Thyroid Influence on Bone Histology during Tooth Movement in Hamsters

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INTRODUCTION

Oppenheim[1] credited Schwalbe and Fluoren with recognition of the nature of physiologic tooth movement due to extrinsic forces. That is, alveolar bone is resorbed on the pressure side of a tooth and deposited on the tension side. In subsequent years this concept was tested by many investigators and expanded, so that presently this theory of tissue response is a fundamental element in orthodontic theory and practice.

The nature of tooth movement, however, is not a simple matter of cause and effect, but one complicated by a multitude of variables. Much is known today about the nature of tooth movement and its concomitant bony changes; but little is known about how general metabolism affects alveolar bone physiology, especially in the variable states of each individual.

Although this paper will, of necessity, deal solely with tooth movement in an elevated thyroid state, one cannot ignore the connection that thyroid hormone has relative to general body-growth, cranial growth, dentofacial growth, tooth eruption and condylar growth in hyperthyroid, hypothyroid and euthyroid individuals. One also must consider thyroid therapy on growing individuals with its effects on general body growth and dental development.

In view of the relationship of thyroid hormone to bony histodifferentiation, this study was undertaken to histologically evaluate the nature of the processes involved in elevated thyroid levels in experimental tooth movement. A review of the literature reveals a scarcity of hormonal studies related to bony changes in orthodontics and the need for further investigation of the basis for tooth movement related to the hormones which influence growth and development.

MATERIALS AND METHODS

A total of 188 golden hamsters (Cricetus auratus), approximately 10 weeks of age, were utilized in this study. The animals were divided into two major groups. Group A was the control group; Group B consisted of those treated with L-thyroxin (3,3', 5,5' tetraiodo-L-thyronine) sodium salt. Both groups were fed a standard diet of Purina laboratory chow and water *ad libitum*. All animals were weighed at the beginning of the experiment, at seven day intervals, and prior to sacrifice. Table I summarizes the groupings and treatment with the number of animals in each group in parentheses.

Elastic separation was achieved between the maxillary left first and second molar teeth. Utilizing light latex elastics and a modified orthodontic ligature tying instrument described by Moskowitz and Kronman,[2] an elastic lubricated with vaseline was placed between the molars. A light sawing motion was used to facilitate placement of the elas-

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TABLE I

I. Control Group A.
   I. Normal, untreated, (12)
   II. Injected with water for 18 days (6)
   III. Elastics inserted 1 day, sacrifice (10)
   IV. Elastics inserted 4 days, sacrifice (12)
   V. Elastics inserted 8 days, sacrifice (14)
   VI. Elastics inserted 1 day, removed, sacrificed 7 days later (10)
   VII. Elastics inserted 4 days, removed, sacrificed 7 days later (12)
   VIII. Elastics inserted 8 days, removed, sacrificed 7 days later (14)

II. Thyroxin Treated Group B
   I. Injected with thyroxin for 18 days (12)
   II. Elastics inserted 1 day, sacrifice (10)
   III. Elastics inserted 4 days, sacrifice (12)
   IV. Elastics inserted 8 days, sacrifice (14)
   V. Elastics inserted 1 day, removed, sacrificed 7 days later (12)
   VI. Elastics inserted 4 days, removed, sacrificed 7 days later (14)
   VII. Elastics inserted 8 days, removed, sacrificed 7 days later (14)

tic interdentally. The animals treated with elastic separation were anesthetized with ether.

The dosage of thyroxin used was 150 micrograms (aqueous solution) per 100 grams of body weight. The solution was prepared fresh every forty-eight hours and injected subcutaneously at the nape of the neck each day. Average dosage based upon the approximate weight of 150 grams for each hamster was 225 micrograms per animal.

The animals were sacrificed by decapitation. The left posterior quadrant of the maxilla was dissected and specimens were decalcified in 10% EDTA (Ethylenediaminetetraacetic acid) solution adjusted to pH 7.0.[3] After decalcification the tissues were fixed in neutral buffered formalin, vacuum-embedded in paraffin and sectioned at eight micra. The histologic stains employed were hematoxylin and eosin and Masson's trichromic method.

Findings

Gross Findings

Elevation of the thyroid level resulted in a slight weight gain in a majority of the animals over the period of the experiment. This was thought to be attributable to both normal growth and increased dietary intake resulting from an elevated basal metabolic rate. When compared with the controls, the thyroxin-treated group was irritable, aggressive, and tended to resist handling prior to injection. The coats of these animals degenerated and took on a moth-eaten appearance. Skin ulcerations frequently occurred at the site of injection.

Two of the thyroxin-treated group died during the course of the experiment. Their deaths occurred after a siege of illness characterized by weight loss, drying of the cornea, degeneration of the coat and severe agitation. It was thought that the loss of these animals resulted from an extreme increase in basal metabolic rate.

Group A

Those animals completely untreated and those injected with distilled water for eighteen days revealed normal tissue morphology (Fig. 1). The sections revealed normally tapered interproximal and interradicular alveolar bone. Numerous osteocytes were present throughout the bone. Rows of osteoblasts were visible on the mesial and distal roots of the first, second, and third molars. Numerous osteoclasts were seen in the alveolar bone, predominantly on the distal aspect of the mesial and distal roots of all molars.

The periodontal membrane displayed uniform thickness. Tension on the

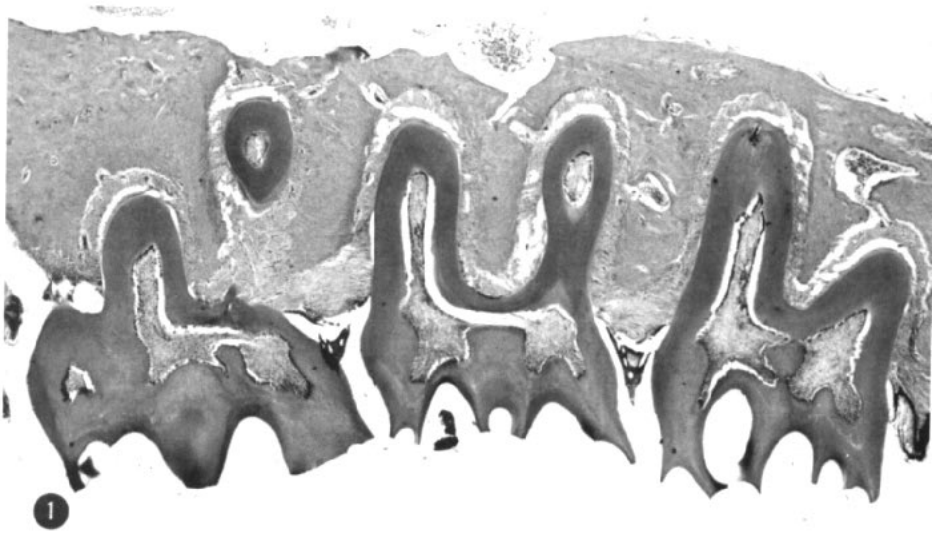

Fig. 1 Sagittal sections of hamster maxilla in control group A I, x 100, H & E stain.

periodontal fibers was evident on the mesial of both roots of each molar. Fibers in relative equilibrium were evident on the distal of the mesial and distal roots. Integrity of the cementum was unchanged. The teeth were upright in the alveolus.

In those animals in which elastics were inserted for one, four and eight days successively and then sacrificed, (Subgroups III, IV, and V) orthodontic movement was successfully accomplished (Fig. 2). The first molar moved mesially and the second and third molars distally. Resultant degrees of adjacent tissue destruction were seen. The normal pattern of distal drift was reversed in the first molar. Osteoclastic activity occurred mesial to the mesial and distal roots of the first molar. Compression of the periodontal membrane was exhibited on the mesial of these roots and tension on the distal. Interdental and interradicular areas of alveolar bone displayed some generalized osteolytic changes and undermining resorption. Similar changes were also evident about the second and third molar teeth. Distal drift of these teeth increased as did the osteoclastic activity on the distal of these roots. Osteoblastic activity on the mesial of these roots increased on their mesial surfaces. Similar compression of the membrane occurred on the distal of the roots and tension on the mesial. Compression effects of the distal tooth movement were dissipated less in the area of the alveolus of the third molar than in the alveolar area mesial to the first molar and distal to the second molar. Root surfaces on the molars showed no alteration in cementum. The one and four-day groups with elastics inserted for eight days showed a tendency to tip.

Subgroups VI, VII, VIII consisted of those animals with elastics inserted for one, four and eight days and then allowed to recover for seven days.

In Subgroup VI, (Fig. 3) destruction of the alveolar crest between the first and second molars and scalloping between the second and third molars occurred. Evidence of osteoclastic changes was seen about the roots. The general bone picture showed gross un-

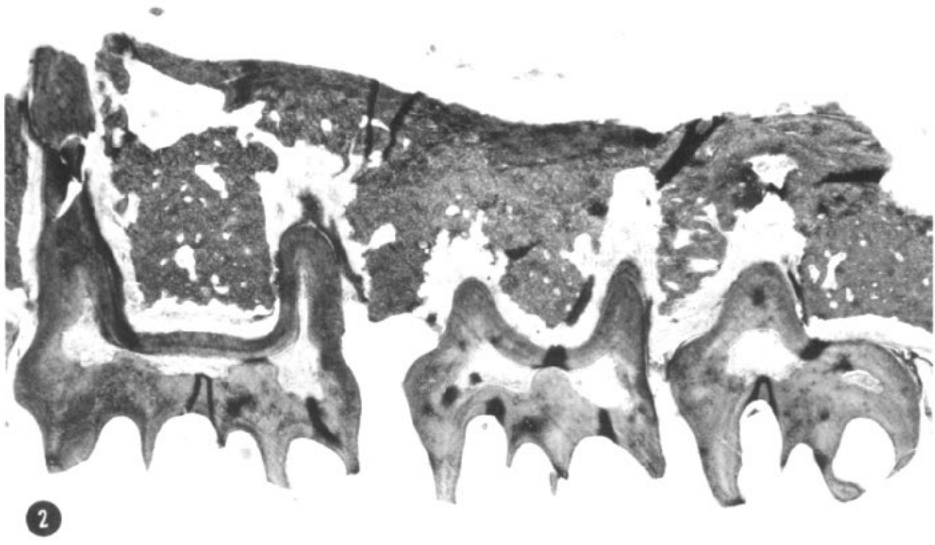

Fig. 2 Sagittal section of group A IV - elastic inserted for 4 days prior to sacrifice. Tooth movement, tissue destruction at site of insertion and undermining resorption are evident, Masson's.

dermining resorption and osteoclasia. Resorption and crushing with tissue necrosis was visible at the site of elastic insertion.

The periodontal fibers of all three molars showed tension consistent with normal distal drift. The periodontal membrane was inflamed but intact. Tension was seen on the mesial of all roots with relative equilibrium of the

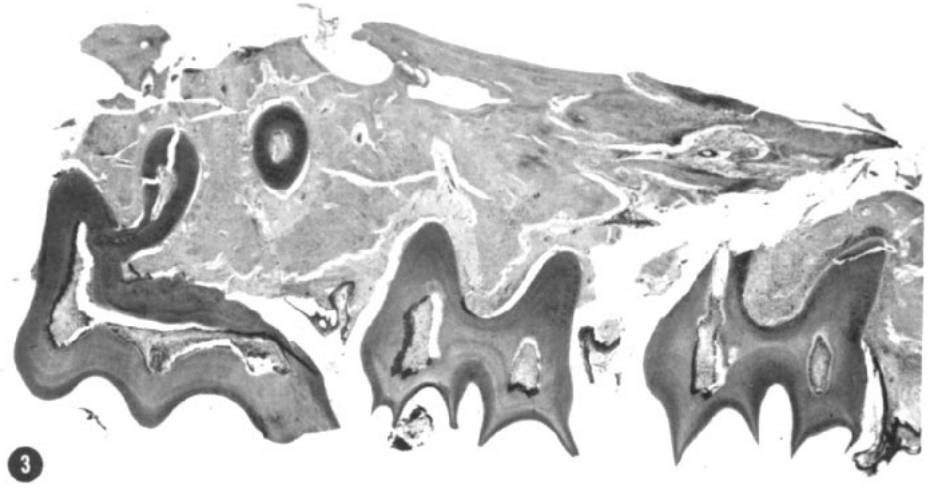

Fig. 3 Group A VI - elastic inserted for 1 day, followed by 7 days recovery, H & E.

fibers on their distal aspect. The first molar repositioned itself so that normal fiber tension reoccurred on the mesial of its roots. Thus the first molar uprighted from being tipped, and then tipped distally into the space made by elastic insertion. The cementum was unchanged, and the second and third molars remained upright in bone.

Subgroup VII, that group with elastics inserted for four days and allowed to recover for one week, showed moderate scalloping of bone and decreased osteoclastic activity. The periodontal membrane appeared to regenerate and reorganize to normal membrane structure and thickness. General bone reorganization and calcification due to osteoblastic activity occurred. The second and third molars were upright. The first molar tipped distally. Reorganization of the papilla and alveolar crest occurred between the first and second molars. Osteoblastic activity occurred on the mesial of all roots and slight osteoclastic activity on the distal of all the roots.

In subgroup VIII, the group with elastics inserted for eight days and allowed to recover for seven days, the alveolar crest appeared to have normal cytoarchitecture. Osteoblastic activity restored the tissue morphology to that seen in the normal control groups. The periodontal membrane showed normal thickness and integrity. The cementum was unchanged. Each molar was upright in the alveolar bone.

Group B

In this control group each animal was injected with thyroxin for eighteen days and then sacrificed. Tissue architecture consistent with a section of normal hamster maxilla was seen. A slight increase in areas of osteoclastic activity was observed.

In the thyroxin-treated groups with elastics inserted for one, four and eight days and sacrificed immediately, scalloping and destruction of the alveolar crest at the point of elastic insertion was observed.

Destruction of the alveolar crest between the second and third molars occurred in those animals sacrificed after one day. In the four-day group similar destruction was visible with a general increase of osteoclastic activity throughout the alveolar bone (Fig. 4). Osteoclastic activity increased where the alveolar crest was compressed between the second and third molars. Scalloping was seen at the upper third of the interradicular bone between all three molars. The periodontal membrane remained intact.

In the eight-day group more than three quarters of the alveolar bone between the molars was destroyed. Gross undermining resorption appeared in the interradicular bone and in the bone adjacent to the root surfaces. Increased osteolytic changes were seen in all adjacent bone. The periodontal membrane was inflamed and had areas of necrosis and degeneration.

The root surfaces of the one-day and four-day specimens showed smooth cementum layers. In the eight-day group half the specimens examined displayed areas of resorption in the cementum. Tipping of the crown occurred at a distance from the area of elastic insertion in the one-day group. The teeth of the four and eight-day groups were upright, and apparently had tipped and subsequently uprighted themselves.

Relative to the groups that had elastics inserted for one, four and eight days and not treated with thyroxin, the similar thyroxin-treated groups showed an exaggerated response to elastic insertion. Increased undermining resorption, membrane inflammation and osteoclastic activity at the alveolar crest and the interradicular areas were observed.

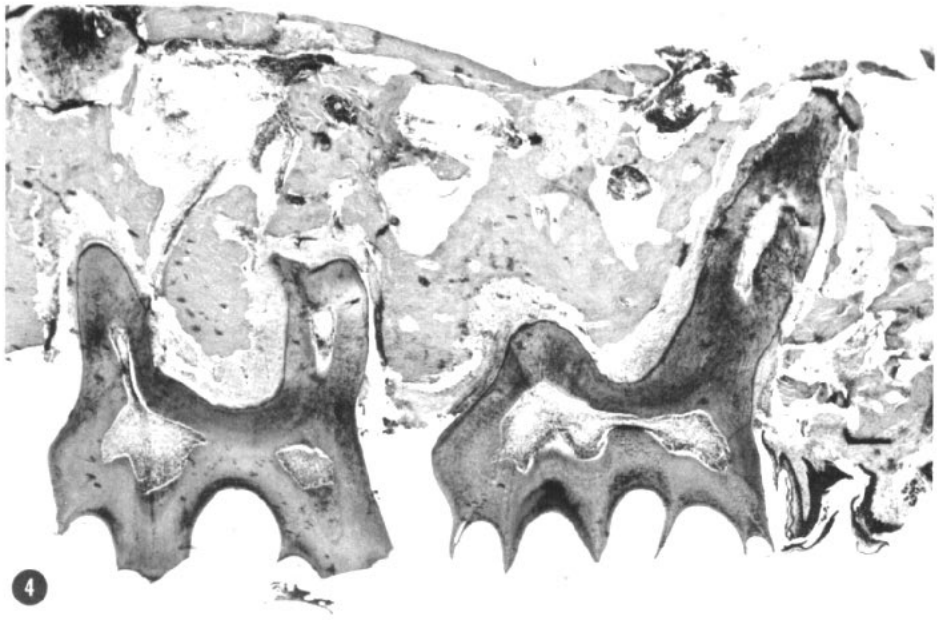

Fig. 4 Group B III - thyroxine - injected, elastics inserted for 4 days prior to sacrifice. Note increased tissue destruction as compared with Fig. 2, in which the same procedure, without thyroxin was employed, H & E.

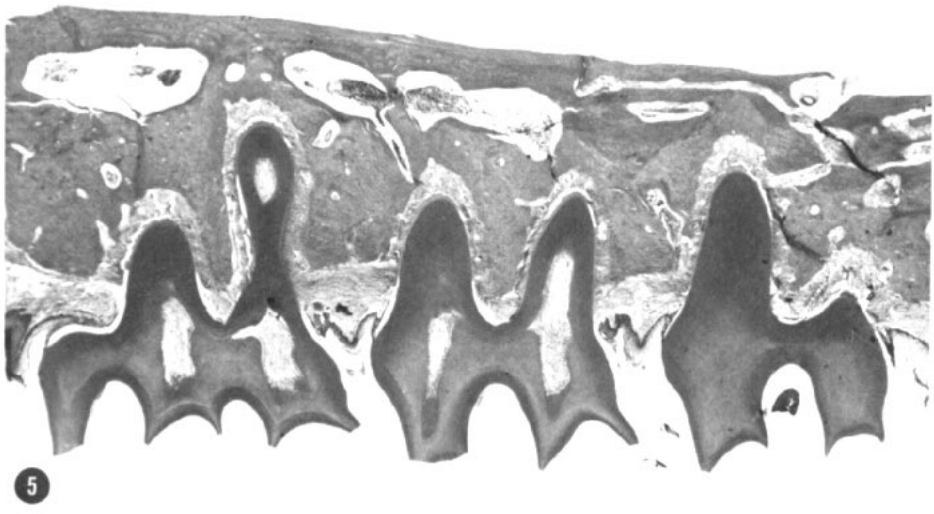

Fig. 5 Group B V - thyroxine-treated, elastic inserted for 1 day and 7 days recovery. Enhanced recovery when compared with Fig. 3 is evident, H & E.

Fig. 6 Group B VI - thyroxine-treated, elastic inserted for 4 days and 7 days recovery. Thyroxine therapy again to promote tissue recovery, Masson's.

Subgroup V, the thyroxin-treated group with elastic insertion for one-day and seven-day recovery (Fig. 5), showed a smooth interdental papilla and alveolar crest. Increased bone repair was observed. Normal distal drift of the first molar was restored. Alveolar bone was replaced about the root surfaces where it had been destroyed. The periodontal membrane was intact and inflammation was minimal. The teeth were upright. Tissue morphology was restored essentially to normal.

Subgroup VI, the thyroxin-treated group with elastic insertion for four days and seven-day recovery, showed a smooth alveolar crest and normal papilla between the molars (Fig. 6). Undermining resorption was repaired by osteoblastic activity. Normal distal drift was resumed. The first molar tipped distally into the space created by the elastic insertion. The periodontal membrane in its entirety was intact and had normal fiber orientation and thickness. No inflammation was present.

Subgroup VII, the thyroxin-treated group which had elastics inserted for eight days and a seven day recovery period, showed normal papilla and alveolar crests. Only slight osteolytic alteration was visible in the general bony architecture. Osteoblastic repair occurred throughout the bone. Normal distal drift was restored. No tipping of the teeth was visible. The periodontal membrane and cementum were essentially normal.

Discussion

In the examination of subgroups I and II of Group A, the normal group and the group injected with distilled water, normal cytoarchitecture was observed. The areas of osteoblastic and osteoclastic activity confirmed the normal distal drift previously reported in rodent teeth.[2,4,5]

In subgroups III, IV, V, those with elastics inserted for one, four and eight days, a progressive degree of destruction was observed as a function of time. The longer the insertion of the elastic, the greater was the destruction.

Changes observed in the one-day group consisted of breakdown of the

alveolar crest and its soft tissue cover. Bone scalloping occurred between the first and second molars. A dual effect was seen to take place in the one-day group: bone scalloping, a biological response and tissue necrosis of the alveolar crest and its soft tissue cover, a response to mechanical trauma.

When one compares the groups with elastics inserted for one, four, and eight days, the changes appear to be comparable and differ only in a matter of degree. The presence, however, of crushed periodontal membrane in the four-day group between the second and third molars was not seen earlier in the group with elastics inserted for one day. This indicated a progressive tissue response to the presence of a consistent force between the first and second molars.

In the eight-day group the greatest response was seen. In this group osteoclastic activity was predominant. Scalloping of the cementum, tooth tipping and generalized tissue necrosis were seen with osteolysis the overwhelming picture.

Thus, the one and four-day groups represent a variance between increased osteoclastic activity with some osteoblastic activity to the point where there is incomplete breakdown of bone.

In subgroup VI, the one day group with seven-day recovery, osteoclastic changes about the roots, gross undermining resorption, and crushing with tissue necrosis at the site of elastic insertion was observed. Bone scalloping was also seen to occur between the second and third molars indicating a minimal amount of tissue recovery in the seven day period with elastic stress removed.

In subgroups VII and VIII, with elastics inserted for four and eight days with seven days of recovery, tissue repair was evident. Mechanical destruction by elastic insertion was thought to have occurred predominantly in the first three or four days, after which an enhanced repair mechanism developed. This was illustrated in the four and eight-day insertion groups with seven days of recovery. The tissue healed to its normal histologic state.

In Group B, the thyroid-treated group, the tissue response to elastic insertion was similar to the response of the nonthyroid groups II, III, IV, except that tissue breakdown and repair were accelerated. The metabolic effect of thyroxin was thought to have enhanced the tissue changes. The metabolism of calcium and potassium from bone (the inorganic portion) was greater due to the relative acceleration of osteoclasia in the thyroid group as opposed to a nonthyroid treated control.

A distinct difference was noted between the one-day insertion group with and without thyroid where a seven day recovery period had elapsed. In the nonthyroid treated group repair lagged behind the similar group with the thyroid supplement. This indicated an influence upon bone repair rate by increasing the amount of healing present at a comparable period in the corresponding thyroid and nonthyroid groups.

From the findings it was not possible to state in absolute terms whether the rate of tissue breakdown was influenced more profoundly than was the rate of repair.

In subgroups VI and VII, the four and eight-day thyroid treated groups with seven day recovery, advanced bony repair was evident with the persistence of only minute areas of osteoclasia. This amount of osteolytic change was seen in the thyroid control group which had no elastics inserted. Increased osteoclasia was quantitatively least significant when comparing the eight-day insertion groups with and without thyroxin. Based upon the findings, one must not conclude that a supplement of thyroxin would be benefi-

cial in clinical orthodontics by shortening the treatment time. The literature clearly indicates that this conclusion is erroneous.[6,7] Thyroid given to normal children might not only induce the symptoms of hyperthyroidism but also attenuate the normal pattern of growth. This occurs due to the premature closure of the epiphyseal cartilages induced by the stimulating effect of thyroxin upon the pituitary gland. Thus, precocious maturation would be the result.

Future investigation may well show thyroxin to be of use in the treatment of adult orthodontic cases by reducing bone resistance and accelerating the rate of breakdown and repair in the alveolar bone. The benefit of thyroxin might thus be realized without the undesirable effects upon growth.

Summary

L-thyroxin sodium salt was used to induce a hyperthyroid state in the golden hamster. The teeth of these animals were moved orthodontically by the placement of an elastic between the first and second maxillary molar teeth. The animals were grouped and sacrificed after one, four and eight days of elastic insertion. Another set of one, four and eight day groups were allowed to recover with the elastics removed for seven days and then sacrificed. All of the groups were compared with identical nonthyroxin treated groups and controls.

The tissue specimens were excised and decalcified in EDTA. They were then fixed in neutral buffered formalin and stained in Massons trichromic stain or hematoxylin and eosin for the evaluation of histomorphology.

This study established the following:

1. It confirmed normal distal drift of molars in hamsters.
2. Excessive orthodontic force created by the insertion of an elastic between the first and second molars resulted in tooth movement by undermining resorption within the alveolar bone as a function of time.
3. L-thyroxin sodium salt resulted in demineralization of the alveolar bone by increasing osteoclastic activity.
4. The force required to move teeth is absorbed in the alveolar bone immediately adjacent to the root surfaces.
5. There was an increase in both the rate and quality of osteoblastic activity in those animals treated with thyroxin when allowed to recover from elastic insertion.

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