Original Article

Decreased alveolar bone turnover is related to the occurrence of root resorption during experimental tooth movement in dogs

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ABSTRACT

Objective: To investigate the relationship between root resorption (RR) and bone turnover in two different types of tooth movement in dogs.

Materials and Methods: A total of 16 dogs in two different groups were used. Tooth movement of dog premolars resulted from approximately 200 g of force. Histomorphometric analysis of premolar roots was assessed after 4 and 12 weeks of tooth movement by comparing nonresorptive to resorptive surfaces.

Results: Histomorphometric analysis indicated a significant decrease in the bone formation rate in the root resorptive areas, which resulted in decreased bone volume after 12 weeks. The threshold to detect RR in periapical radiographs was about 1.0 mm^2.

Conclusions: A sustained mechanical load, due to the prolonged stress and strain of continuous mechanics, induces elevated bone metabolic activity, such as the bone turnover (remodeling) and change in bone volume (modeling). Therefore, our data support the hypothesis that increased RR is related to decreased bone formation (turnover) in high stress areas exposed to prolonged orthodontic tooth movement. (*Angle Orthod.* 2015;85:386–393.)

KEY WORDS: Root resorption; Alveolar bone turnover; Histomorphometric analysis; Tooth movement; Biomechanics

INTRODUCTION

External apical root resorption (EARR) and root resorption (RR) are common problems associated with orthodontic treatment. EARR is a permanent blunting of the apical roots associated with orthodontic treatment, and RR is a more generalized phenomena that includes the lateral regions of the roots and may occur in other circumstances.[1,2] One of the suggested causes for RR during orthodontic tooth movement is biochemical or mechanical factors related to the magnitude,[3] duration,[4] direction,[5,6] and type of the orthodontic force.[7] However, the specific etiology and interrelationship of EARR and RR is elusive.

One of the reasons for the high occurrence of EARR at the apical region is that the center of the rotation of the teeth usually is located in or near the apical one third of the root.[8] Stress analysis of orthodontically stimulated rat molars suggests that mechanically induced stress results in bone resorption.[1] In the past, Engström et al.[9] have defined the link between stress-induced bone resorption and RR in normal and hypocalcemic rats. In that study, RR was related to the degeneration process occurring in the vicinity of the pressure areas. Especially in the hypocalcemic

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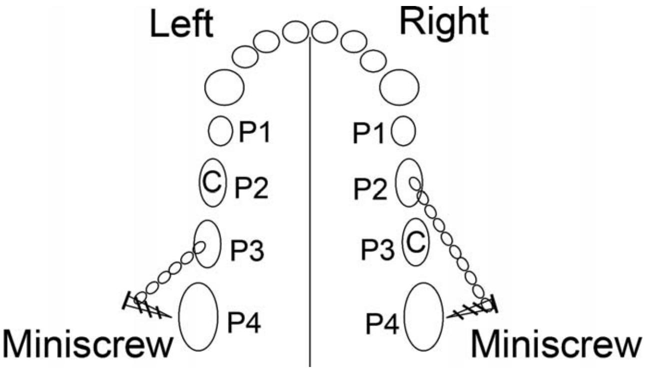

Figure 1. A schematic drawing demonstrates miniscrew-anchored mechanics to move premolars. (P1 indicates first premolar; P2, second premolar; P3, third premolar; P4, fourth premolar; and C, control).

rats, alveolar bone resorption in the compression zones seemed more rapid and extensive than in the normal rats. There is also a study that investigated the relationship between the bone turnover and RR after corticotomy.[10] However, there are few studies investigating the effect of RR relative to the change in the rate of surrounding alveolar bone turnover during tooth movement using histomorphometric analysis.

Intrusion and tipping movements are known to be associated with RR.[5,6] With tipping, the periodontal ligament (PDL) peak stresses are known to be about three times greater than those with translation, and intrusion causes about four times more RR than extrusion.[5,6] Thus, investigating the incidence and the amount of RR in different types of tooth movement would be helpful in directing controlled tooth movement to avoid severe RR.

Therefore, we hypothesized that there will be a reduced alveolar bone turnover adjacent to the root resorptive areas where high stress is associated with prolonged tooth movement.

MATERIALS AND METHODS

Experimental Design

The study protocol was reviewed and approved by the Institutional Board of Animal Research Ethical Committee of Tohoku University. Sixteen 8-month-old beagle dogs (eight each for 4- and 12-week groups) were used. A total of 32 mandibular teeth were examined in each of four tooth movement groups ($n = 8$); 4-week mainly intruded, 4-week mainly tipped, 12-week mainly intruded, and 12-week mainly tipped. The mainly tipped specimens were group A, and mainly intruded specimens were group B. The modifier "mainly" is used because the two groups were not exclusively tipped or intruded. The name of the group signifies the predominant type of tooth movement. Contralateral premolars were used as unloaded controls ($n = 8$) (Figure 1). Impressions of the jaws for casts were taken before and after the tooth movement. Lidocaine (2% epinephrine) was injected into the mucoperiosteal flap. A crown with a hook was bonded to the second (group A) and third (group B) premolars. A 1-mm hole was drilled into the bone. Miniscrews (Titanium screw, Stryker Leibinger, Kalamzoo, Mich; 1.0 mm in diameter and 5.0 mm in length) were inserted between the roots of the fourth premolars. Orthodontic force of 200 g was applied by the power chain attached from the miniscrew to the hook of the cast crown. Immediately before and after the tooth movement, radiographs were taken with the digital Schick x-ray computer program (CDR Schick Tec Inc, Long Island, NY). At 3 days and 10 days before humanely killing the animal, a sequence of two fluorochrome labels, calcein green (Sigma Chemical Co, St Louis, Mo) and tetracycline (Lederle Laboratories, American Cyanamid Co, Pearl River, NY), was administered by intravenous injection. After 4 or 12 weeks of experimental tooth movement, the dogs were euthanized.

Tissue Preparation

Specimens were fixed in 70% ethyl alcohol, and then dehydrated in an ascending series of ethyl alcohol baths, cleared in xylene, and infiltrated with methylmethacrylate for 20 hours. The tissues were placed in methylmethacrylate containing 3% dibutyl phthalate and 0.5% initiator (Perkodox 16, AKZO, Chicago, Ill). Before the specimen blocks were sectioned, they were all numbered and blinded. The Exakt cutting/grinding system (Exakt Medical Instruments, Oklahoma City, Okla) was used to finish the specimens after serial sectioning with a Leica 1600 Saw Microtome (Deerfield, Ill). Sections were polished to approximately 100 μm and mounted for bright field, fluorescent, and polarized light microscopy. Microradiographs were also produced using a Faxitron (Hewlett Packard, Beaverton, Ore). Since microradiographs enable us to distinguish the extent of mineralization, it was used to identify the area of root resorption and/or quality of surrounding bone.

Histomorphometry

The area analyzed in this study was defined by a test line (dashed) bisecting the distal roots longitudinally and three solid lines perpendicular to the test line (Figure 2). The test line was defined as a perpendicular line to the line connected to the alveolar crest of the mesial and distal of the distal root. The distal alveolar surfaces, within 1.5 mm that directly faced the PDL in all three levels, were measured (Figure 2).

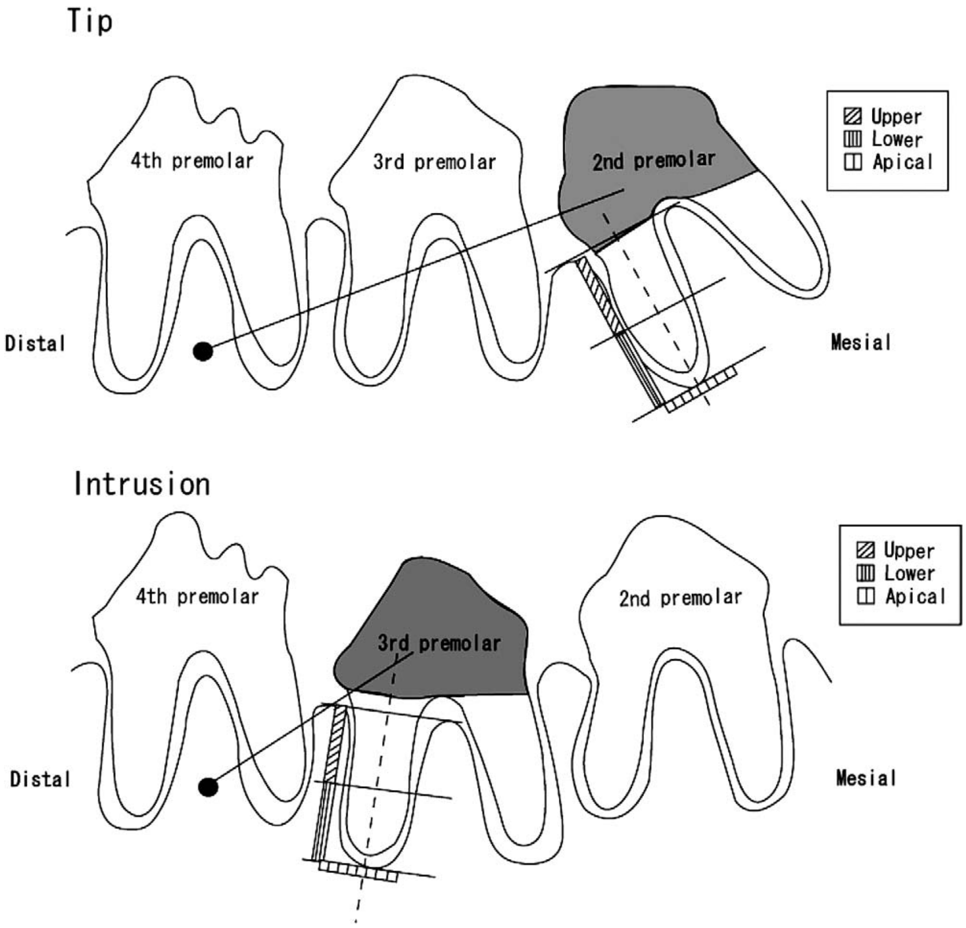

Figure 2. A drawing shows how the premolars were moved by the miniscrew-anchored mechanism. Histomorphometric analysis was performed in three different regions at the distal root of the premolars (upper, lower, apical: average region of interest in all three areas was 1.5 × 8.9 mm^2).

Histomorphometric analysis (Table 1) was performed on a Nikon FXA epifluorescent microscope (Nikon Inc, Melville, NY) utilizing stereological point-hit and linear intercept methods at magnifications of 100× to 250× with a 10 × 10 ocular square grid.[11]

Our definition of RR is microscopic (histologic) lesions in areas of resorption lacunae on cementum surface. Distinction between the neighboring alveolar bone of the nonresorptive and the resorptive area was identified by a perpendicular line to the line bisecting the root drawn at root resorptive areas (Figure 3). Measurement was performed within 1.5 mm from the surface that directly faced the PDL. Histomorphometric measurements and calculations in these two areas followed the standard nomenclature and formulae described by Parfitt.[12]

Statistics

Mann Whitney *U*-test was performed to examine the effects of types of tooth movement on the histomorphometric indices of rate and amount of RR, and

Table 1. Derived Histomorphometric Indices

	Abbreviation	Formula
Static Indices		
Root resorption index	RR; %	Resorptive hits/total hits × 100
Bone volume/total volume	BV/TV; %	Bone hits/total hits × 100
Eroded surface/bone surface	ES/BS; %	Erosion surface hits/total hits × 100
Dynamic Indices		
Mineralizing surface/bone surface	MS/BS; %	[(Double label intercept + ½ single label intercept) × 100]/BS
Mineral appositional rate	MAR; μm/d	Interlabel width/7 d
Bone formation rate	BFR; %/y	MAR × [(double label intercept + ½ single label intercept) × d/Bh × d2] × 100 × 365

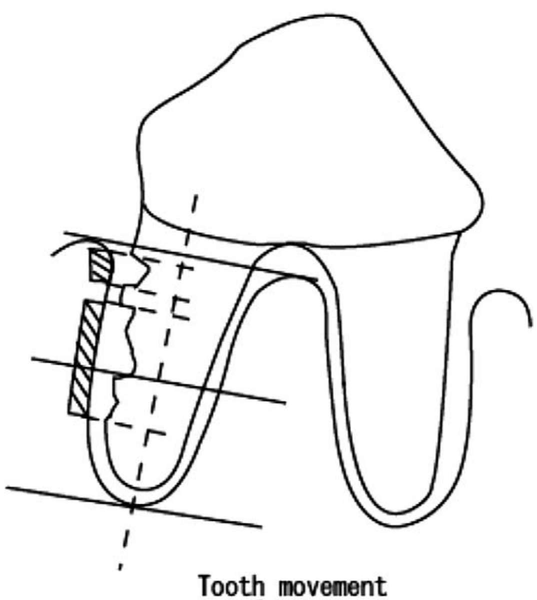

Figure 3. Schematic drawing presents the comparison of the histomorphometric analysis between the nonresorptive surface (nonshaded area) and resorptive surface (shaded area: width of 1.5 mm).

between nonresorptive and resorptive area. P values $< .05$ were considered significant. All of the histomorphometric data are presented as average + the standard error.

RESULTS

Root Resorption Index

Group A (tipping). In the control group, there was no significant difference in any of the three regions within the group (Table 2).

After 4 weeks (Figure 4; Table 2), there was no significant difference compared to the control. Decreased bone labeling with increased RR was observed at the mesial upper region (pressure area; Figure 4) compared to the distal upper region (tension area). After 12 weeks (Figure 5; Table 2), significant increase of RR was observed. Among the regions, the mesial upper (Figure 5) and lower regions showed significantly higher RR rate.

Group B (intrusion). In the control, there was no significant difference in the three regions within each group.

After 4 weeks (Figure 4; Table 2), significant increased RR was observed at the mesial apical region compared to the distal apical region. After 12 weeks (Figure 5), a significant increase was observed in the apical region (Table 2).

Root Resorptive Area vs Nonresorptive Area

Group A (tipping). In group A, bone volume/total volume (BV/TV) significantly decreased at both 4 and 12 weeks of root resorptive areas and at 4 weeks of nonresorptive area. Eroded surface/bone surface (ES/BS) significantly increased in both areas in both groups. Significantly increased ES/BS was observed at the root resorptive area at 12 weeks (Table 3).

Mineral appositional rate (MAR) significantly increased at nonresorptive areas at 4 and 12 weeks, and at resorptive area at 4 weeks. At 12 weeks, a significant increase was observed at the nonresorptive area. Mineralizing surface/bone surface (MS/BS) resulted in a significant increase in both areas in both groups. A significantly lower rate was observed in the resorptive areas at 12 weeks. Bone formation rate (BFR) resulted in a significant increase in both areas in both groups. A significantly lower BFR was observed in the resorptive area in both groups. A significantly higher BFR was observed at 12 weeks compared to 4 weeks in the nonresorptive area.

Group B (intrusion). In group B, BV/TV significantly decreased in both areas at 4 weeks and resorptive area at 12 weeks. A significantly lower BV/TV was observed in the resorptive area at 12 weeks. Significantly higher

Table 2. Root Resorption Index (Total is Total Average RR Index of All Three Regions)

	Control								4-Week							
	Upper		Lower		Apical		Total		Upper		Lower		Apical		Total	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Group A (tipping)	0.9	0.5	0.5	0.5	1.5	1.3	1.0	0.5	16.1	8.3	14.4	8.6	13.2	8.0	14.6	4.6
Group B (intrusion)	1.4	0.7	1.2	0.8	1.0	1.0	1.2	0.5	22.6	12.1	24.9	14.3	25.2	11.7	24.2*	7.0
	Control								12-Week							
	Upper		Lower		Apical		Total		Upper		Lower		Apical		Total	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Group A (tipping)	2.0	1.1	2.3	1.2	1.9	1.2	2.0	0.7	55.0*	20.8	33.6*	12.3	27.0	9.8	38.5[a]*	8.7
Group B (intrusion)	1.3	0.7	1.1	0.9	2.4	0.8	1.6	0.5	32.8	16.4	38.9	15.9	50.1*	11.0	40.6*	8.2

[a] Significant difference compared with the 4-week group ($P < .05$).

[c] Significant difference compared with the control.

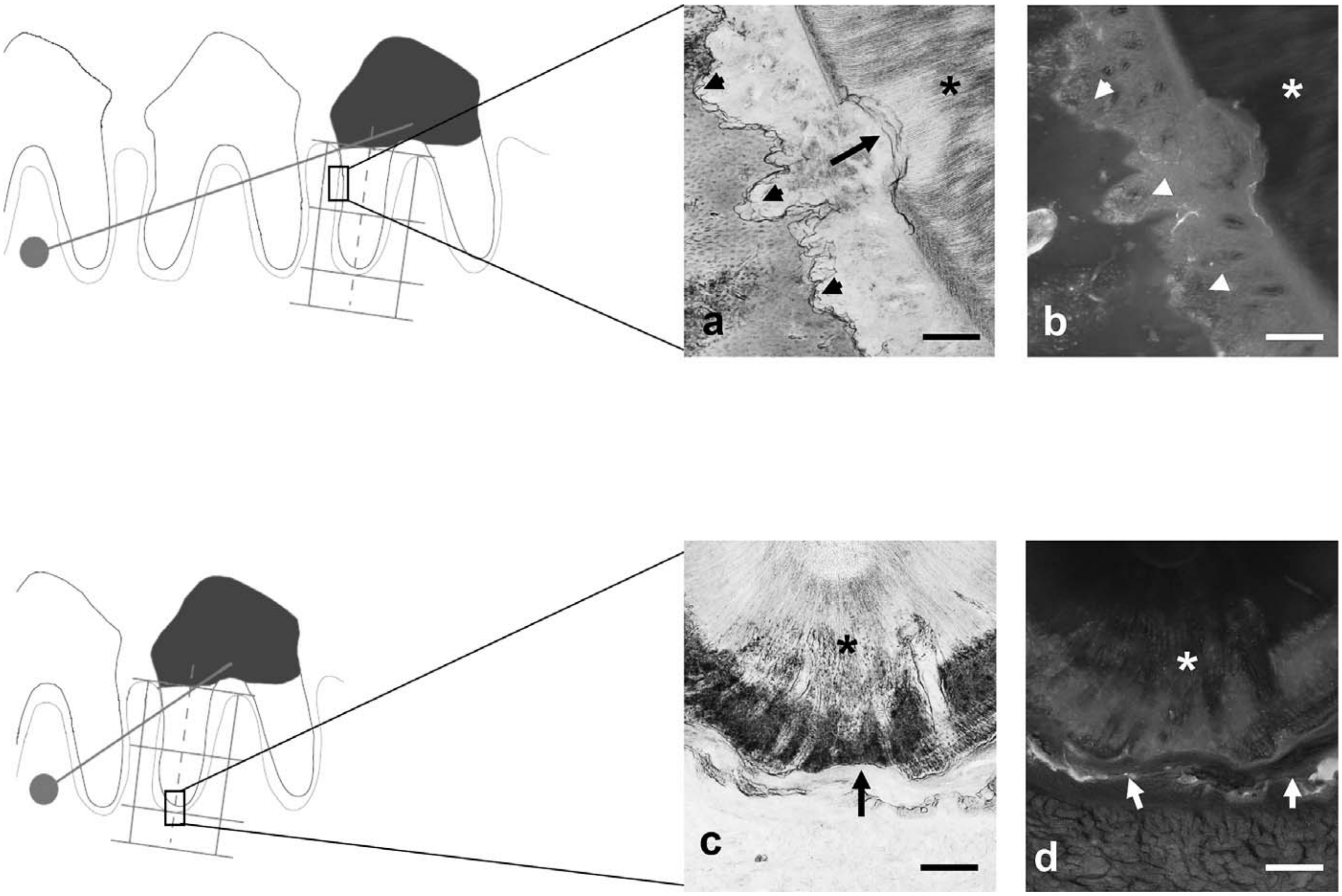

Figure 4. Light (a,c) and fluorescent (b,d) microscopic photographs of RR (arrows) demonstrate tipping (a,b) and intrusion (c,d) after 4 weeks. Eroded surface (arrow heads in c) results in decreased bone labeling (arrow heads in d) in the distal upper area. Decreased bone labeling is observed at the mesial apical area (c,d) adjacent to the RR (arrow in c). * Tooth side. (Bars = 50 μm).

BV/TV was observed in 12 weeks compared to 4 weeks in the nonresorptive area. ES/BS showed significant increase in both groups in both areas. Significantly higher ES/BS was observed in the root resorptive area in both groups. There was a significant difference in MAR at 4 weeks and nonresorptive 12 weeks. A significantly higher MS/BS was observed in nonresorptive areas at 4 and 12 weeks, and in resorptive area at 4 weeks. A significantly lower MS/BS was observed in the resorptive area at 12 weeks. A significantly higher MS/BS was observed at 12 weeks. BFR was significantly higher in both areas in both groups. A significantly lower BFR was observed in the resorptive area at 12 weeks. Furthermore, a significantly higher BFR was observed at 12 weeks compared to 4 weeks in the nonresorptive area.

Radiographic Observations

Although a significant amount of RR was observed along the root surface of experimental teeth from the histologic sections, only few periapical radiographs resulted in moderate (approximately 10%) to severe (approximately 1%) RR (>1.0 mm^2) (Figure 6).

DISCUSSION

The average root resorption index in the control was less than 2% of the total examined area. These data suggest that the dogs used in this study did not have any systematic factors that might have influenced the fraction of the root surface involved with RR. Increase in the amount of RR was observed after the initiation of tooth movement. This is consistent with previous reports that the longer the duration of treatment, the more extensive the RR in both clinical[13] and animal studies.[14] Especially after 12 weeks, the amount of RR significantly increased. At 4 weeks, RR was up approximately 50% in both groups. These data are consistent with the concept that the amount of RR tends to increase with longer treatment duration.

After 12 weeks of tooth movement, the most RR was observed at the upper region of the distal root in the tipping group A. In the intrusion group B, the most significant RR was observed at the apical region.

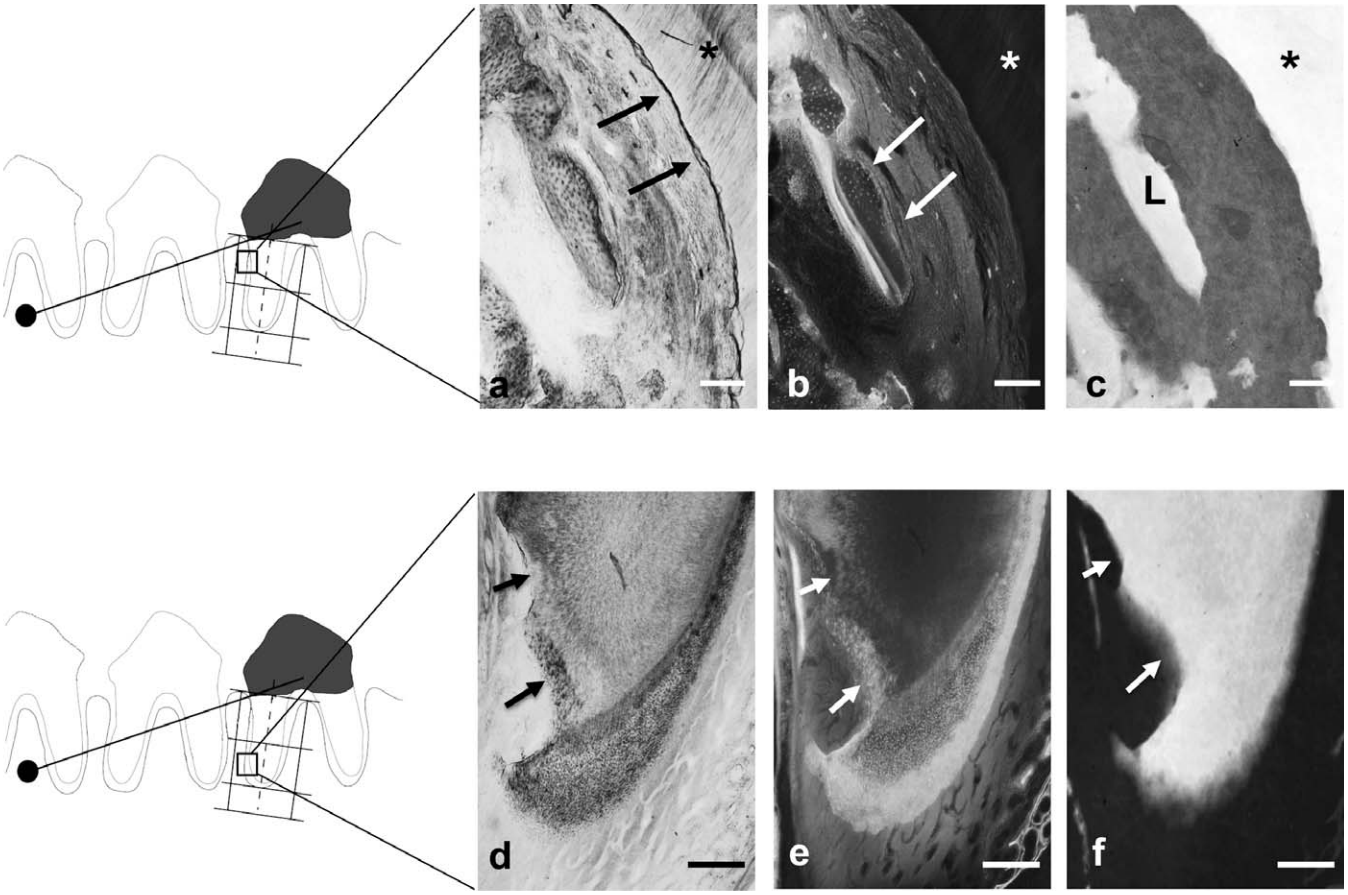

Figure 5. Light (a,d) and fluorescent (b,e) microscopic photographs, and microradiographs (c,f) demonstrate tipping (a,b,c) and intrusion (d,e,f) after 12 weeks. At the upper region of the distal root (a,b,c) a significant amount of RR (arrows in a), with decreased bone labeling (arrows in b) was observed. Microradiographs showed a lamellar bone (L) formation at mesial upper area (c). At the lower region of the distal root (d,e,f), increase of RR (arrows) was observed. (Bars = 50 μm).

Table 3. Histomorphometric Indices Between Root Resorptive Area and Nonresorptive Area

			4-Week						12-Week			
Group A (Tipping)	Control (4-Week)		Nonresorption		Root Resorption		Control (12-Week)		Nonresorption		Root Resorption	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
BV/TV, %	60.4	1.5	43.6*	6.0	41.4*	5.2	63.9	2.5	57.1	3.9	48.2*	4.7
ES/BS, %	13.8	3.5	50.0*	4.6	59.7*	4.1	14.2	2.3	36.6*	6.2	59.2[a]*	5.8
MAR, μm/d	1.4	0.1	1.9*	0.2	1.9*	0.2	1.3	0.1	2.3*	0.2	1.6[a]	0.2
MS/BS, %	14.9	2.9	30.6*	2.0	25.7*	3.2	14.9	1.5	47.1*	5.7	30.3[a]*	3.3
BFR, %	21.5	2.8	142.3*	10.8	100.3[a]*	11.4	19.2	1.5	204.7[b]*	12.5	98.3[a]*	10.0
			4-Week						12-Week			
Group B (Intrusion)	Control (4-Week)		Nonresorption		Root Resorption		Control (12-Week)		Nonresorption		Root Resorption	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
BV/TV, %	61.8	1.7	45.1*	3.0	36.7*	3.5	63.3	2.9	56.8[b]	3.6	39.0[a]*	4.3
ES/BS, %	13.8	2.1	26.3*	2.8	46.3[a]*	4.4	10.9	1.8	31.4*	5.3	57.0[a]*	8.1
MAR, μm/d	1.3	0.1	1.7*	0.2	1.8*	0.1	1.2	0.1	1.7*	0.1	1.4	0.2
MS/BS, %	16.1	3.0	28.9*	2.5	28.1*	3.2	15.5	1.9	48.8*	6.9	22.4[a]	4.2
BFR, %	17.8	2.5	108.5*	9.6	92.2*	8.5	18.4	2.7	155.5[b]*	6.9	84.4[a]*	12.1

[a] Significant difference compared with nonresorption area.

[b] Significant difference compared with 4-week ($P < .05$).

[c] Significant difference compared with control.

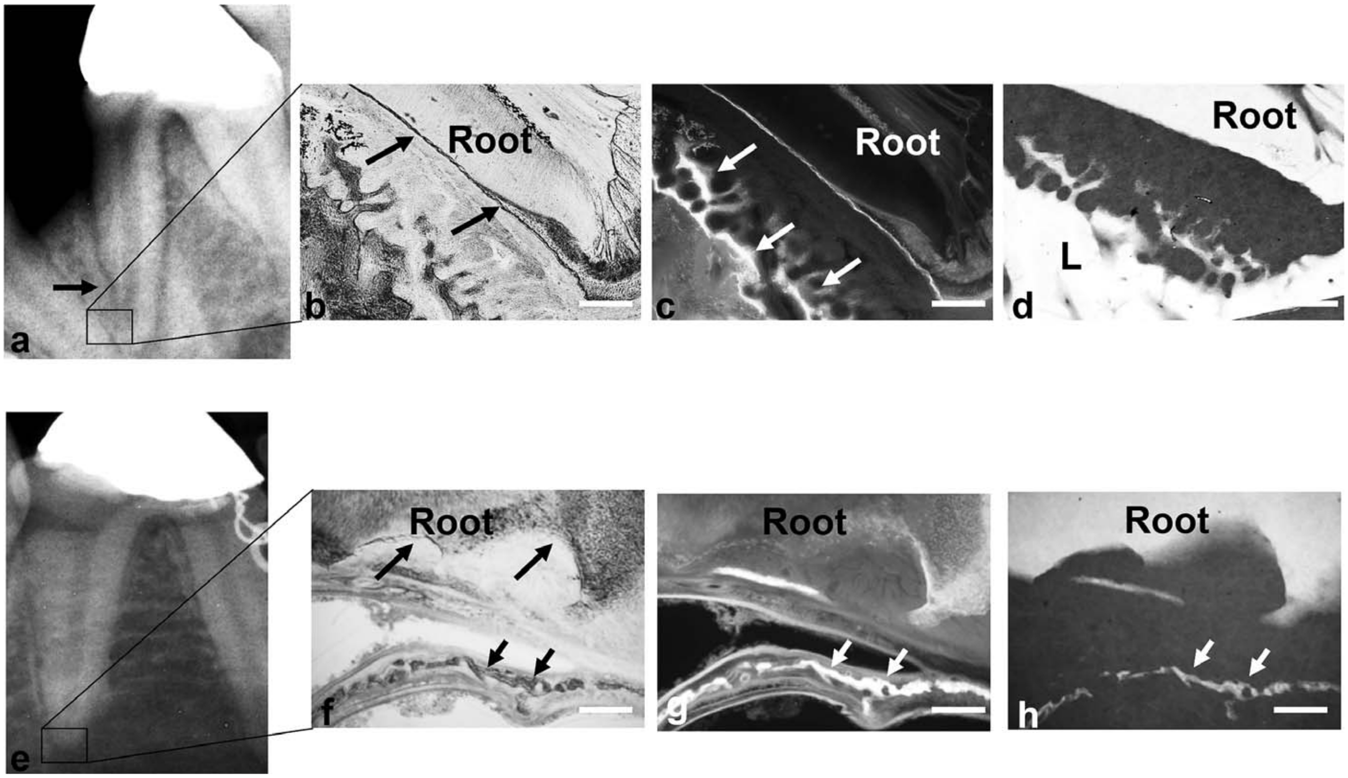

Figure 6. Periapical radiographs (a,e), light (b,f) and fluorescent (c,g) microscopic photographs, and microradiographs (d,h) of intrusion group after 12 weeks. RR is observed (arrow in a,b) from the periapical radiographs and light microscopic photograph with decreased bone labeling (arrows in c) adjacent to the lamellar bone (L). There was also a significant amount of RR at the apical areas (arrows in f) with decreased adjacent bone volume (arrow heads in f,g,h). (Bars = 50 μm).

These two regions are considered to be pressure areas, where the most stress concentration is observed.[15] Thus, this study demonstrates that when a tooth is tipped distally, RR mainly occurs at the upper distal region. This finding is in agreement with the finite element analysis that has shown that stress magnitude depends on the type of tooth movement and corresponds to the RR pattern.[15] During intrusion, RR mainly occurs at the apical region (apex) where the highest stress concentration is expected. Intrusion is suggested to be the most susceptible type of movement.[5,6] However, in this study, there was no significant difference in the total amount of RR between intrusion and tipping groups. The reason for this might be that in the comparative clinical studies, the tooth analyzed is usually an incisor. Molars may be less prone to RR because they are teeth that are designed to resist greater occlusal loading compared to incisors.

In this study, significant differences in histomorphometric indices were observed among the locations of RR, treatment duration, and type of tooth movement. After 4 weeks, significant decrease in the amount of BFR and increase in the amount of ES/BS were observed between the nonresorptive and resorptive areas. Thus, it appears there is suppression of bone turnover and increased bone resorption at the area where RR occurs during the initial stage of tooth movement.

In both groups at 12 weeks, the BFR in the root resorptive areas was approximately half that of the nonresorptive areas. MAR and MS/BS were also significantly decreased at resorptive areas. These data suggest there is an inhibition of osteoblastic activity and alveolar bone mineralization in the alveolar bone, adjacent to the resorptive area, resulting in a decrease of active bone formation. Significant decrease in the BV/TV was observed along with decreased BFR in the root resorptive area, especially in the intrusion group. These data can be explained by the mechanostat theory,[16,17] which holds that when mechanical loading exceeds the physiologic range, a pathologic overload occurs, which results in a decrease in prevalence of bone remodeling and a fatigue failure response.[1]

At 12 weeks, an increased BFR was observed along the nonresorptive area compared to the 4-week group. Moreover, the ES/BS% significantly increased at the resorptive areas compared to the nonresorptive areas at 12 weeks in both groups. Bone formation parameters such as MS/BS and BFR increased at the nonresorptive areas, while they tend to decrease in resorptive areas. Taken together, this evidence suggests that the concentration of high stress, caused by the functional prematurities resulting from orthodontic tooth movement, results in suppression of the normal bone modeling and/or remodeling phenomenon. This delayed bone response exposes the roots to excessive flexure resulting in fatigue failure of the root surface which is manifest as RR.[1] In addition, with a large amount of force, not only the root but the bone may be destroyed. Thus, a controlled amount and direction of force is required to minimize root and bone resorption, such as in the case of intrusion where less bone is observed in the apex.

Relevant studies indicated that persons homozygous for the interleukin-1 beta (IL-1β) allele 1 have a 5.6-fold increased risk of EARR greater than 2 mm.[18,19] From the results of our study, reduced rates of alveolar bone resorption were observed at root resorptive areas that were associated with compressed areas of PDL. Therefore, it is suggested that prolonged stress concentrated along the root of the tooth resulted in a slowing down of the alveolar bone resorption, which led to RR. The present data strongly support the previous studies suggesting that the excessive RR observed in patients homozygous for allele 1 of IL-1β may be manifest by an initial impairment of alveolar bone resorption, producing prolonged stress and strain of the adjacent tooth root because of dynamic functional loads.[1,18,19]

Significant histologic RR was observed in this study. Some RR with a total area greater than $>$1.0 mm^2 was evident on periapical radiographs, suggesting this is the detection limit for routine radiographic detection. Moreover, orthodontic force (200 g) used in this study is often used clinically. Clinicians must evaluate the amount and the direction of mechanical force when using miniscrews as anchorage to prevent, or at least control, RR during orthodontic treatment.

CONCLUSIONS

- The results confirmed the hypothesis: a significant decrease of bone turnover was noted at areas of root resorption that occurred in zones of high, concentrated stress.
- A sustained mechanical load, due to the prolonged stress and strain of continuous mechanics, induces both tooth movement and elevated bone metabolic activity, such as the bone turnover (remodeling) and change in bone volume (modeling).

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