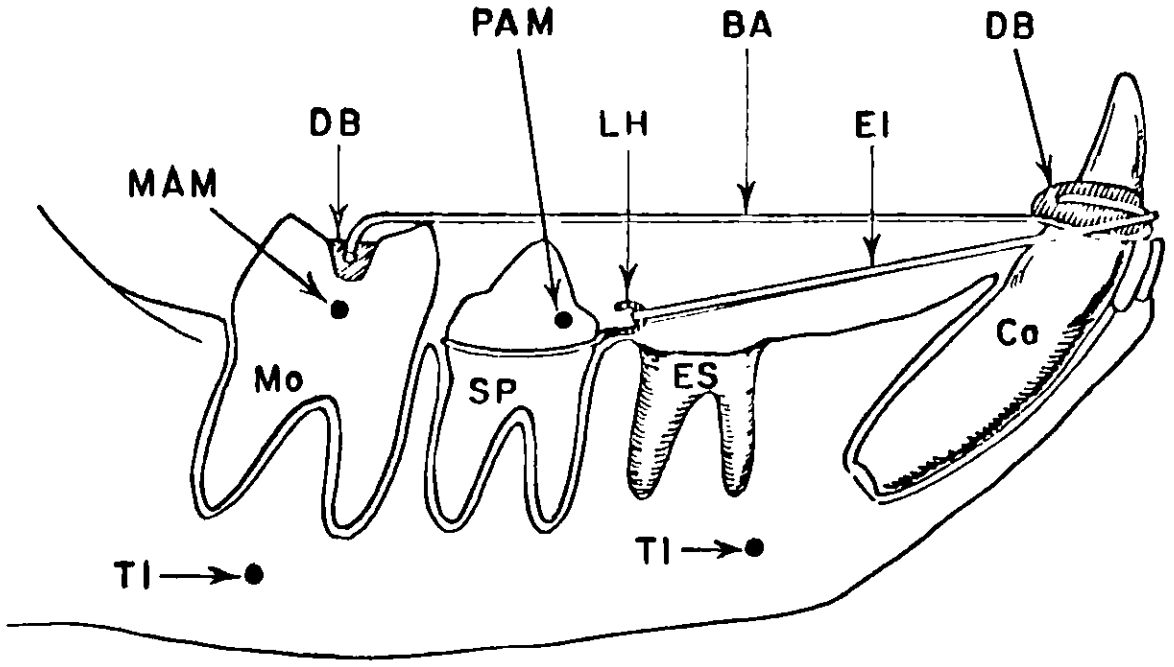

PAM
BA
DB
DB
LH
EI
MAM
Mo
SP
ES
Co
TI
TI

Figure 4.--Dorsal view of mandible, teeth, metallic markers and tooth moving appliance.

TI tantalum implant
AM amalgam marker
EL elastic
BA base arch
Mo molar
SP second premolar
ES extraction sites

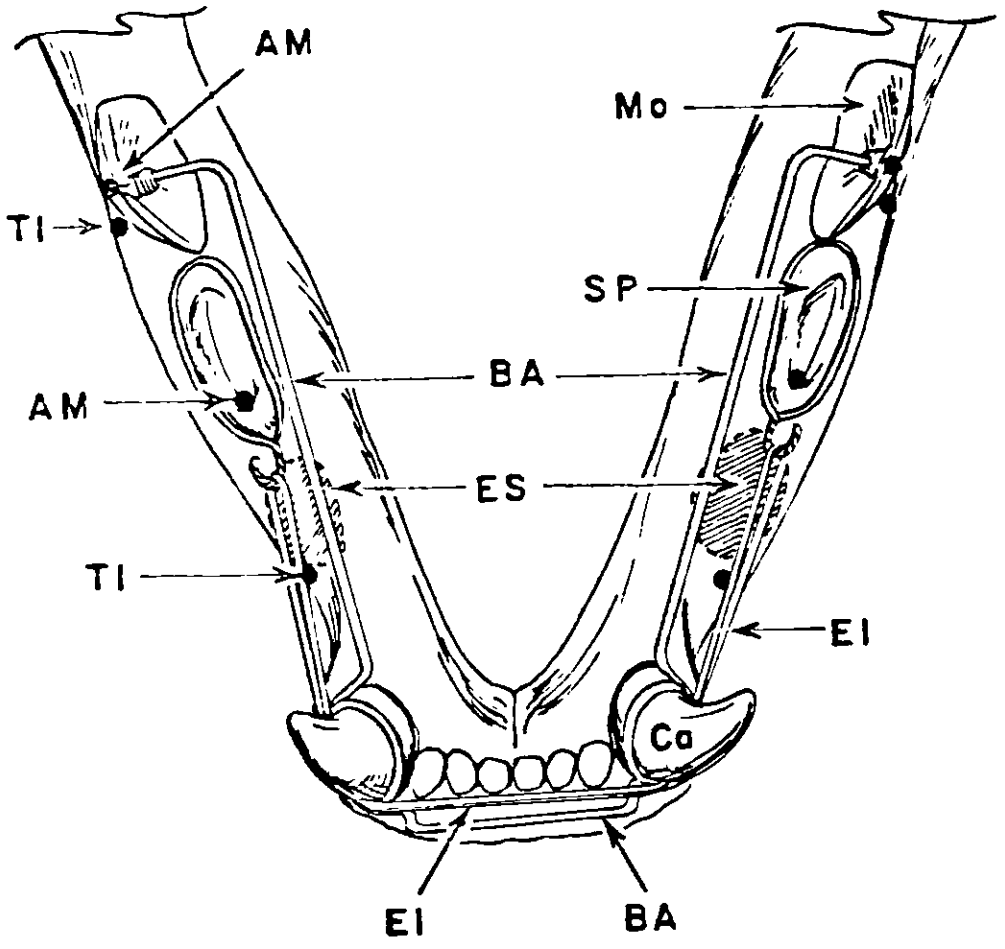
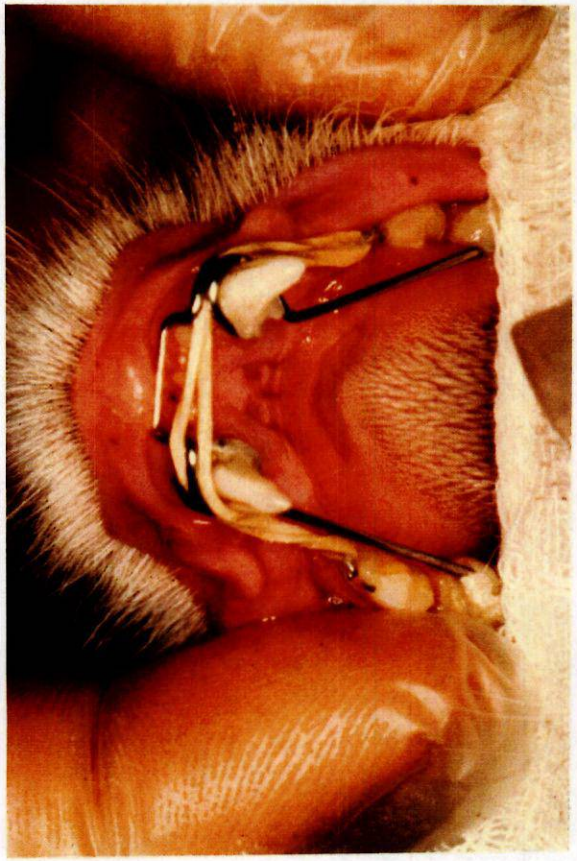
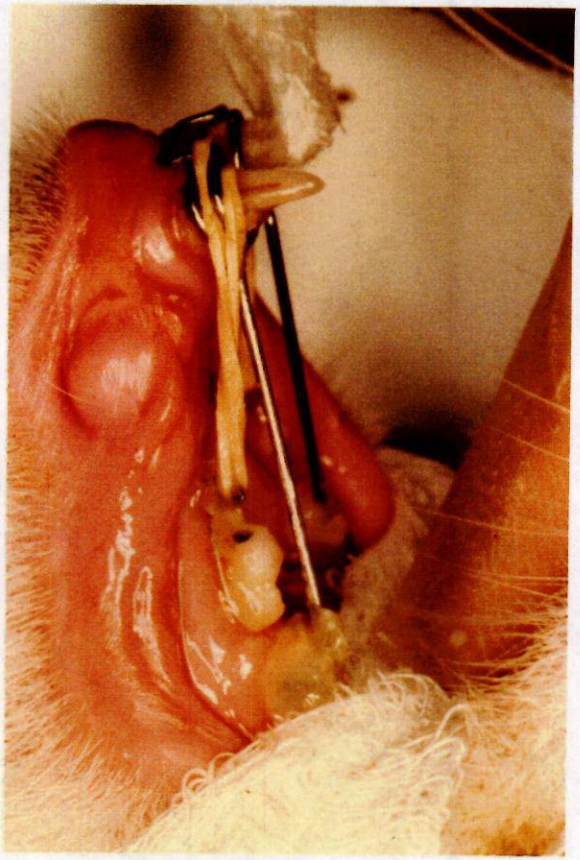

AM
Mo
TI
SP
BA
AM
ES
TI
EI
Ca
EI
BA

PLATE I

Intra-oral Photographs
of Tooth Moving Appliance





occlusal interferences (Figures 3 and 4, Plates I and II). The animals were fed a liquid diet (CD cat food, sustagin and water) for the remainder of the study.

Activation of the Appliance

The appliance was activated by stretching an elastic (TP Latex Colortech, orange or green) from the mesial hook of the second premolar around each cuspid and through the trough created by the base arch, to the mesial hook on the other second premolar (Figures 3 and 4, Plate I). Consequently, the contralateral second premolars were protracted by a reciprocal force.

Although the magnitude of the force varied greatly, from around 7 ounces at elastic insertion to approximately 2 ounces before the weekly elastic change, the force was theoretically always equal on each pair of teeth in a single animal, at any given time, because the force applied to the teeth was reciprocal.

Vital Dyes

In order to microscopically identify regions of new bony deposition, procion vital dyes (Imperial Chemical Ind.) were administered intraperitoneally to four of the cats; procion red MX-8B (125 mg/Kg) before the appliances were activated, and procion blue MX-R (100 mg/Kg) two weeks before they were killed. Because these animals became very ill, as a result of the dye administration, almost dying, the remaining cats were not injected with the dye, and the dye-treated cats were not given the dye again until

near the termination of the study.

The procion dyes are derivatives of trichlorazine and have two reactive chlorines in their structure, which enables them to form covalent bonds with protein matrices. Effective blood levels are sustained for approximately 10 days (Seiton and Engel, 1969; Prescott et al., 1968).

The dye solution (125 mg/ml saline) was sterilized by filtration with a 0.45 miliport filter (Gelman Instrument Co.). These dyes are unstable and react freely with hydroxyl groups, including water, especially under alkaline conditions. For this reason, solutions were freshly prepared before use, with no alkali added (Raper, 1977).

Data Collection

The animals were sedated for collection of data and adjustment of appliances before the appliances were activated at weekly intervals. At these times, the appliances were cleaned, direct measurements and cephaloradiographs were taken, elastics changed, and all interferences (i.e., apposing teeth, excess bonding agent, base wire) were removed from the path of the moving tooth.

Intra-oral Measurement

Direct intra-oral distances were measured with the aid of a Helios caliper while the animals were sedated. Distances were measured, on both the surgically treated and untreated sides, from the amalgam markers in the first molars to the amalgam markers in

the second premolars (Figure 5).

Cephalostat

A cephalostat was specially constructed for the use with cats (Plate III). The head of the cat was secured by a palatal bar which supported the hard palate and the maxillary canine teeth. This allowed for accurate repositioning of the head in the transverse and frontal planes, but with some variation in the sagittal plane. The source-film distance was fixed at 1.775 m and the object-film distance at 11.0 cm.

Right and left radiographs were taken with the head turned so that the respective side of the mandible was parallel to the film. Thus, both the alveolar ridge and the film were perpendicular to the central ray of the x-ray beam (Plates II and III). Although this determination was visual and only an approximation, it was held constant for each animal on all subsequent radiographs. Exposure was varied according to animal weight and ranged from 2.5 seconds to 3.1 seconds at 85 KVP and 10 MA, using Kodak no screen film (NS-2T ready-pack, 5" x 7", Schein, Inc.).

Cephalometric Measurements

Four measurements were recorded from each radiograph. The first measurement was a radiographic duplication of the same distance measured by the direct intra-oral technique (i.e., from second premolar to molar). The second distance recorded was measured from the posterior mandibular tantalum implant to the

Figure 5.--Lateral view of mandible, teeth and metallic markers, showing the four basic distances or angles measured cephalometrically.

A premolar to molar distance
B premolar to implant distance
C molar to implant distance
D angle measuring amount of premolar tipping

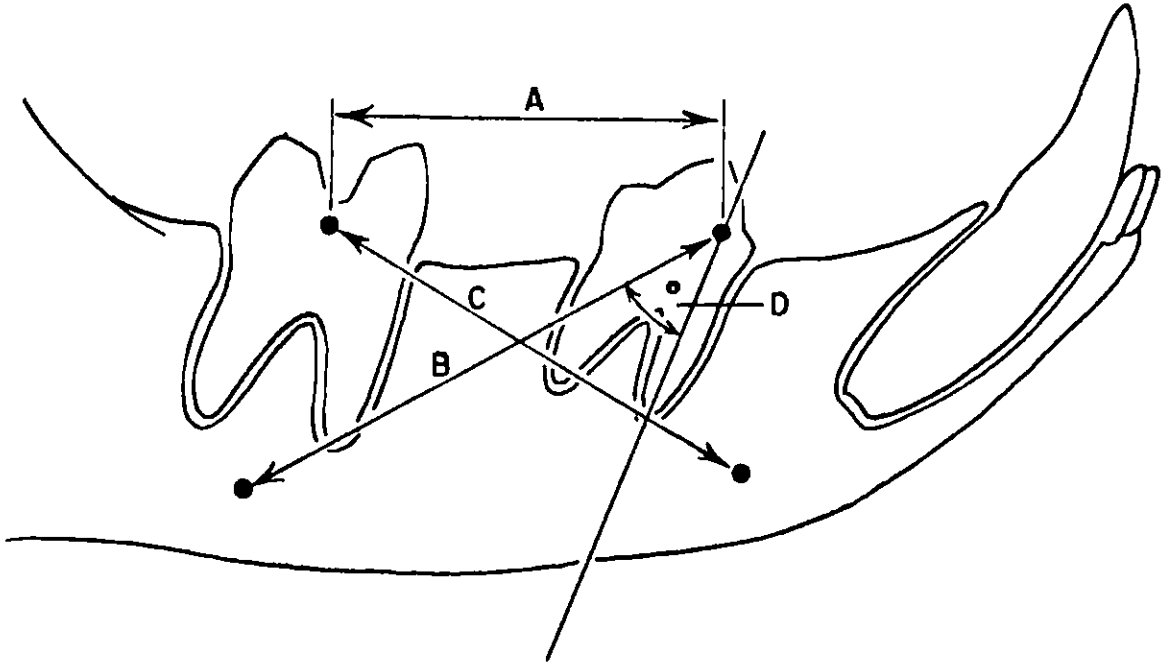

A
B
C
D

PLATE II

CEPHALOMETRIC RADIOGRAPHS

1. Right side

2. Left side


THE BOLTON FUND
CASE WESTERN RESERVE
3 6 1

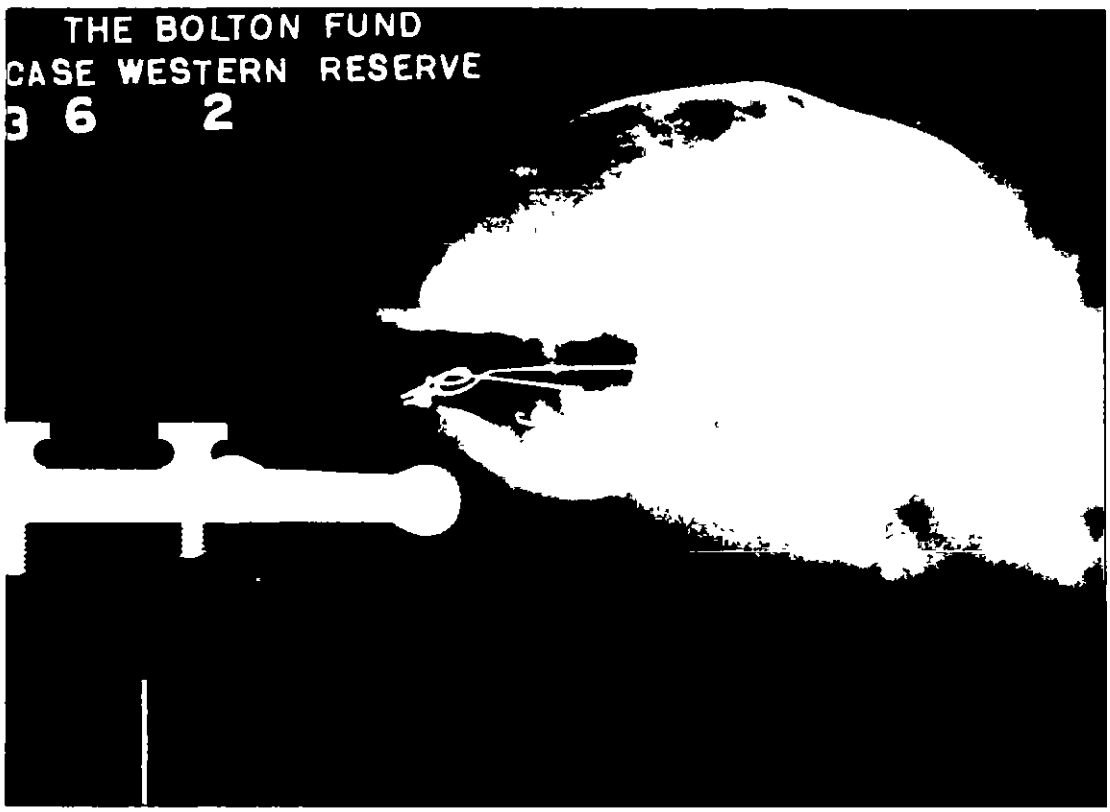
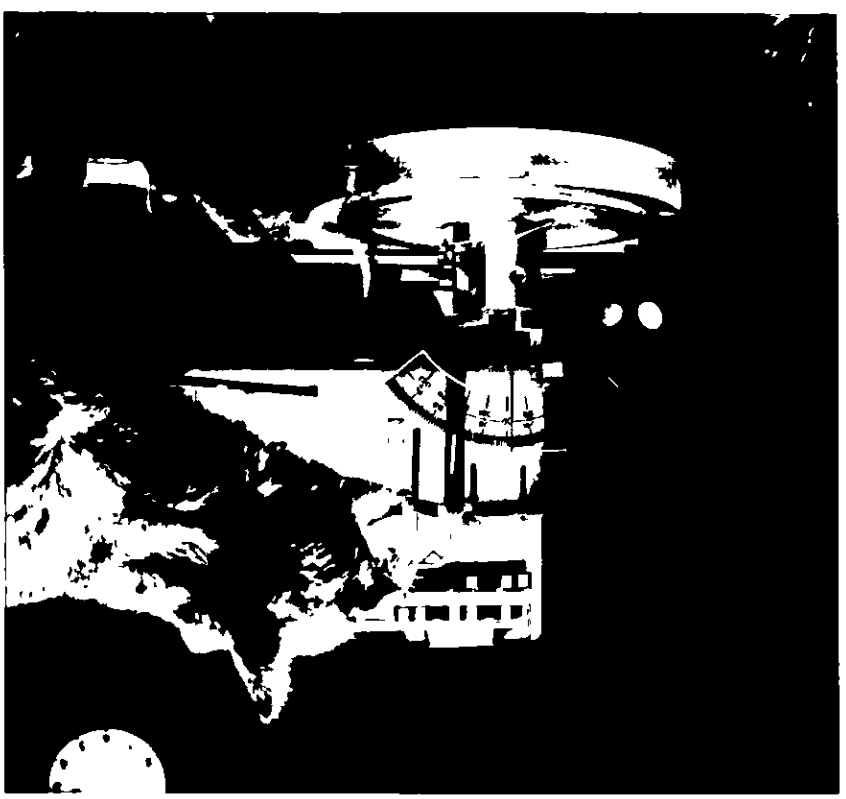

THE BOLTON FUND
CASE WESTERN RESERVE
3 6 2

PLATE III

Cephalostat with Cat in Place





amalgam marker in the molar. This distance was measured to determine if the molar had been driven distally, in order to properly evaluate the amount of premolar protraction represented by the tooth-to-tooth measurement. Finally, the degree of tipping of the second premolar was determined by measuring the angle formed by the intersection of a line from the second premolar amalgam marker through the apex of its root, and a line from the posterior mandibular implant to the second premolar amalgam (Figure 5).

Termination of Study

After a period of 9 weeks, or whenever any of the moving teeth were therapeutically extracted, whichever occurred first, the study was terminated. The animals were sedated with 1 cc ketamine hydrochloride (100 mg/ml), injected intramuscularly, and killed with a 5 cc intracardial injection of sodium pentobarbitol (60 mg/ml). The animals that were bone-stained had tissue blocks immediately excised for histological preparation as described below. An autopsy was then performed on all animals to determine if any visible nerve regeneration had taken place. Tissue suspected to be of inferior alveolar nerve origin was also removed for histological preparation. The intact, non-resected mandibles were removed from the animal, and dissected free of soft tissue to determine if implants were firmly fixed in bone.

Data Reduction

Each animal contributed a set of data to both the control sample and to the experimental sample (Table 3). All measurement types were analyzed separately with comparisons made between the control and experimental groups. For statistical analysis, a Student t-test was used for each set of measurements to determine if a significant difference existed between control and experimental states. Because only a fraction of the animals received a sham operation, this variant was not statistically considered, and because the study was conducted over a different time span for certain animals, weekly comparisons were not made.

Histologic Preparations

The segments of tissue removed from the mandibular canal were fixed in 10% neutral buffered formalin for a period of two days. Dehydration was accomplished with successive washes of 70%, 80%, 95% and absolute ethol alcohol. After clearing with xylene, the tissues were infiltrated and embedded in parafin. Sections were cut at 6 microns and stained with luxol fast blue.

RESULTS

The results of this investigation will be presented in the following manner: (1) general observations, (2) descriptive results, (3) statistical analyses of results, (4) autopsy results, and (5) descriptive histological results.

General Observations

Following the surgical resection of the superior cervical ganglion and inferior alveolar nerves, the animals required a recovery period of 3 to 10 days, during which time they would not eat or freely move about and their body temperatures increased 2 to 4 degrees above normal. They received supportive therapy during this time, after which, they regained normal appetites and physical activity.

Immediately after the surgical procedure, all of the animals experienced a pupillary constriction, a draping of the nictitating membrane and increased lacrimal secretion of the operated side, suggesting that sympathetic innervation to that side of the head was interrupted. These signs existed for 2 to 6 weeks postoperatively, after which, normal appearance and function of the eye were restored to all cats. No other gross signs or symptoms resulted from the surgical resection of the nerves.

Two weeks after the administration of the vital dyes and activation of the appliances, one animal died as a result of a septicemia. This was apparently due to a rupture of the intestine during the intraperitoneal injection of the vital dye. Four weeks after the activation of the applicances, three animals developed a seasonal, respiratory viral infection, from which one of the cats died. The other two cats completely recovered.

The teeth moved at quite different rates among the different animals, and it was necessary to terminate the study on certain cats before the specified term of the investigation (9 weeks of tooth movement), because of very rapid movement. Consequently, no attempt was made to compare weekly movements among cats, nor collective weekly movements. Rather, only individual cumulative weekly movements or collective total movements were considered. One cat failed to have any significant tooth movement on either side, and this data was rejected from the results, leaving a total sample size of five animals.

Descriptive Results

Intra-Oral Measurements

The weekly cumulative movement of both the control and experimental sides of each animal is presented in Table 4. From this data, it can be seen that one animal was terminated after three weeks of tooth movement, one animal after seven weeks, and the remaining three after nine weeks.

Table 4

Intra-Oral Measurements, Weekly Cumulative

Movement (millimeters)

Week	Side	Cat				
		0506	0517	0520	0536	0537
1	C*	0.09	0.66	0.92	0.70	0.35
	E*	0.26	0.05	1.46	0.01	0.36
2	C	0.49	0.65	2.59	1.07	0.92
	E	0.28	0.75	4.10	0.10	0.96
3	C	0.74	0.75	5.27	1.49	2.67
	E	0.64	1.43	11.44	0.41	2.16
4	C	1.56	0.98	. .	1.69	2.96
	E	1.82	1.36	. .	0.52	2.69
5	C	2.40	1.00	. .	2.23	4.17
	E	2.56	2.52	. .	0.89	3.15
7	C	4.76	1.50	. .	2.70	5.52
	E	3.71	3.85	. .	1.09	5.83
9	C	10.91	1.97	. .	2.91	. .
	E	9.95	4.50	. .	1.11	. .

*C--Control
*E--Experimental

Table 5

Intra-Oral Measurements

Total Tooth Movement

(millimeters)

	Side	
Cat	Control	Experimental
0506	10.91	9.95
0517	1.97	4.50
0520	5.27	11.44
0536	2.91	1.11
0537	5.52	5.83
Total	26.58	32.83
$\bar{X}$	5.32	6.57

Figure 6.--Intra-Oral Measurement
Total Movement

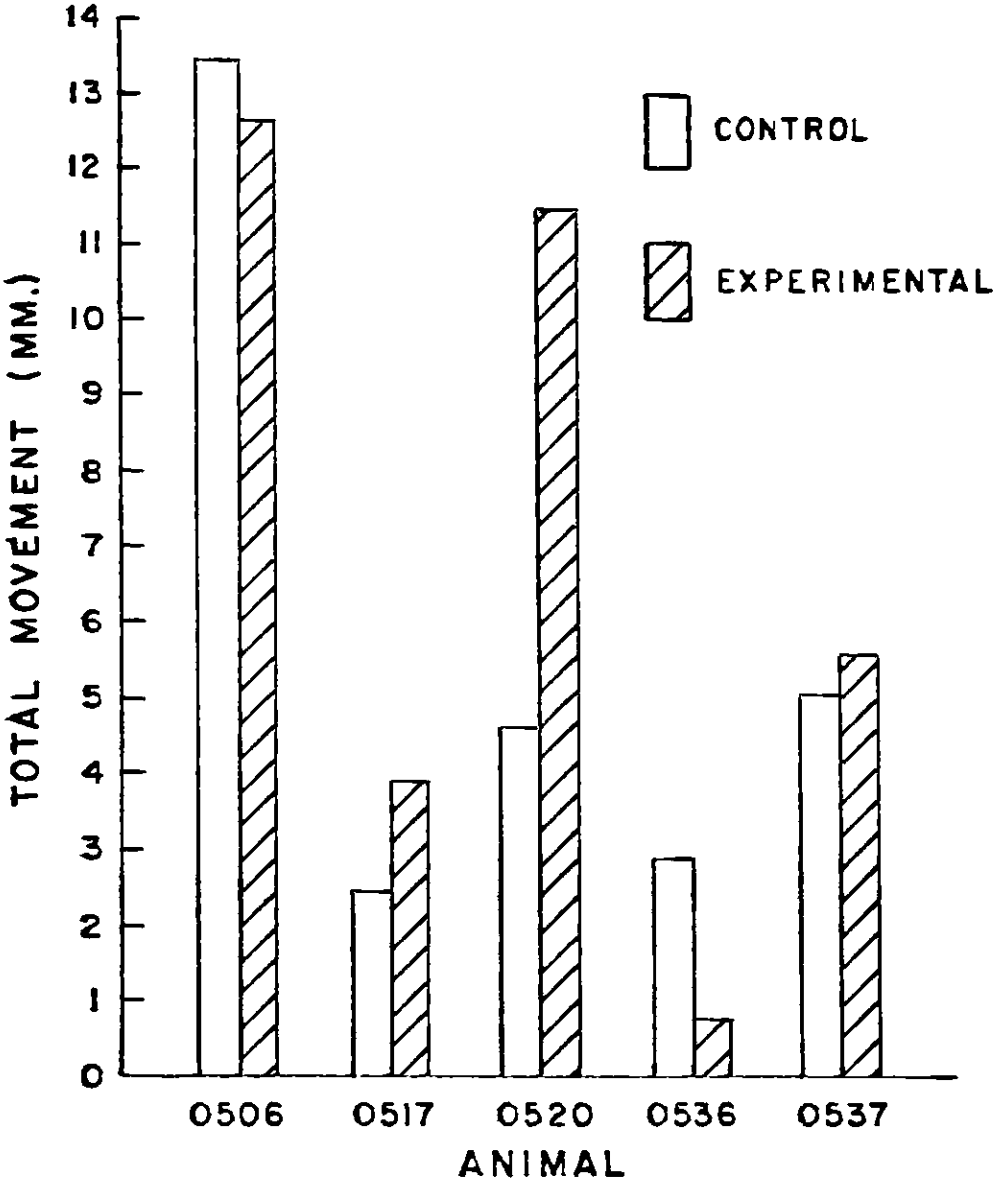

TOTAL MOVEMENT (MM.)
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
CONTROL
EXPERIMENTAL
0506
0517
0520
0536
0537
ANIMAL

Figure 7.--Intra-oral Measurement #0506
Weekly Cumulative Movement

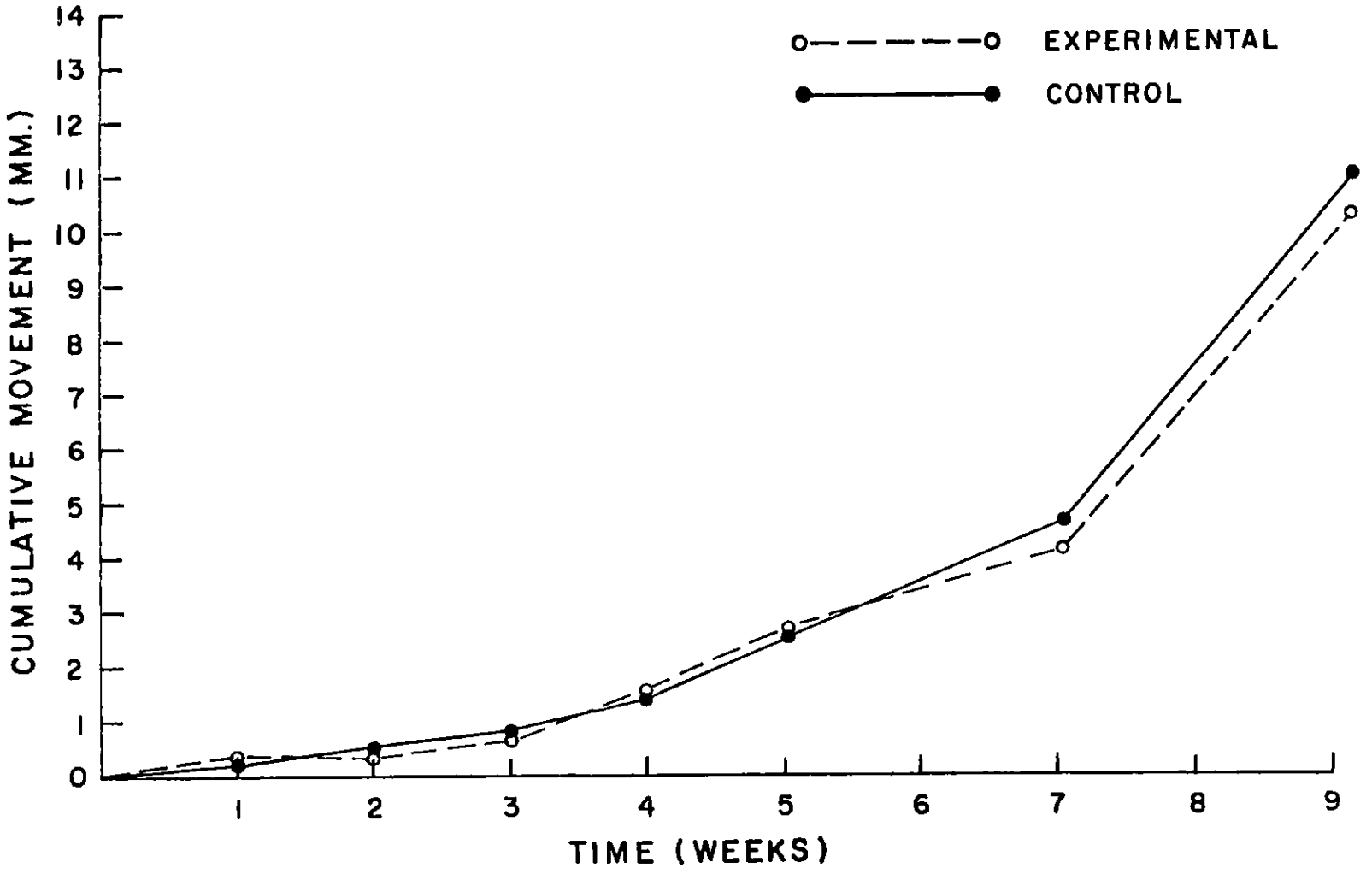

EXPERIMENTAL
CONTROL
CUMULATIVE MOVEMENT (MM.)
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
1
2
3
4
5
6
7
8
9
TIME (WEEKS)

Figure 8.--Intra-oral Measurements #0517
Weekly Cumulative Movement

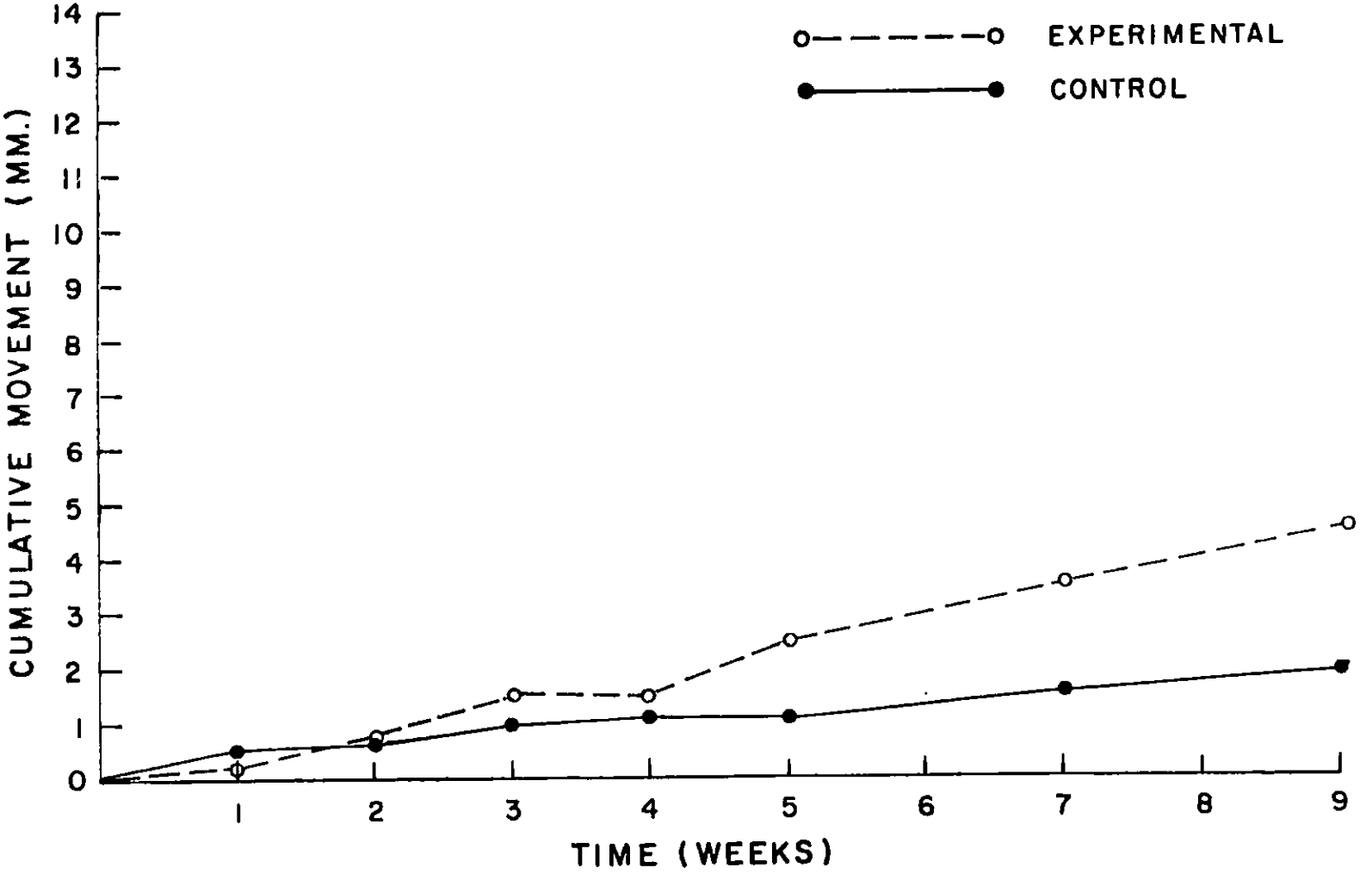

EXPERIMENTAL
CONTROL
CUMULATIVE MOVEMENT (MM.)
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
1
2
3
4
5
6
7
8
9
TIME (WEEKS)

Figure 9.--Intra-oral Measurements #0520
Weekly Cumulative Movement

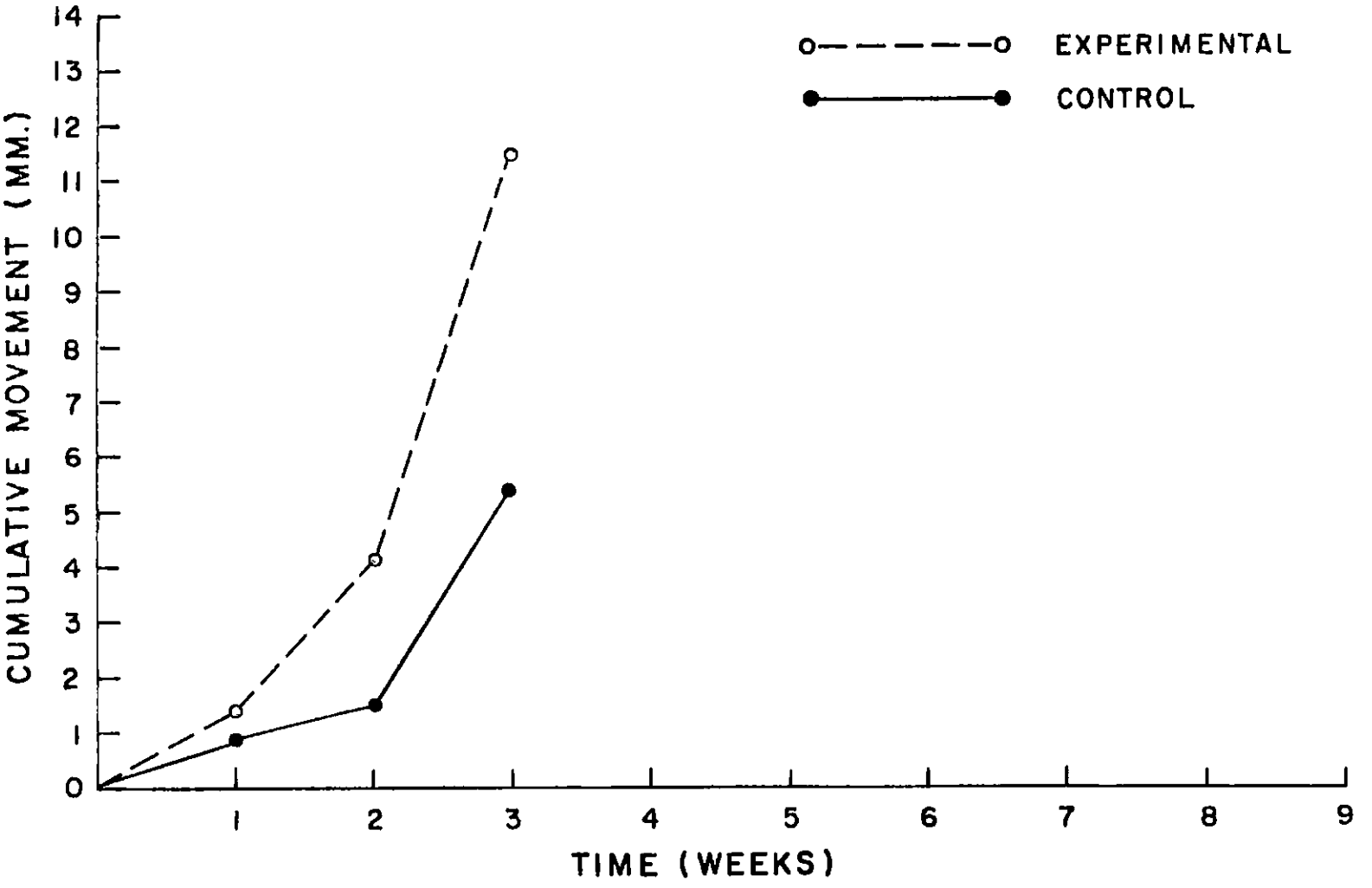

EXPERIMENTAL
CONTROL
CUMULATIVE MOVEMENT (MM.)
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
1
2
3
4
5
6
7
8
9
TIME (WEEKS)

Figure 10.--Intra-oral Measurement #0536
Weekly Cumulative Movement

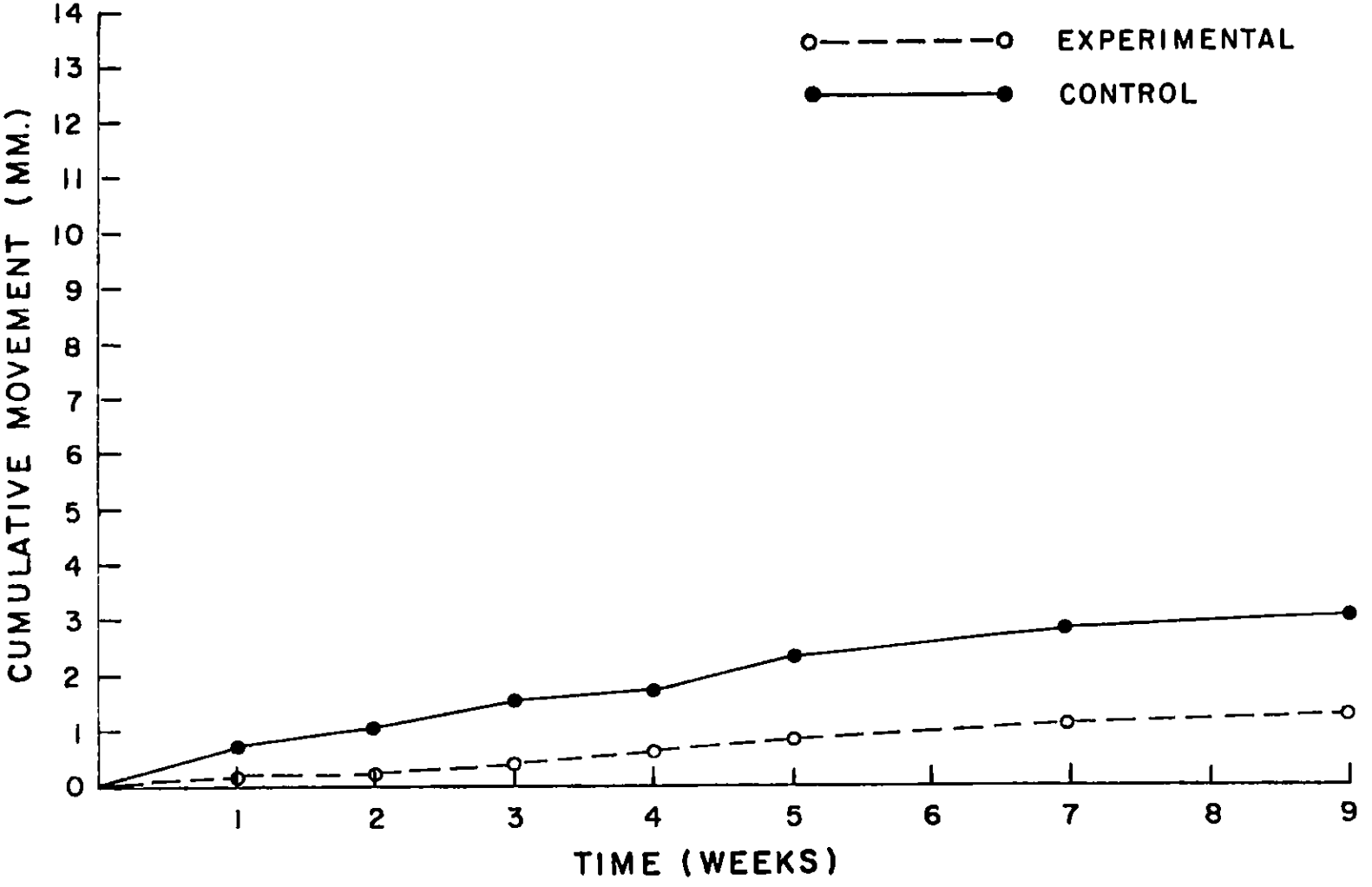
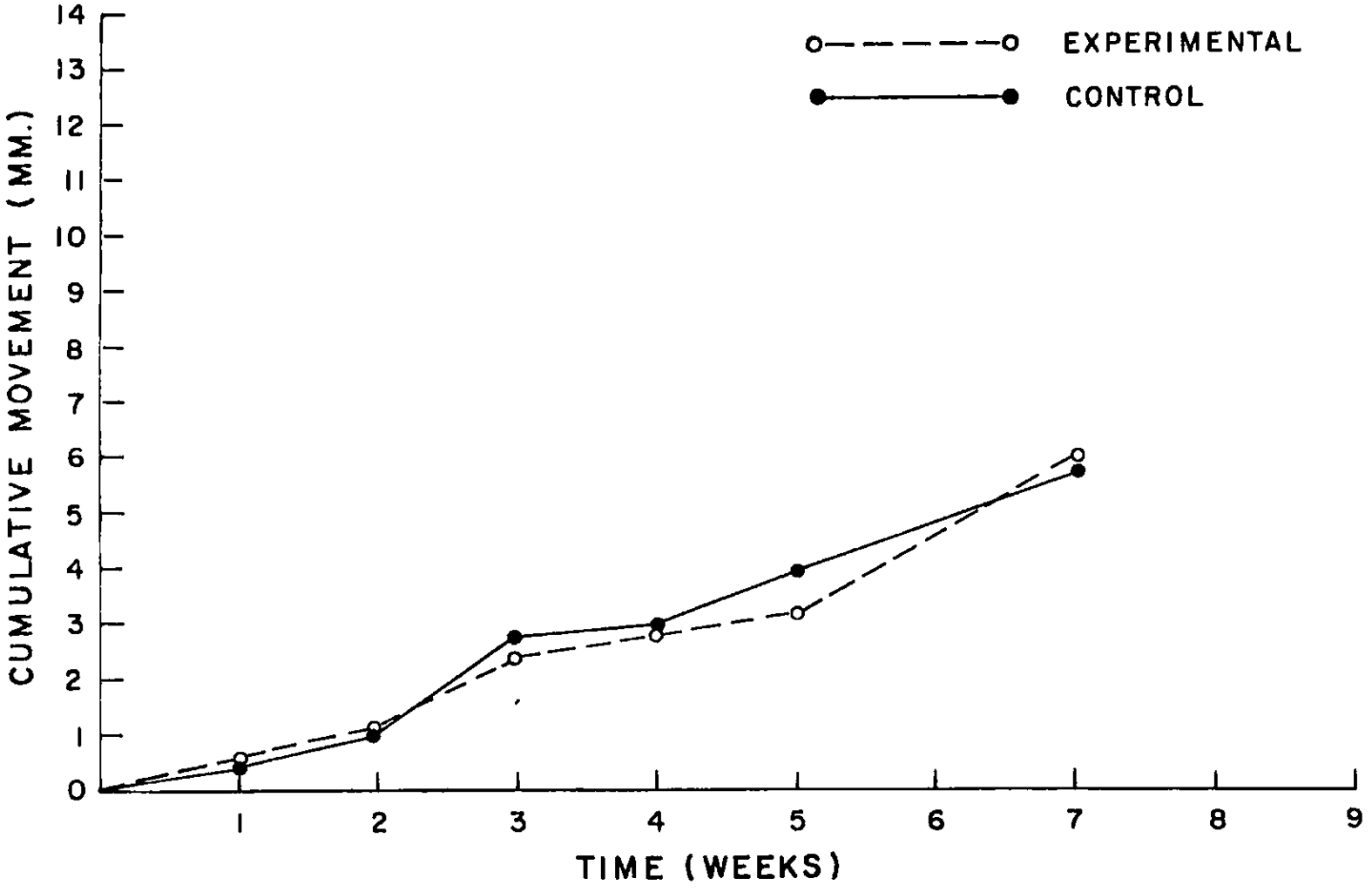

EXPERIMENTAL
CONTROL
CUMULATIVE MOVEMENT (MM.)
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
1
2
3
4
5
6
7
8
9
TIME (WEEKS)

Figure 11.--Intra-oral Measurement #0537
Weekly Cumulative Movement


EXPERIMENTAL
CONTROL
CUMULATIVE MOVEMENT (MM.)
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
TIME (WEEKS)
1
2
3
4
5
6
7
8
9

The total tooth movement in each cat, of right and left sides, regardless of the time required to achieve that movement, is presented in Table 5. The mean total movement for the control sides was 5.32 mm and 6.57 mm for the experimental sides. Individual magnitudes of tooth movement are represented by a histogram (Figure 6), from which it can be seen that three of the five cats did experience a noticeable difference in the amount of tooth movement between the control and experimental sides. Although the rate of tooth movement varied among animals, and between right and left sides in certain cats, control and experimental sides of any given animal showed the same basic slope or trend on a weekly basis. The two remaining animals which received sham operations (#0536, 0537) did not demonstrate any pattern of tooth movement that was inconsistent with the other animals.

Cephalometric Measurements

The following four cephalometric measurements were recorded: (1) second premolar to molar distance, (2) second premolar to bony implant distance, (3) bony implant to molar distance, and (4) premolar tipping (Figure 5).

The cumulative weekly movements represented by these measurements are presented in Table 6. The bony implant to molar distance was recorded to determine if the molar was driven distally. From the data presented, it can be seen that it was not, and this measurement will not be considered further. The mean total movement of the

Table 6

Cephalometric Measurements

Weekly Cumulative Movement

Week	Measurement	Side	Cat 06	Cat 17	Cat 20	Cat 36	Cat 37
1	Premolar to Molar (millimeters)	C*	1.06	0.38	0.31	-0.01	0.25
		E*	1.09	0.21	0.83	0.05	0.79
	Premolar to Implant (millimeters)	C	0.77	0.41	0.48	0.21	0.26
		E	0.62	. .	0.38	0.27	0.40
	Implant to Molar (millimeters)	C	0.24	0.34	-0.17	-0.15	-0.55
		E	-0.05	1.78	-0.08	0.01	0.16
	Premolar Tipping (degrees)	C	-4.0	6.00	88.00	-4.0	-4.5
		E	15.50	5.00	-8.00	-8.0	4.0
2	Premolar to Molar (millimeters)	C	1.81	0.40	2.71	0.60	-1.15
		E	1.19	0.62	6.74	0.37	1.01
	Premolar to Implant (millimeters)	C	0.92	0.17	1.14	0.84	1.38
		E	0.45	. .	5.46	0.32	1.19
	Implant to Molar (millimeters)	C	0.69	0.17	0.31	-0.14	-0.87
		E	-0.20	0.02	1.34	0.31	-0.44
	Premolar to Tipping (degrees)	C	-1.0	6.00	60.00	-3.00	-17.50
		E	5.00	-5.00	-44.00	-3.00	-7.00
3	Premolar to Molar (millimeters)	C	2.30	0.38	4.64	1.18	2.00
		E	2.24	1.49	11.40	0.59	2.22
	Premolar Implant (millimeters)	C	1.31	0.11	1.60	1.32	1.88
		E	0.84	. .	10.30	0.57	2.08
	Implant to Molar (millimeters)	C	0.77	-1.7	0.25	-0.13	-0.01
		E	0.25	0.41	0.82	0.15	-0.40
	Premolar Tipping (degrees)	C	-10.50	4.0	9.00	-14.00	-14.00
		E	. .	-7.5	-85.00	-9.00	-10.00

Table 6 continued

Week	Measurement	Side	Cat 06	Cat 17	Cat 20	Cat 36	Cat 37
4	Premolar to Molar (millimeters)	C	2.59	0.28	. .	0.81	2.68
		E	3.09	1.62	. .	0.45	2.80
	Premolar to Implant (millimeters)	C	1.73	0.49	. .	0.70	2.67
		E	1.65	. .	. .	0.78	2.14
	Implant to Molar (millimeters)	C	0.33	-0.17	. .	0.01	-0.57
		E	0.63	0.91	. .	0.22	1.13
	Premolar Tipping (degrees)	C	-15.50	4.00	. .	-16.00	-22.50
		E	1.00	-15.50	. .	-14.00	-10.00
5	Premolar to Molar (millimeters)	C	3.23	0.53	. .	0.82	4.05
		E	3.60	2.35	. .	0.96	3.65
	Premolar to Implant (millimeters)	C	1.69	0.42	. .	0.84	3.99
		E	2.11	. .	. .	0.90	2.78
	Implant to Molar (millimeters)	C	0.75	-0.20	. .	-0.10	-0.15
		E	0.75	0.77	. .	0.31	-0.04
	Premolar Tipping (degrees)	C	-14.50	-2.00	. .	-10.00	-29.50
		E	1.00	-10.00	. .	-5.50	-14.50
7	Premolar to Molar (millimeters)	C	6.43	1.31	. .	1.76	5.32
		E	5.11	3.45	. .	0.75	5.61
	Premolar to Implant (millimeters)	C	4.81	1.23	. .	2.01	5.10
		E	2.55	. .	. .	1.26	4.52
	Implant to Molar (millimeters)	C	1.19	-2.30	. .	-0.41	-0.47
		E	1.15	1.34	. .	-0.16	0.31
	Premolar Tipping (degrees)	C	-32.50	-5.00	. .	-14.50	-39.00
		E	-3.00	-13.00	. .	-17.00	-25.00

Table 6 continued

Week	Measurement	Side	Cat 06	Cat 17	Cat 20	Cat 36	Cat 37
9	Premolar to Molar (millimeters)	C	13.32	2.44	. .	2.87	. .
		E	12.61	3.77	. .	0.77	. .
	Premolar to Implant (millimeters)	C	11.36	2.07	. .	2.98	. .
		E	9.92	. .	. .	0.91	. .
	Implant to Molar (millimeters)	C	1.79	0.05	. .	-0.60	. .
		E	1.75	1.02	. .	-0.12	. .
	Premolar Tipping (degrees)	C	-43.50	-12.50	. .	-39.00	. .
		E	-40.50	-13.00	. .	-19.00	. .

*C--control
*E—experimental

Table 7

Cephalometric Measurements

Total Movement

	Measurement					
	Premolar to Molar (millimeters)		Premolar to Implant (millimeters)		Premolar Tipping (degrees)	
	Side					
Cat	C*	E*	C	E	C	E
0506	13.32	12.61	11.36	9.92	43.5	40.5
0517	2.44	3.77	2.07	**	12.5	13.0
0520	4.64	11.40	1.60	10.30	9.0	85.0
0536	2.87	0.77	2.98	0.91	39.0	19.0
0537	5.32	5.61	5.10	4.52	39.0	25.0
Total	28.59	34.16	23.11	25.65	143.0	182.5
$\bar{X}$	5.72	6.83	4.62	6.41	28.6	36.5

*C--Control
*E--Experimental
**--Implant lost

Figure 12.--Cephalometric Measurement
Premolar to Molar
Total Movement

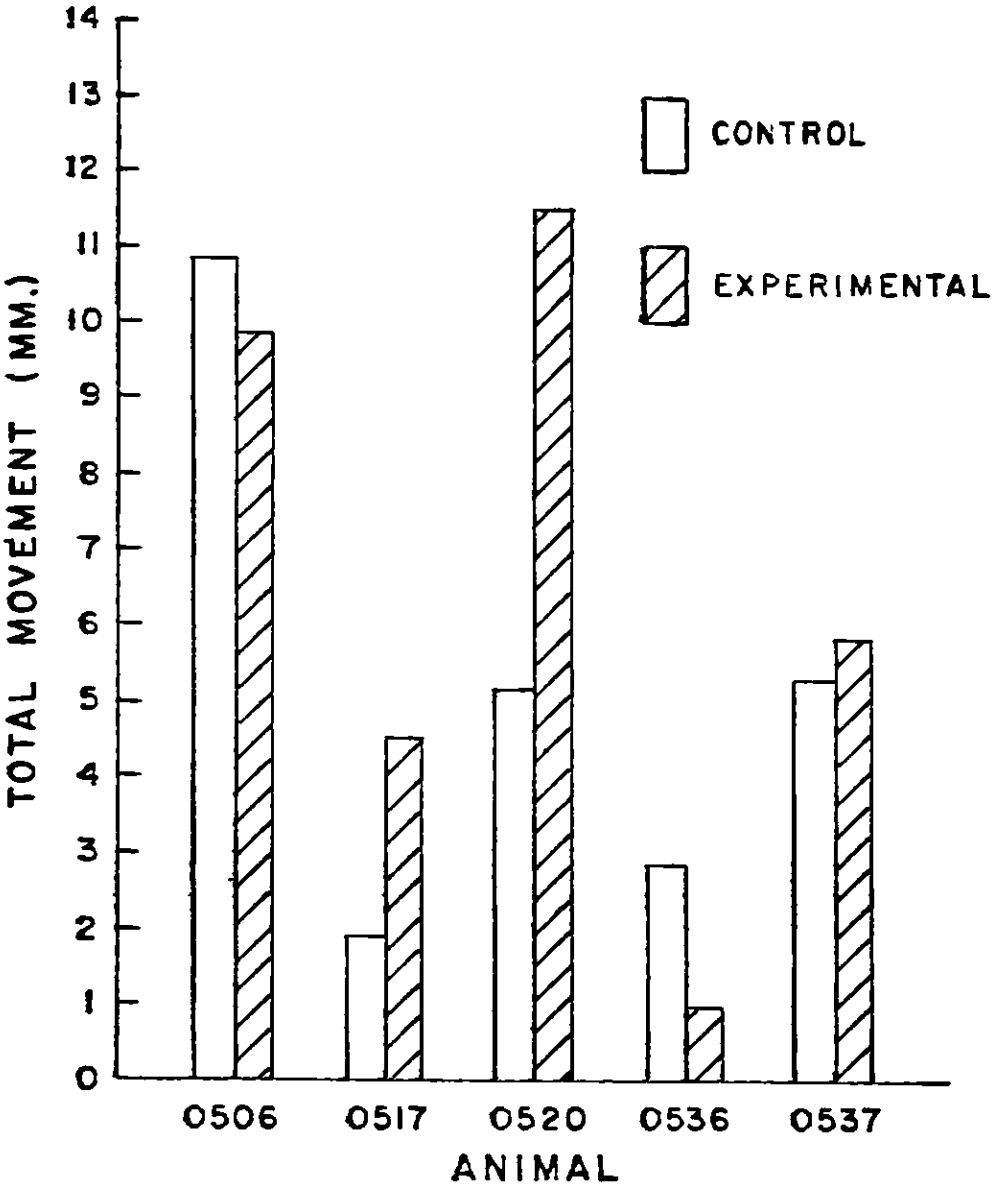

TOTAL MOVEMENT (MM.)
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
CONTROL
EXPERIMENTAL
0506
0517
0520
0536
0537
ANIMAL

Figure 13.--Cephalometric Measurement
Premolar to Implant
Total Movement

* implant lost

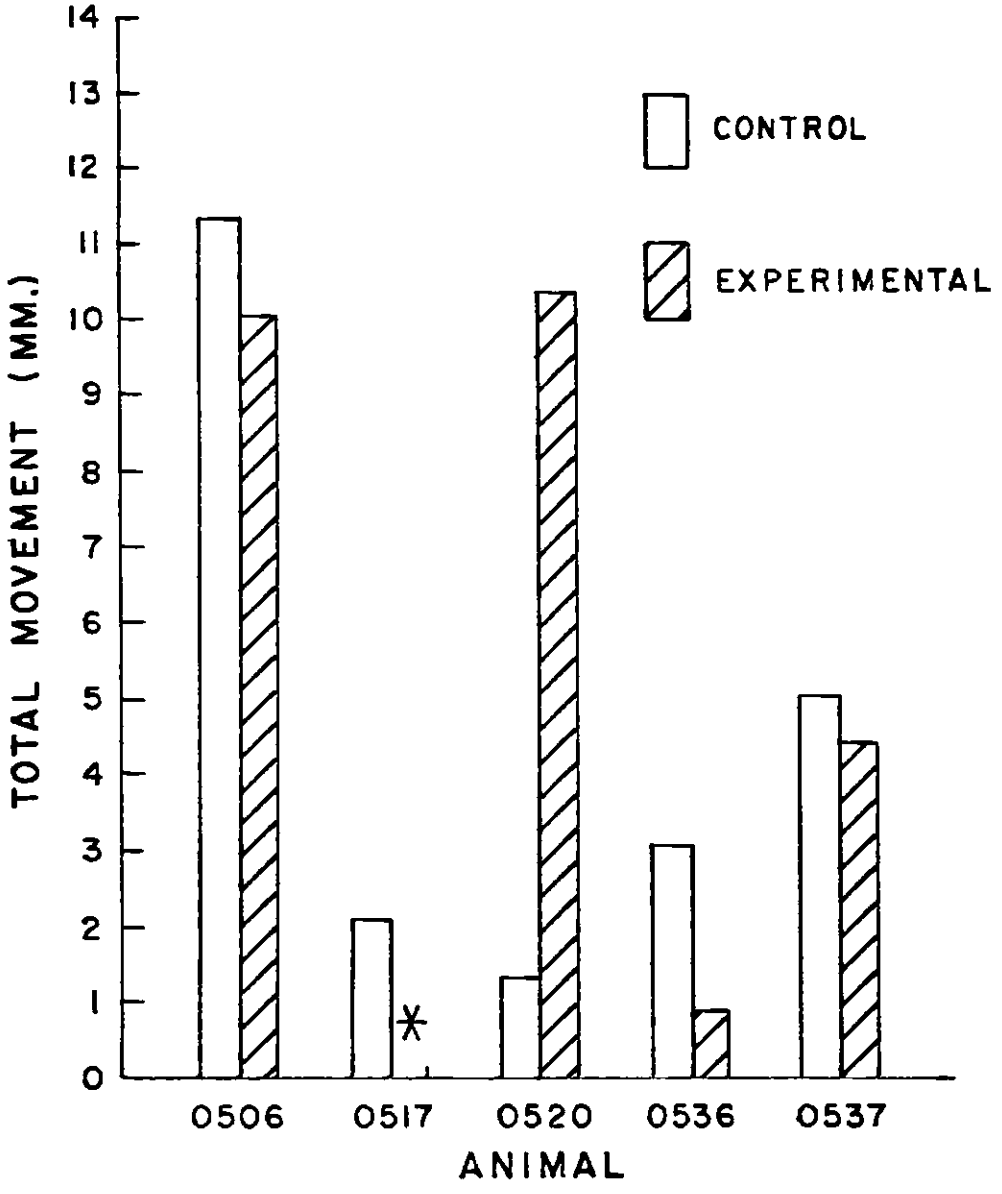

14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
TOTAL MOVEMENT (MM.)
CONTROL
EXPERIMENTAL
*
0506
0517
0520
0536
0537
ANIMAL

Figure 14.--Cephalometric Measurement
Total Premolar Tipping

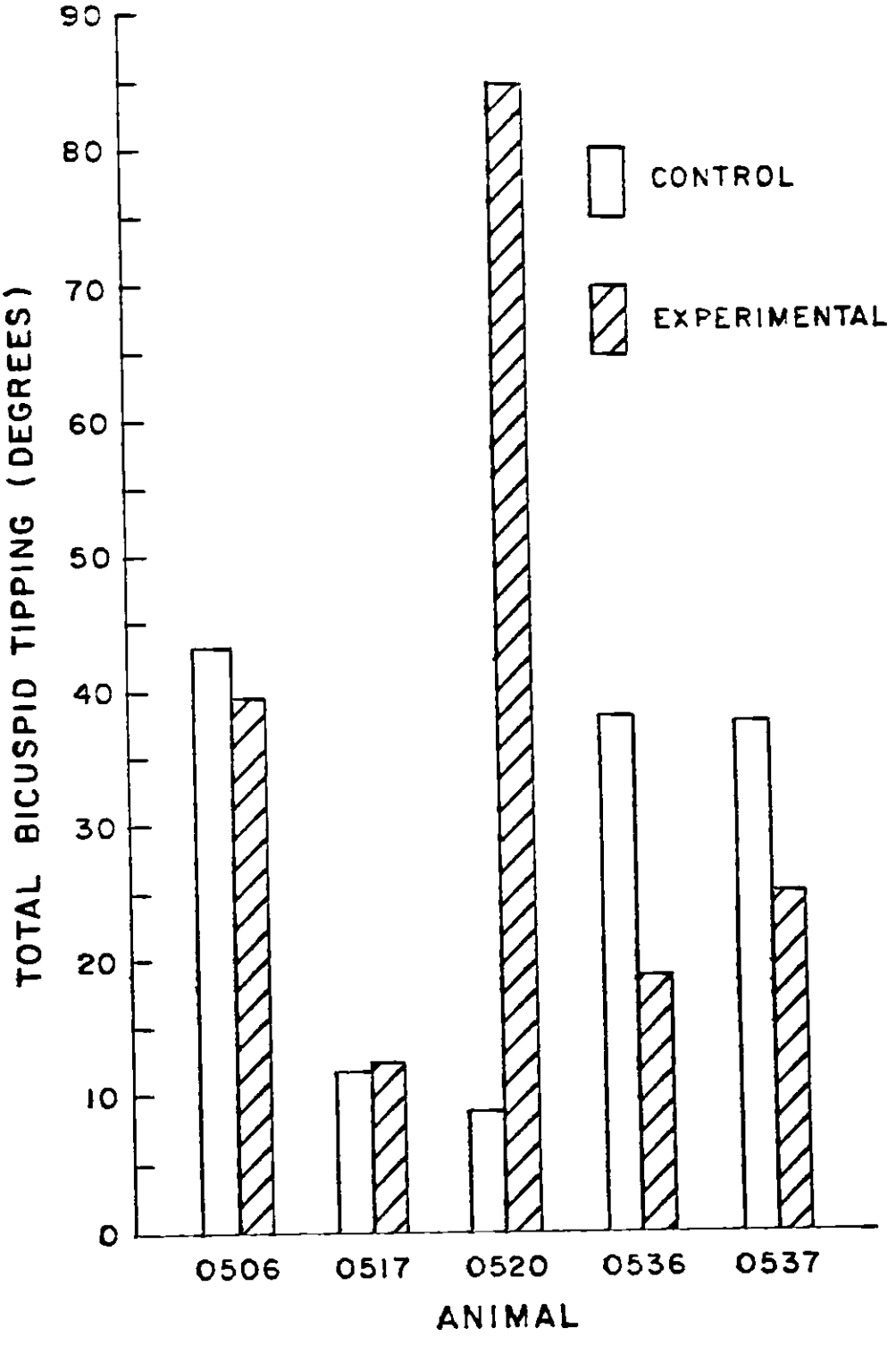

90
80
70
60
50
40
30
20
10
0
TOTAL BICUSPID TIPPING (DEGREES)
CONTROL
EXPERIMENTAL
0506
0517
0520
0536
0537
ANIMAL

PLATE IV

FINAL CEPHALOMETRIC RADIOGRAPHS

A. #0506 Right Left

B. #0517 Right Left

C. #0520 Right Left

D. #0536 Right Left

E. #0537 Right Left

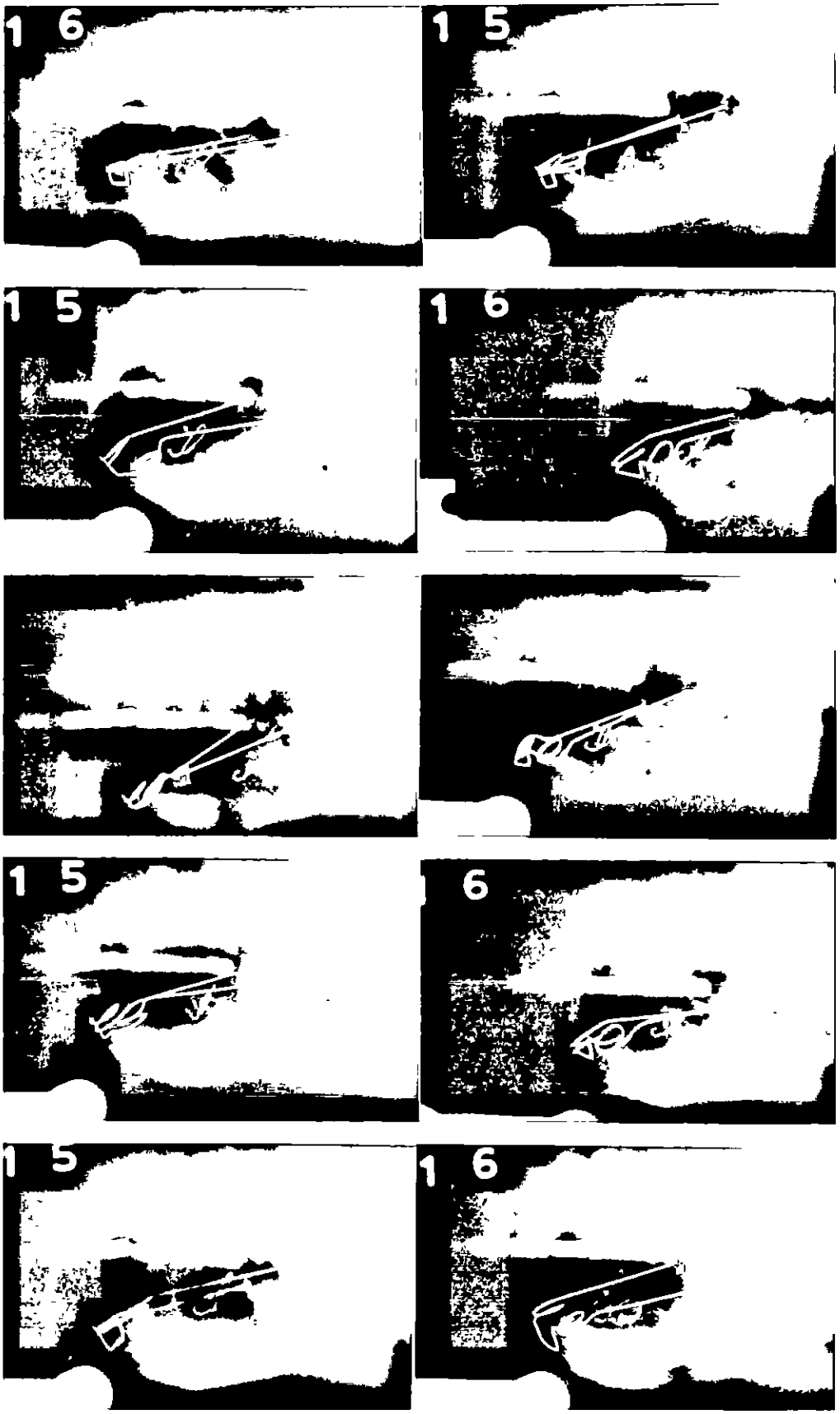
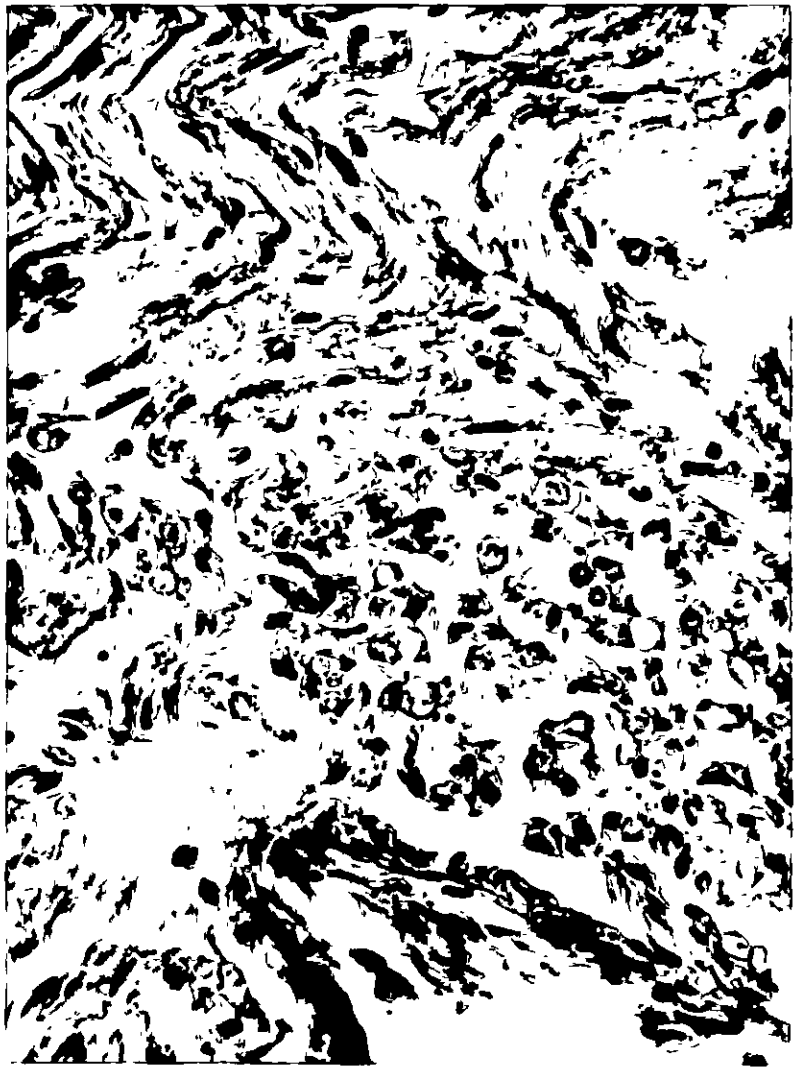

1 6
1 5
1 5
1 6
1 5
6
1 5
1 6

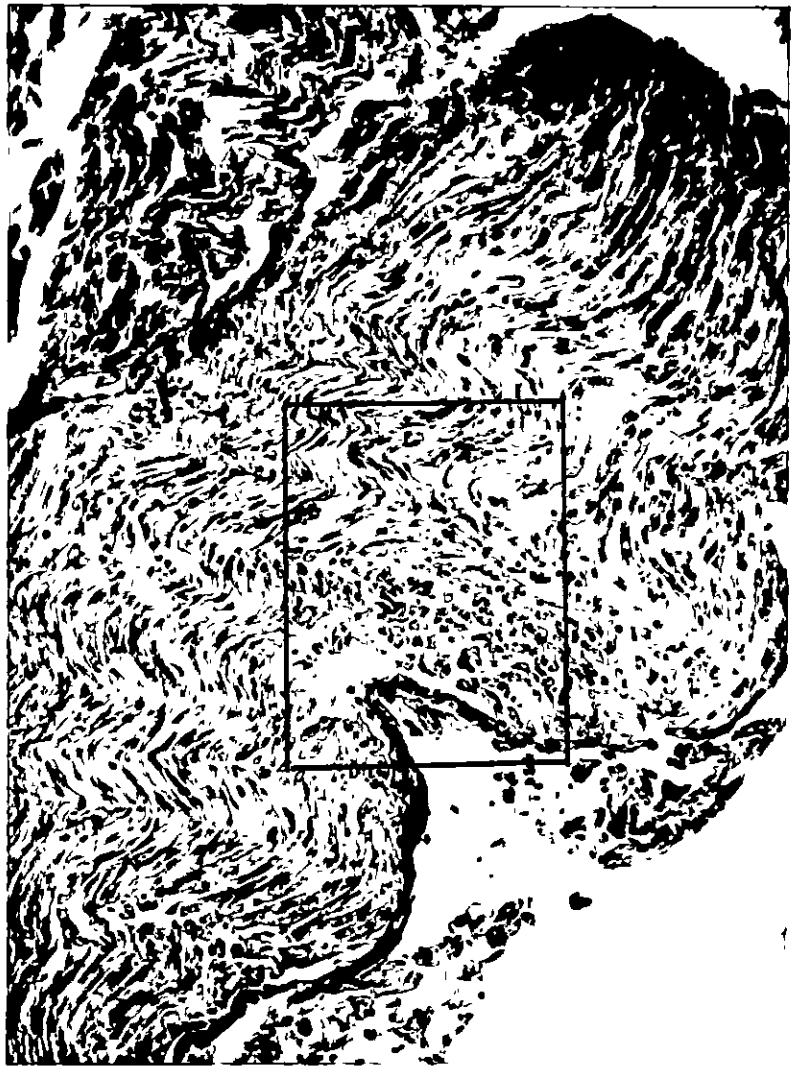
PLATE V

Histological Confirmation of Inferior
Alveolar Nerve Regeneration

A. 140X

B. 450X





tooth-to-tooth measurement was 5.72 mm on the control side and 6.83 mm on the experimental. The tooth-to-implant distance averaged 4.62 mm on the control side and 6.41 mm on the experimental. The premolar tipped an average of 28.6 degrees on the control side and 36.5 degrees on the experimental side (Table 7, Plate IV). All of these measurements are consistent in pattern and magnitude with the intra-oral measurements (Figures 12, 13 and 14).

Statistical Analysis of Results

Although the sample size was extremely small, a Student t-Test was performed to determine if there was any significant (95% confidence) effect or difference between the control and experimental sides (Table 8). There was no effect or difference in any of the measurements, statistically speaking. An F-Test of variance was first performed and the variances between the two groups (control and experimental) were found to be comparable, thus making the Student t-Test applicable.

Autopsy Results

A postmortem examination was performed on each animal to determine if any visible nerve regeneration had occurred. In all animals, examination of the vagosympathetic trunk revealed that no visible sympathetic ganglion regeneration had occurred, but an unidentified nerve was found joining the nerve trunk. This nerve was of the approximate size and location that would be expected of

Table 8

Analytical Statistics

Student t-test

Measurement	N_1	N_2	$\bar{X}_1$	$\bar{X}_2$	S_1^2	s_2^2	$t_{df}^{.05}$	t	Effect
I.O. Premolar to Molar	5	5	5.32	6.57	12.08	17.45	±2.31	-0.52	no
Ceph. Premolar to Molar	5	5	5.72	6.83	19.49	25.47	±2.31	-0.37	no
Premolar to Implant	5	4	4.62	6.41	15.99	20.42	±2.36	-0.63	no
Premolar Tipping	5	5	28.60	36.50	270.43	839.75	±2.31	-0.53	no

the postganglionic sympathetic nerve.

Examination of the mandibular canal revealed that total regeneration of the inferior alveolar nerve had taken place in all animals. Upon further examination of the mandibles, the tantalum markers were found to be firmly implanted in bone.

Histologic Results

The tissue removed from the mandibular canals of the nerve resected side of the mandibles is shown in Plate V to be nerve tissue. The low power view (140X) shows the typical wavy pattern of the longitudinal sectioned fibers and nerve fiber axons can be seen in the cross sectioned portion in the higher power view (450X).

DISCUSSION

Discussion of results from this study will be separated into two categories: (1) discussion of tooth movement results, and (2) discussion of technical and procedureal details.

Tooth Movement Results

Three of the five animals that survived this study showed rates of tooth movement that were substantially different for the right and left sides. Two of these animals had teeth on the experimental side move more than twice as fast and as far as the control side. One animal showed just the opposite results. As previously noted, none of these differences are statistically significant.

Although these results are inconclusive, they perhaps lend new insight to the results of King (1936), Edwards and Kitchen (1938), Taylor and Butcher (1951), Miller (1957), Brown et al. (1961), and Rehak (1963), in which denervation of the PDM of rodents or rabbits produced an increase in incisor eruption rate (i.e., faster tooth movement). The above studies concluded that this faster eruption rate was the result of increased attrition subsequent to loss of sensation. However, the results of this study raise the possibility that some cellular mechanisms within the PDM or other supporting structures of the teeth may be responsible

for altered eruption rate.

The question arises: what target cells or tissues are the recipients of the speculated neurological initiation and direction of tooth movement? Clearly, vasomotor alterations would result from sympathectomy. Avery et al. (1971) has demonstrated that resection of the superior cervical ganglion in rabbits causes a vascular dilatation in the tooth pulp and PDM. It easily can be argued that PDM vascular variation would affect every cell within and around the PDM. Therefore, it can also be argued that via vasomotor influence, neurologic variation would also affect every cell within and around the PDM. Consequently, all arguements in support of a vascular theory of tooth movement also apply to a neurologic theory.

Another mode of action that nerves might employ to influence PDM or other tooth supporting tissues is the "neurotrophic effect." Neurotrophism, as it applies to craniofacial growth, has been most extensively investigated by Moss (1971, 1972, 1974) who suggests that specific "trophic substances" descend down the nerve axons to the periphery, and are released at nerve terminals. Current knowledge regarding which substances are suspected of being "trophic" has been reviewed by Behrents (1976). These "trophic" substances" presumably influence, directly or indirectly, soft and hard tissue growth, remodeling and/or function. Although this mechanism does appear to exist, Behrents (1976) has concluded that such influences play a relatively minor role in the overall process

of craniofacial growth. He has stated:

> It is most plausible that during the growth of the facial complex, growth centers, sites, and soft tissues are, under various temporal and environmental conditions, modified by many things, one of which is neurotrophism.

The possibility must also be entertained that nerves more directly influence certain cells within or around the PDM. The degree to which this may apply to the myofibroblast has been reviewed at length above. A cell which structurally and functionally resembles smooth muscle cells in many ways, may respond neurophysiologically in much the same manner that smooth muscle cells react to neural transmission. Gorgas and Bock (1974) have reported that this is indeed the circumstance that exists in the capsule of the rat testis. Of course, the present study does not attempt to specify how nerves may or may not act on the PDM or associated structures; rather it is intended only to suggest whether or not neural action affects orthodontic tooth movement.

In spite of the attempts made to minimize unwanted variables in this study, some cannot be said, conclusively, to have been eliminated. Vascular interruptions could possibly impair the ability of the PDM or bone to remodel. Osteoclastic activity has been shown by Miller (1957) to be directly related to vascularity of the PDM. In addition, fluid dynamics and local concentration of hormones or unknown influential substances would be decreased with impaired vascularity. However, in all animals, the inferior alveolar artery was not visibly damaged by the resection of the accompanying nerve, and the preservation of the PDM blood supply was the

reason that the mandibular canal was not plugged to prevent nerve regeneration.

Trauma could also result in altered muscular action, especially with the masseter and internal pterygoid muscles. Although this possibility is undeniable, the altered masticatory function that might result should have been minimal influence on the moving teeth due to lack of occlusion of the moving teeth and the liquid diet given the animals.

One variable that could have tremendous influence on the results of this study, is the rate of nerve regeneration. Given the fact that regeneration did occur in all animals, although whether or not full re-establishment of periodontal innervation was attained is not known, and given the hypothesis that nerve degeneration may affect tooth movement, this variable becomes crucial. The need to move teeth before substantial regeneration has occurred and to monitor nerve regeneration is discussed below.

In order to arrive at a proper perspective of the results and issues within this study, one must refrain from making overly simplistic hypotheses which attempt to give any one cell type, tissue or biological process full credit for such a complex event as tooth movement. It has been shown that many factors influence tooth movement. Although it seems likely that, under normal physiologic conditions, some primary mechanism (e.g., neurologic function) must exist to initiate and direct this multifactorial event, it also seems likely that many compensatory mechanisms exist

that could negate much of the loss of physiologic function encrued by the removal of this primary mechanism. This is perhaps more eloquently explained by Latham's concept of "multiple assurance" (Latham, 1970). Briefly, this concept contends that in the living organism, certain biologic processes are so important to the normal function of that organism, that these events are assured by virtue of alternative mechanisms available to accomplish them. This concept appears applicable to tooth movement.

Technical and Procedural Details

Regarding the experimental design of this study, the foremost problem was the small size of the sample subsequent to the loss of some animals. It becomes almost impossible to reach a statistically significant result with a final sample size of five, and any conclusions at best must be labeled as speculation based on suggestive results. Even though this investigation was conceived as a pilot study, a final sample size numbering 12 to 15 animals, would give more credence to any speculations made.

Certain animals did show an effect. That is to say, the experimental side of the animal produced either much more or less tooth movement as compared to the untreated (control) side. An original presumption early in the study was that teeth on the right and left sides will move at approximately the same rates when exactly equal forces are applied to both sides in untreated animals. However, in retrospect, this presumption may have been unwarranted,

and for this reason, it is suggested that further studies of this nature should also include a separate control group that has teeth moved bilaterally, but without nerve resections (sham operations could be included).

An attempt was made to minimize bilateral variation as a result of surgical trauma by performing sham operations on the contralateral side from the resections. Since all animals did not receive treatment, no conclusions could be derived from the sham. Nonetheless, given the number of animals to work with, the experimental design was well conceived, for it did serve to minimize the substantial systemic influences exerted on these animals (e.g., viral respiratory infections, varied surgical trauma, illness from vital dye administration, variations in amount and reactions to drugs, variation in appetite and weight gain or loss). Also, the variations between control and experimental sides, as a result of the slightly different time schedule to which each animal was subjected, was minimized.

It was most disconcerting to find that considerable nerve regeneration had occurred by the end of the study in all animals. At autopsy, the regenerated inferior alveolar nerve was visible within the mandibular canal, and was microscopically confirmed as nerve tissue containing axons (Plate V). Although no superior cervical ganglion regeneration was found, post-ganglionic sympathetic regeneration apparently did occur in four out of five animals. Postmortem examination revealed a nerve of the same size

and location as the postganglionic sympathetic nerve. However, this nerve could also be a branch of the vagus. Even more suggestive evidence of sympathetic nerve regeneration was supplied by the pupil size. Immediately after the nerve resection operation, the eye of the operated side showed pupillary constriction. This parasympathetic action was expected, because the postganglionic sympathetic innervation to the eye originates from the superior cervical ganglion (Pansky, 1969). This diagnostic sign disappeared in most animals before the end of the study. Whether or not innervation (sympathetic or somatic) had been fully re-established in the PDM is not known. It is interesting to note that the one animal to have extremely rapid tooth movement and which displayed the greatest difference between control and experimental sides (cat #0520), was the only animal which still had pupillary constriction and drooping of the nictitating membrane on the treatment side for the entire period of tooth movement. This may be due to the fact that tooth movement was terminated after only three weeks.

This study was designed so that the nerve resection operation was performed first. A considerable period of time transpired between this operation and the commencement of tooth movement (4 to 6 weeks) because of the time required to extract teeth, place implants, and to construct the tooth moving appliances. In view of the rapid rate of nerve regeneration, the nerve resection procedure would better have been done as the last procedure before activation of the appliances. Also, a more careful monitoring of nerve regeneration would be helpful to interpretation of the results. This could

perhaps have been accomplished by tooth vitality tests in the case of the inferior alveolar nerve, and by measuring pupillary diameters in the case of the sympathetic innervation to the head.

Aldskorgius and Arvidsson (1978), Grant and Arvidsson (1975), and Westrum et al. (1976) have reported, from studies on cats and rats, that transection of peripheral nerves (e.g., frontal, inferior alveolar) gives rise to substantial retrograde degeneration of nerve tissue that progresses to and includes central nervous tissue (e.g., spinal trigeminal tract, main sensory trigeminal nuclei). If retrograde nervous degeneration occurs to this extent as a rule, then regeneration would be impossible. The rapidity with which regeneration occurred here seems to suggest that this retrograde degeneration was not widespread.

Westrum et al. (1976) also reported contralateral central nervous tissue degeneration following pulpectomy in cats. If this process were widespread, it would certainly tend to neutralize any affect unilateral nerve resection might have on tooth movement. Although the rapidity of nerve regeneration pointed out above tends to cast doubt on this consideration, it still remains as a possibility.

As it is apparently a new finding, it is worth restating that a right/left dimorphism was observed in the relative positions of the nodose ganglion of the vagus nerve and the superior cervical sympathetic ganglion. On the left side of all eight animals (plus three trial animals), these two ganglia were found side by side and in intimate approximation. On the right side however, the superior

cervical ganglion was positioned superior to the nodose ganglion (Figure 2).

Certain technical details also warrant discussion. All drugs used for the purpose of anesthesia were extremely effective and safe, despite the frequency of use. Ketamine hydrochloride was administered approximately twenty times to each animal over a period of three months. No appreciable tolerance or sensitivity to any drugs was observed.

The cephalometric techniques employed were also quite effective. The implant markers were clearly visible on x-ray film and, with one exception, remained fixed in bone throughout the study. The cephalostat allowed for accurate head positioning, as demonstrated by the consistency of the three cephalometric measurements among themselves, and their good correlation with the intra-oral measurements.

The tooth moving appliances worked well. They were well tolerated by all animals, moved teeth effectively, and were easy to re-activate. The maxillary second premolar teeth required frequent grinding to remove them from the path of movement of the mandibular second premolars. In retrospect, the maxillary second premolars should have been extracted prior to appliance activation.

The cats proved to be extremely sensitive to the procion vital dyes employed. For this reason, only four animals were subjected to this procedure, and only at the beginning of the tooth movement and two weeks before the study was terminated. Animal studies utilizing cats, with small sample sizes, should probably

avoid using procion dyes, so as not to endanger the sample.

Due to the fact that histologic sections of the teeth, PDM and bone are not presently available, the discussion of the effectiveness of the procion dyes, and of the cellular changes and responses observed, is not possible.

In conclusion, the fact that a more convincing pattern of tooth movement did not result in all of the animals shows that either neurologic transmission is not a primary factor involved in the control of tooth movement, or that other mechanisms exist which tend to compensate for the loss of nerve innervation to the PDM and associated structures. However, the results of this preliminary study do suggest that interruption of the nervous supply to the PDM in cats may affect orthodontic tooth movement. Therefore, based on the results of this study, a larger, more comprehensive investigation of the same basic issue, with the changes in experimental design, chronological order of procedures, and in methods employed as recommended above, appears warranted if the role of neural influence on tooth movement is to be resolved.

SUMMARY AND CONCLUSIONS

A review of the literature makes it clear that many factors influence the various types of tooth movement. Past studies treated active eruption, passive eruption, drift, and orthodontic tooth movement as separate entities, which were examined on an individual basis. In this study, the premise was made that all types of tooth movement, whether physiologic or therapeutic, are variations of a single process involving common basic cellular mechanisms and components. As a consequence, the multitude of factors reported to influence individual types of tooth movement (e.g., vascularity, hormones, piezoelectricity, fluid dynamics, cellular contractility, diet, neurologic innervation), were theorized to also influence other types of tooth movement. In addition, the basic factors or influences of tooth movement mentioned above were theorized to be interrelated and controlled during normal physiologic conditions by some overriding primary mechanism. It was suggested that this primary mechanism involves the neurophysiologic component of the PDM.

To test the hypothesis that tooth movement is controlled by, or at least involves nerve transmission, the superior cervical ganglion and a segment of the ipsilateral inferior alveolar nerve were surgically resected from one side of eight cats. Mandibular first premolars were extracted, and bilateral second premolars were protracted by reciprocal forces. The rate and amount of tooth movement

on each side of the mandible were determined by direct intra-oral and by cephalometric measurements, with the aid of amalgam tooth markers and tantalum bony implants. Procion vital dyes were also used to aid in the microscopic analysis of the bony changes.

Teeth were moved for a period of nine weeks or until therapeutic exfoliation occurred. At the termination of the study, all animals were examined for nerve regeneration, and appropriate tissue samples were taken for histologic preparation. These tissue samples were of two types: (1) tissue suspected to be of inferior alveolar nerve origin, and (2) tooth, PDM and surrounding bone which had been biologically stained in vitro. The latter tissue sections were not available for examination in time to be included herein.

The results of this study may be summarized as follows:

1. A new approach to the investigation of possible PDM mediated influences on orthodontic tooth movement has been developed that utilizes unilateral sympathetic and somatic denervation of the mandible.

2. Three out of five surviving animals showed substantially different rates of tooth movement for the control and experimental sides; two out of these three showed an increase in the rate of tooth movement on the denervated side over the control side by a factor of 2:1 or greater, and one animal showed the opposite trend.

3. These results are compared with past studies which showed an increase in incisor eruption rate following PDM denervation, and with studies that demonstrated the presence of mechanisms by which nerves might control tooth movement (e.g., myofibroblastic model), but no definite correlation could be made.

4. Regeneration of resected nerve tissue occurred at a rapid rate and was complete in most animals before the termination of the study. This is in contrast to the findings of Aldskorgius and Arvidsson (1978), Grant and Arvidsson (1975), and Westrum et al. (1976), which showed retrograde neural degeneration and nerve cell death following peripheral nerve transection.

5. A new finding is reported in which a right/left side anatomical dimorphism of the relative positions of the superior cervical ganglion and the nodose ganglion of the vagus nerve exists (Figure 2).

6. On the basis of these results, tooth movement appears to be a multifactorially influenced process; if neurologic transmission is a primary controlling factor in tooth movement, then alternate mechanisms may exist which tend to compensate for the loss of this primary component.