Original Article

The effect of alveolar decortication on orthodontically induced root resorption

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ABSTRACT

Objective: To determine the effect of alveolar decortication on orthodontically induced root resorption.

Materials and Methods: A total of 24 male Wistar rats (14 week old) were used. The rats were randomly divided into one of the following three groups: group 1 (control group), orthodontic tooth movement (OTM) for 2 weeks; group 2, OTM for 2 weeks + two alveolar decortications (2AD); group 3, OTM for 2 weeks + four alveolar decortications (4AD). The first molar was moved mesially for 2 weeks. Micro computed tomography was used to analyze root volume. In addition, histological sections were stained with Tartrate Resistant Acid Phosphatase (TRAP) to quantify the osteoclast number.

Results: The buccal root volume in OTM + 4AD group was decreased by 8.92% and 6.11% when compared with the OTM-only group and OTM + 2AD group, respectively. Similarly, the other four root volumes in the OTM + 4AD group was decreased by 8.99% and 5.24% when compared with the OTM-only group and OTM + 2AD group, respectively. There was a decrease in buccal root density in the OTM + 4AD group by 4.66% and 3.56% when compared with the OTM-only group and the OTM + 2AD group, respectively. In addition, there was an increase in the number of osteoclasts by 195.73% and 98.74% in OTM + 4AD group in comparison with the OTM and OTM + 2AD group.

Conclusions: The amount of orthodontically induced root resorption was positively correlated with the extent of surgical injury used to accelerate orthodontic tooth movement. (*Angle Orthod.* 2020;90:524–531.)

KEY WORDS: Root resorption; Alveolar decortication

INTRODUCTION

Orthodontically induced inflammatory root resorption is a pathologic side effect of orthodontic treatment.[1] This condition is difficult to predict and it is usually identified by routine X-rays or at the finishing stages of orthodontic treatment, when the amount of sequela may not be reversible.[2] The etiology of root resorption may be the result of a combination of individual predisposition, genetics, and external mechanical factors. Approximately 5% of adults and 2% of adolescents are likely to have at least one tooth with severe resorption during active orthodontics.[3,4] Prolonged active treatment is highly correlated with root resorption as a result of the longer period of hyalinization preceding root resorption.[5]

Because of the complications associated with long orthodontic treatment duration, interventions to shorten treatment time have gained momentum in the past decade. Special interest has been given to surgical interventions to accelerate tooth movement, including alveolar perforations/decortication, piezocision, corticision, corticotomy, and dental distraction.[6] It is unclear if the surgical adjunctive procedures in an attempt to accelerate orthodontic tooth movement have an effect on orthodontically induced root

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resorption. Several studies have shown that corticotomy and piezocision do not cause root resorption,[6–8] whereas other studies have shown that periodontal distraction causes root resorption in one of six cases.[9] A study on the effects of micro-osteoperforation on root resorption showed that this intervention resulted in significantly increased root resorption.[10] A Cochrane review indicated that there was a paucity of high-quality evidence regarding the effects of surgical adjuncts to accelerate orthodontic tooth movement on root resorption.[1] Therefore, the existing literature lacks sufficient evidence regarding the extent of surgical insult and its effect on orthodontically induced root resorption. Consequently, the goal of this study was to investigate the effect of differing amounts of surgical insult (alveolar decortication) on orthodontically induced root resorption. The null hypothesis was that alveolar decortication would not result in significant increase in the amount of orthodontically induced root resorption. The specific objectives were (1) to determine the amount of orthodontically induced root resorption with alveolar decortication and (2) to investigate whether the extent of injury (alveolar decortication) was positively correlated with orthodontically induced root resorption.

MATERIALS AND METHODS

Animals and Experimental Design

All animal procedures in this study were approved by the Institutional Care Committee of the University of Connecticut Health Center. A total of 24 14-week-old male Wistar rats were obtained from Charles River Laboratories (Wilmington, Mass).

The rats were randomly divided into one of the following three groups: group 1 ($n = 8$), orthodontic tooth movement (OTM) for 2 weeks (OTM only); group 2 ($n = 8$), orthodontic tooth movement for 2 weeks + two alveolar decortications (OTM + 2AD); and group 3 ($n = 8$), orthodontic tooth movement for 2 weeks + four alveolar decortications (OTM + 4AD).

Force Application and Appliance Delivery

The rats were anesthetized with xylazine (13 mg/kg) and ketamine (87 mg/kg). A custom spring was fabricated using 0.036-inch stainless steel (SS) wire to keep the mouth open during the experimental procedure; 5 to 8 grams of protraction (mesialization) force was applied to the maxillary first molar using a nickel titanium coil spring (Ultimate Arch Wires, Bristol, Conn). To attach the coil spring to the molar, a 0.008-inch SS ligature wire was passed beneath the contact between the first and second maxillary molars and threaded to the first maxillary molar (Figure 1). The other end of the spring was attached to the maxillary incisors using SS ligature wire.

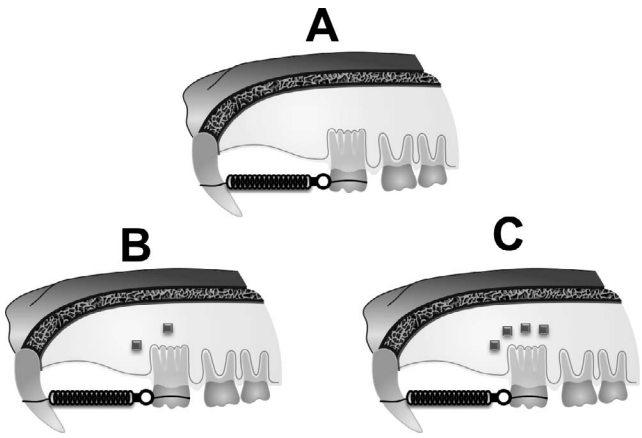

Figure 1. (A) Schematic of orthodontic tooth movement for 2 weeks only group. (B) Schematic of orthodontic tooth movement for 2 weeks + two alveolar decortications group. (C) Schematic of orthodontic tooth movement for 2 weeks + four alveolar decortications group.

To prevent the dislodgement of the spring from the maxillary incisors, 0.5-mm deep groves were prepared on the facial, lingual, and distal surfaces of the maxillary incisors. Self-etching primer and light cured adhesive resin cement (Transbond, 3M Unitek Corp, Monrovia, Calif) were applied to the lingual surface of the first molar and incisors to secure the ligature wire. To reinforce the anterior anchorage, the right and left incisors were joined to act as a unit (Figure 1). The appliance was checked twice a week, and additional bonding material was added as necessary. The maxillary incisors were trimmed twice a week to keep the force at a constant plane and to prevent dislodgement of the spring.

Surgical Insult through Alveolar Decortications

Alveolar decortications (ADs) were made using a quarter round bur and a high-speed hand piece with a saline wash. In group 2, two ADs were made on the palatal alveolar bone adjacent to the first maxillary molar, whereas in group 3, four ADs were made on the palatal alveolar bone (Figure 1).

Micro Computed Tomography

The root volume and density were analyzed using micro computed tomography (micro-CT; SCANCO Medical AG, Bruttisellen, Switzerland). The raw data obtained by the scanning procedures were reconstructed and evaluated using the image processing language analysis tool. Root volume measurement (including root dentin and cementum) was used to

Table 1. Distribution of Data for Buccal Root Volume

	Group		
	Orthodontic Tooth Movement	Orthodontic Tooth Movement + Two Alveolar Decortication	Orthodontic Tooth Movement + Four Alveolar Decortication
Minimum	78.1	74.2	69.2
25% percentile	78.13	74.55	69.35
Median	78.4	75.95	70.6
75% percentile	78.83	77.8	74.4
Maximum	78.9	78.3	75.4
Mean	78.45	76.1	71.45
Standard deviation	0.3697	1.707	2.792
Standard error of mean	0.1848	0.8534	1.396
Lower 95% confidence interval	77.86	73.38	67.01
Upper 95% confidence interval	79.04	78.82	75.89

quantify root resorption of the five roots of the maxillary first molar.

Histological Staining

Subsequently, the samples were decalcified and processed for paraffin embedding. Sagittal sections of 5 to 7 μm in thickness were obtained. Tartrate Resistant Acid Phosphatase (TRAP) staining was performed using a leukocyte acid phosphatase (TRAP) kit (386-1 KT; Sigma-Aldrich, St. Louis, Mo). TRAP-positive, multinucleated cells were counted on the alveolar bone surfaces on the mesial sides of the distobuccal roots. The region of interest for osteoclast quantification on the alveolar bone was identified as a rectangle parallel to the sagittal axis of the distobuccal root of the first molar with 200 μm width and with the length extending from the bifurcation to the apex. The osteoclast numbers were counted in triplicate from four rats in each group, and the values were then averaged for each animal.

Statistical Analysis

Means, standard deviations, percentile distributions, and confidence intervals were computed for root volume and density and osteoclast number. A one-sample Kolmogorov-Smirnov test was used to examine the normality of distribution of the outcomes examined. All of the examined outcomes were distributed normally. The power analysis was based on a previously published study.[11] The number of animals was calculated by G-power software and was determined to be 8 in each group. For this calculation, an α level of 0.05 and β level of 0.8 were selected. Statistical analyses were carried out using Graph Pad Prism version 7 (GraphPad Software Inc., LaJolla, Calif). Statistical significance of differences among means were determined by one-way analysis of variance with a Bonferroni post-hoc test. All statistical tests were two sided, and a P value of <0.05 was deemed to be statistically significant.

RESULTS

All rats in different groups tolerated the appliance well with no net loss in weight.

OTM and Micro-CT Quantification of Root Resorption (Buccal Root of Maxillary First Molar)

The OTM + 4AD had significantly ($P < 0.05$) more orthodontic tooth movement than the OTM + 2AD and OTM-only groups as reported elsewhere.[12] The root volume of the buccal root was calculated individually, and the remaining four roots were calculated together because the alveolar decortication was closer to the buccal root, which was also the leading root with orthodontic force application. Micro-CT quantification of the buccal root volume showed a significant increase of 8.92% ($P < 0.05$) and 6.11% ($P < 0.05$) in root resorption (decrease in root volume) in the OTM + 4AD group when compared with the OTM-only and OTM + 2AD groups (Figure 2, Figure 3, and Table 1), respectively.

Micro-CT Quantification of Root Resorption (Remaining Roots of Maxillary First Molar)

Root volume of the other four roots was calculated to evaluate whether the surgical insult had any effect on the trailing roots. Micro-CT quantification of the volume of the remaining four roots showed a 8.99% ($P < 0.05$) and 5.24% ($P > 0.05$) increase in root resorption (decreased root volume) in the OTM + 4AD group when compared with the OTM-only and OTM + 2AD groups (Figure 3, Figure 4, and Table 2), respectively.

Micro-CT Quantification of Buccal and Other Root Density

Micro-CT quantification of buccal root density showed a decrease of 4.66% in the OTM + 4AD group when compared with the OTM-only group, and a decrease of 3.56% when compared with the OTM +

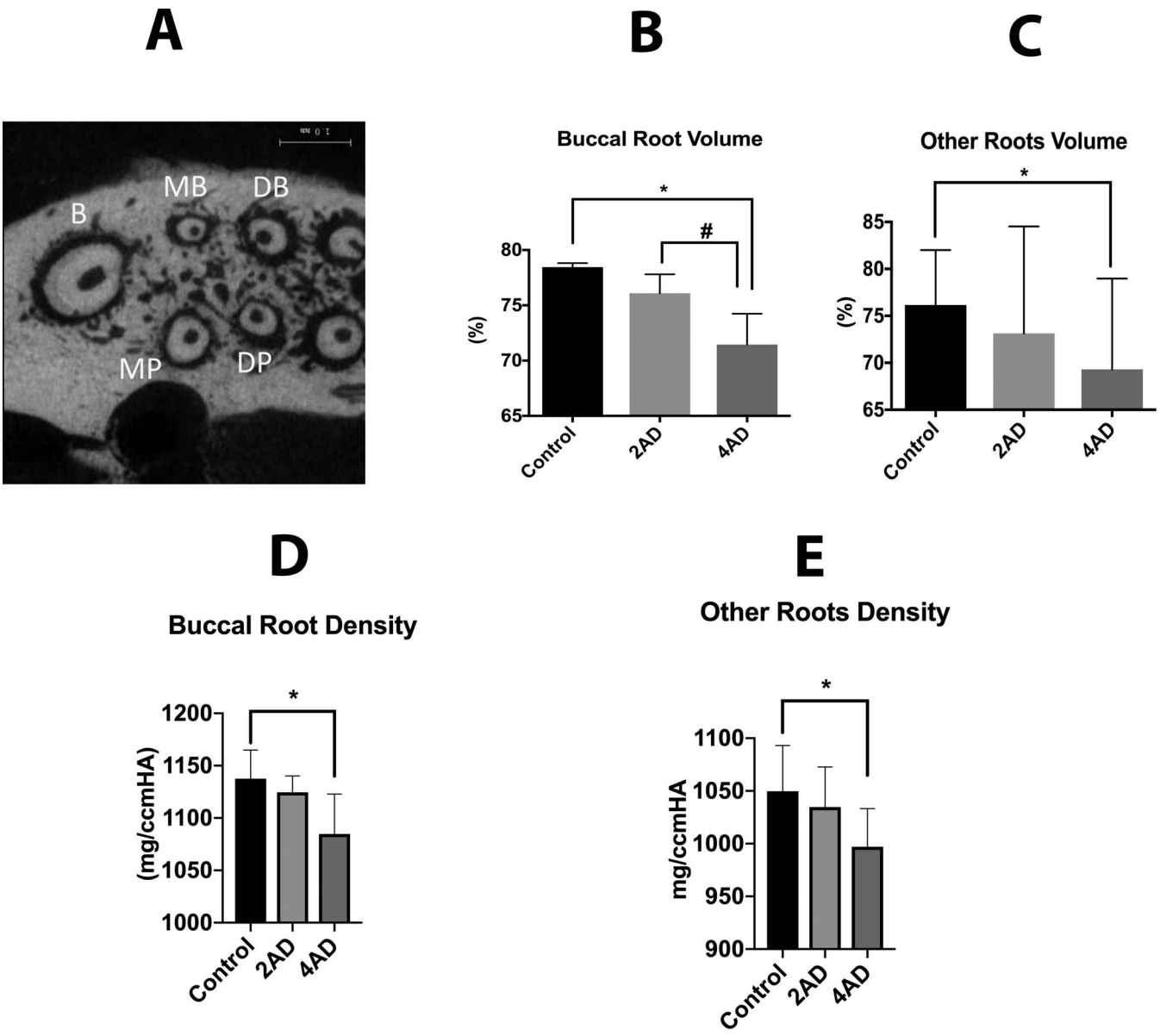

Figure 2. (A) Different root locations on the reconstructed micro computed tomography image; B indicates buccal; MB, mesio-buccal; DB, disto-buccal; MP, mesio-palatal; DP, disto-palatal. (B) Histogram showing a significant decrease ($P < 0.05$) in the buccal root volume in the OTM + 4AD group. (C) Histogram showing a significant decrease ($P < 0.05$) in the other root volume in the OTM + 4AD group. (D) Histogram showing a significant decrease ($P < 0.05$) in the buccal root density in the OTM + 4AD group. (E) Histogram showing a significant decrease ($P < 0.05$) in the other root density in the OTM + 4AD group. 2AD, two alveolar decortications; 4AD, four alveolar decortications; OTM, orthodontic tooth movement.
* $P < 0.05$, # $P < 0.05$.

2AD group (Table 3). The density of the other roots was decreased 5.04% and 3.66% in the OTM + 4AD group when compared with the OTM-only and OTM + 2AD groups, respectively (Table 4).

Histological Quantification of Osteoclast Number

TRAP staining showed an increase of 373.3% ($P < 0.05$) and 98.74% ($P < 0.05$) in the number of osteoclasts in the OTM + 4AD group when compared with the OTM-only and OTM + 2AD groups, respectively (Figure 4 and Table 5).

DISCUSSION

The null hypothesis was rejected, and a significant increase in orthodontically induced root resorption was found with an increasing extent of injury to accelerate orthodontic tooth movement. Previous studies have mostly investigated root resorption as a result of

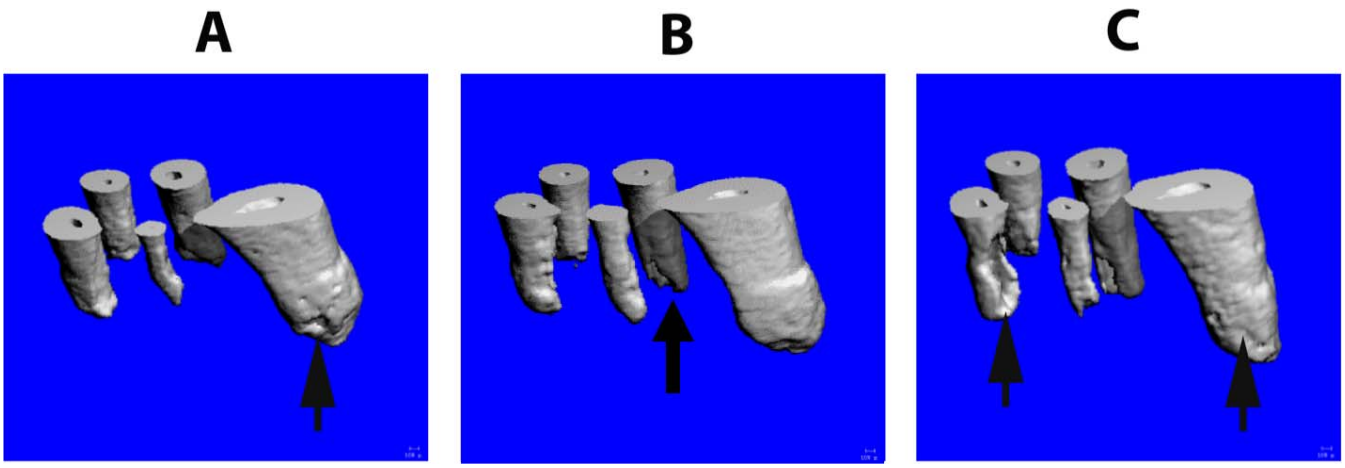

Figure 3. Micro computed tomography reconstructed image of the root resorption in the (A) orthodontic tooth movement for 2 weeks only group, (B) orthodontic tooth movement for 2 weeks + two alveolar decortications group, and (C) orthodontic tooth movement for 2 weeks + four alveolar decortications group. Black arrow denotes root resorption.

surgical insult, but no studies have reported the correlation between the increase of surgical insult and orthodontically induced root resorption.[13–15] The results suggested the amount of orthodontically induced root resorption was directly associated with the extent of injury.

The biological mechanisms behind the surgically facilitated acceleration of tooth movement and its effects on root resorption are multifactorial and not completely understood. It has been shown that the regional acceleratory phenomenon after surgical procecures increased alveolar bone and paradental tissue turnover through increasing the activity of associated cells such as osteoblasts, fibroblasts, cementoblasts, and osteoclasts.[10,11,16,17] Enhanced tissue turnover leads to an osteoporotic and osteopenic environment and a reduction in resistance to tooth movement through alveolar bone.[18,19] Theoretically, reducing the potential for hyalinization development could reduce the amount of root resorption associated with alveolar decortication, but the relationship between alveolar bone density and the root resorption process is still unclear. Although some studies have suggested that increased bone turnover and reduced bone density favored remodeling of the bone over the root surface, but other studies have shown that root resorption increased with increased bone turnover.[15,20,21]

Several cells are involved in the orthodontically induced root resorption, but the main player of this process are mature odontoclasts, cells with morphological and functional features substantially similar to osteoclasts.[22,23] Hematopoietic precursor cells locally derived from the periodontal ligament or from bone marrow are directed to differentiate into odontoclasts/osteoclasts through a complex and coordinated molecular cascade of events, leading ultimately to maturation and clastic activity on alveolar bone and/or dentin.[24] In the current study, it was observed that increased turnover of the alveolar bone (increased osteoclast numbers) led to significantly increased root resorption (decreased root volume) and decreased root density. It was understood that the increase in orthodontically induced root resorption was the result of an increase in multinucleated osteoclasts in the OTM + 4AD group.

Table 2. Distribution of Data for Other Four Root Volume

	Group		
	Orthodontic Tooth Movement	Orthodontic Tooth Movement + Two Alveolar Decortication	Orthodontic Tooth Movement + Four Alveolar Decortication
Minimum	54	47.1	39
25% percentile	75.1	66.4	67.28
Median	77.3	74.35	71.45
75% percentile	78.7	79.6	74.73
Maximum	83	98	78.9
Mean	76.16	73.14	69.31
Standard deviation	5.841	11.39	9.671
Standard error of mean	1.275	2.428	2.062
Lower 95% confidence interval	73.5	68.09	65.02
Upper 95% confidence interval	78.82	78.19	73.6

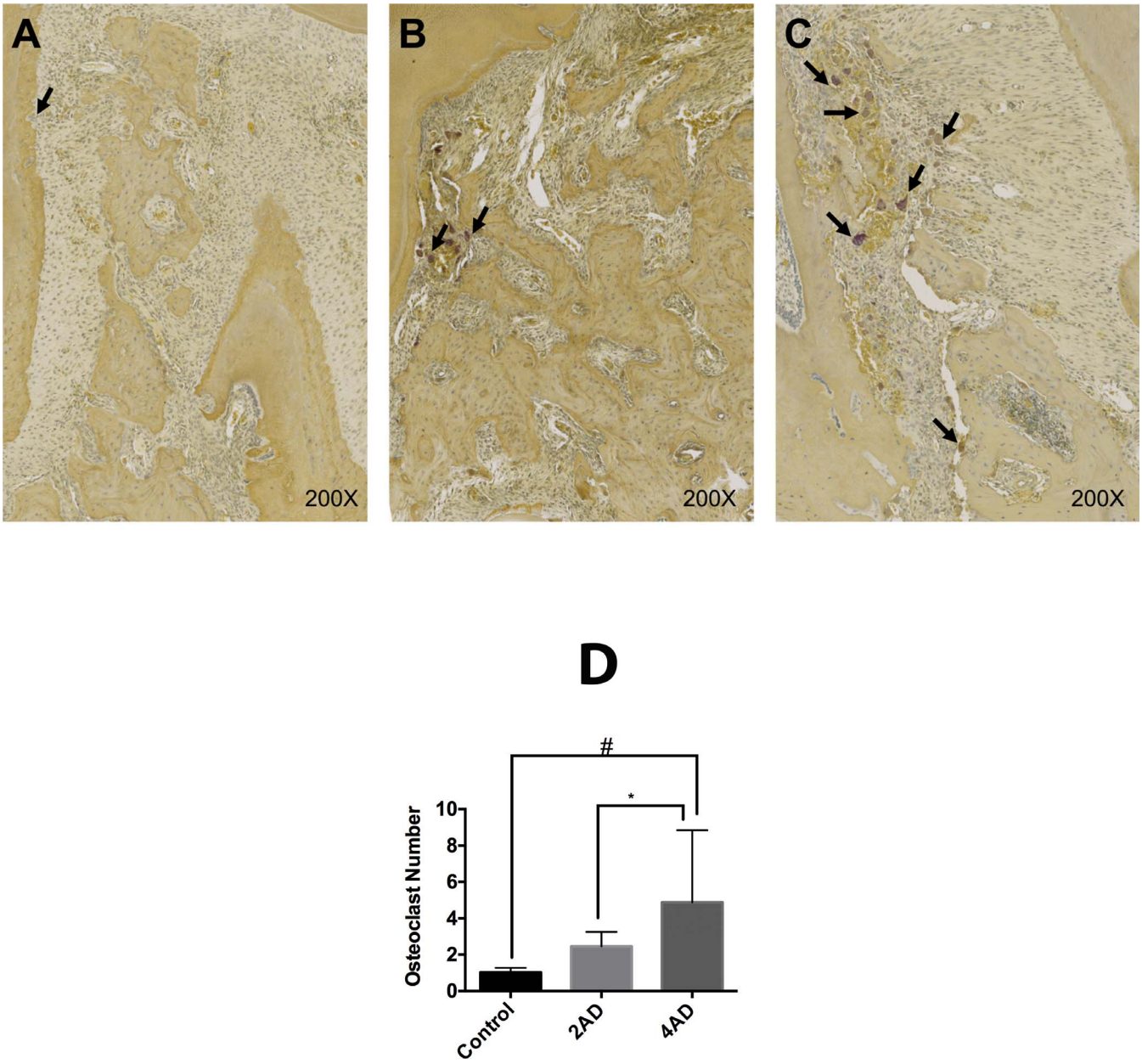

Figure 4. Histological examination and quantification of Tartrate Resistant Acid Phosphatase (TRAP) in the OTM-only, OTM + 2AD, and OTM + 4AD groups. (A) TRAP positive cells in the OTM-only group. (B) TRAP positive cells in the OTM + 2AD group. (C) TRAP positive cells in the OTM + 4AD group. (D) Histogram showing a significant increase ($P < 0.05$) in the TRAP activity in OTM + 4AD group. Black arrow denotes TRAP-positive cells. 2AD, two alveolar decortications; 4AD, four alveolar decortications; OTM, orthodontic tooth movement.
* $P < 0.05$, # $P < 0.05$.

Other studies have also demonstrated an increased osteoclast number after alveolar decortication.[11,19]

Alveolar decortication (surgical insult) might induce a considerable amount of proinflammatory markers around the periodontal tissue, which is beneficial for osteoclastogenesis and the acceleration of tooth movement.[25] However, the inflammatory chain reaction in the alveolar bone may also lead to an exponential resorption of the cementum/dentin of the roots as shown in this study. The root resorption observed in the OTM-only group was the result of external applied load to move the tooth, whereas the root resorption observed in the OTM + 2AD and OTM + 4AD groups was the result of a combination of applied load to move the tooth and alveolar decortication to accelerate the tooth movement. Teixeira et al.[19] demonstrated an increase in cytokines and chemokines after cortical alveolar perforations in rats, and this increase in inflammatory mediators also led to an increase in orthodontically induced root resorption. Similarly, a

Table 3. Distribution of Data for Buccal Root Density

	Group		
	Orthodontic Tooth Movement	Orthodontic Tooth Movement + Two Alveolar Decortication	Orthodontic Tooth Movement + Four Alveolar Decortication
Minimum	78.1	74.2	69.2
25% percentile	78.13	74.55	69.35
Median	78.4	75.95	70.6
75% percentile	78.83	77.8	74.4
Maximum	78.9	78.3	75.4
Mean	78.45	76.1	71.45
Standard deviation	0.3697	1.707	2.792
Standard error of mean	0.1848	0.8534	1.396
Lower 95% confidence interval	1104	1105	1038
Upper 95% confidence interval	1172	1144	1132

Table 4. Distribution of Data for Other Root Density

	Group		
	Orthodontic Tooth Movement	Orthodontic Tooth Movement + Two Alveolar Decortication	Orthodontic Tooth Movement + Four Alveolar Decortication
Minimum	948	967	933
25% percentile	1030	1004	964.5
Median	1067	1034	1007
75% percentile	1075	1073	1025
Maximum	1099	1090	1062
Mean	1050	1035	997.1
Standard deviation	43.24	37.87	36.17
Standard error of mean	10.81	9.468	9.042
Lower 95% confidence interval	1027	1015	977.8
Upper 95% confidence interval	1073	1055	1016

Table 5. Distribution of Data for Osteoclast Number

	Group		
	Orthodontic Tooth Movement	Orthodontic Tooth Movement + Two Alveolar Decortication	Orthodontic Tooth Movement + Four Alveolar Decortication
Minimum	0.9	1.738	0.625
25% percentile	0.9	1.738	0.625
Median	1.7	2.3	5.5
75% percentile	2.32	3.32	8.5
Maximum	2.32	3.32	8.5
Mean	1.64	2.453	4.875
Standard deviation	0.7119	0.802	3.975
Standard error of mean	0.411	0.463	2.295
Lower 95% confidence interval	−0.1285	0.4605	−4.998
Upper 95% confidence interval	3.408	4.445	14.75

short-term clinical trial with osteoperforations showed an increased amount of root resorption craters attributed to the regional acceleratory phenomenon.[10]

There is a lack of long-term studies on root resorption after surgical interventions to accelerate the rate of tooth movement. It is not known whether the sequela of orthodontically induced root resorption enhanced by local surgical procedures would have any potential of self-repair. It has been suggested that removal of active orthodontic treatment usually terminates active root resorption; therefore, a 2- to 3-month pause in treatment is recommended to decrease further root resorption in suspect patients.[26,27] Importantly, patients receiving adjacent surgical procedures during orthodontic treatment usually receive active orthodontic forces for a period of time (no pause in treatment for possible root repair), possibly increasing the risk for significant root resorption depending on the extent of surgical intervention and duration of orthodontic treatment.

One of the limitations of this study was studying only male Wistar rats and evaluating the effects of the extent of surgical insult at only one time point. To determine the mechanism behind increased orthodontically induced root resorption and to investigate root

self-repair, different time point evaluations and observations for longer periods of time will be pursued.

Another limitation of this study was that rats were used, which lack osteonal remodeling present in humans and higher vertebrate animals. Because this was an animal study, extrapolation of the research findings to the clinical scenario must be done with caution. Nevertheless, this study has given information regarding the side effects of surgically facilitated orthodontics.

CONCLUSIONS

- There was a significant increase in orthodontically induced root resorption with the increase in the extent of surgical insult.
- Micro-CT results show a decrease in root volume and root density with the increase in the extent of surgical insult.
- Histological analyses showed that the increase in the number of the osteoclasts corresponded with an increase in the extent of surgical insult.

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REFERENCES

1. Brezniak N, Wasserstein A. Root resorption after orthodontic treatment: part 1. Literature review. *Am J Orthod Dentofacial Orthop*. 1993;103:62–66.
2. Topkara A, Karaman AI, Kau CH. Apical root resorption caused by orthodontic forces: a brief review and a long-term observation. *Eur J Dent*. 2012;6:445–453.
3. Mirabella AD, Artun J. Prevalence and severity of apical root resorption of maxillary anterior teeth in adult orthodontic patients. *Eur J Orthod*. 1995;17:93–99.
4. Linge BO, Linge L. Apical root resorption in upper anterior teeth. *Eur J Orthod*. 1983;5:173–183.
5. Segal GR, Schiffman PH, Tuncay OC. Meta analysis of the treatment-related factors of external apical root resorption. *Orthod Craniofac Res*. 2004;7:71–78.
6. Hoogeveen EJ, Jansma J, Ren Y. Surgically facilitated orthodontic treatment: a systematic review. *Am J Orthod Dentofacial Orthop*. 2014;145:S51–S64.
7. Aboul-Ela SM, El-Beialy AR, El-Sayed KM, Selim EM, El-Mangoury NH, Mostafa YA. Miniscrew implant-supported maxillary canine retraction with and without corticotomy-facilitated orthodontics. *Am J Orthod Dentofacial Orthop*. 2011;139:252–259.
8. Yi J, Xiao J, Li Y, Li X, Zhao Z. Efficacy of piezocision on accelerating orthodontic tooth movement: a systematic review. *Angle Orthod*. 2017;87:491–498.
9. Kharkar VR, Kotrashetti SM, Kulkarni P. Comparative evaluation of dento-alveolar distraction and periodontal distraction assisted rapid retraction of the maxillary canine: a pilot study. *Int J Oral Maxillofac Surg*. 2010;39:1074–1079.
10. Chan E, Dalci O, Petocz P, Papadopoulou AK, Darendeliler MA. Physical properties of root cementum: part 26. Effects of micro-osteoperforations on orthodontic root resorption: a microcomputed tomography study. *Am J Orthod Dentofacial Orthop*. 2018;153:204–213.
11. Dutra EH, Ahmida A, Lima A, Schneider S, Nanda R, Yadav S. The effects of alveolar decortications on orthodontic tooth movement and bone remodelling in rats. *Eur J Orthod*. 2018; 40:423–429.
12. Chang J, Chen PJ, Dutra EH, Nanda R,Yadav S. The effect of the extent of surgical insult on orthodontic tooth movement. *Eur J Orthod*. 2019;41:601–608.
13. Murphy C, Kalajzic Z, Chandhoke T, Utreja A, Nanda R, Uribe. The effect of corticision on root resorption with heavy and light forces. *Angle Orthod*. 2016;86:17–23.
14. Peron AP, Johann AC, Papalexiou V, Tanaka OM, Guariza-Filho O, Ignacio SA, Camargo ES. Tissue responses resulting from tooth movement surgically assisted by corticotomy and corticision in rats. *Angle Orthod*. 2017;87: 118–124.
15. Cheung T, Park J, Lee D, Kim C, Olson J, Javadi S, Lawson G, Moon W, Ting K, Hong C. Ability of mini-implant-facilitated micro-osteoperforations to accelerate tooth movement in rats. *Am J Orthod Dentofacial Orthop*. 2016;150:958–967.
16. Frost HM. The biology of fracture healing. An overview for clinicians. Part I. *Clin Orthop Relat Res.* 1989;248:283–293.
17. Frost HM. The biology of fracture healing. An overview for clinicians. Part II. *Clin Orthop Relat Res.* 1989;248:294–309.
18. Killiany DM. Root resorption caused by orthodontic treatment: an evidence-based review of literature. *Semin Orthod*. 1999;5:128–133.
19. Teixeira CC, Khoo E, Tran J, Chartres I, Liu Y, Thant LM, Khabensky I, Gart LP, Cisnero G, Alikhani M. Cytokine expression and accelerated tooth movement. *J Dent Res*. 2010;89:1135–1141.
20. Verna C, Dalstra M, Melsen B. Bone turnover rate in rats does not influence root resorption induced by orthodontic treatment. *Eur J Orthod*. 2003;25:359–363.
21. Acar A, Canyurek U, Kocaaga M, Erverdi N. Continuous vs. discontinuous force application and root resorption. *Angle Orthod*. 1999;69:159–163; discussion 163–154.
22. Wang Z, McCauley LK. Osteoclasts and odontoclasts: signaling pathways to development and disease. *Oral Dis*. 2011;17:129–142.
23. Sasaki T. Differentiation and functions of osteoclasts and odontoclasts in mineralized tissue resorption. *Microsc Res Tech*. 2003;61:483–495.
24. Iglesias-Linares A, Hartsfield JK Jr. Cellular and molecular pathways leading to external root resorption. *J Dent Res*. 2017;96:145–152.
25. Baloul SS. Osteoclastogenesis and osteogenesis during tooth movement. *Front Oral Biol*. 2016;18:75–79.
26. Weltman B, Vig KW, Fields HW, Shanker S, Kaizar EE. Root resorption associated with orthodontic tooth movement: a systematic review. *Am J Orthod Dentofacial Orthop*. 2010; 137:462–476; discussion 412A.
27. Remington DN, Joondeph DR, Artun J, Riedel RA, Chapko MK. Long-term evaluation of root resorption occurring during orthodontic treatment. *Am J Orthod Dentofacial Orthop*. 1989;96:43–46.