

Labial and palatal alveolar bone changes during maxillary incisor retraction at the Universitas Sumatera Utara Dental Hospital

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ABSTRACT

Background: The fundamental concept of tooth movement during orthodontic treatment is the occurrence of bone remodelling accompanied by tooth movement in equal proportions. The thickness of the alveolar bone, which supports incisors, is important in estimating the direction of tooth movement. **Purpose:** The study aimed to measure labial and palatal alveolar bone thickness changes after maxillary incisor retraction using lateral cephalograms. **Methods:** Cephalograms of 40 patients (18.58 ± 4.2 years) with skeletal Class I bimaxillary protrusion after maxillary first premolar extraction for incisor retraction had been taken before (T0) and after (T1) orthodontic treatment. Changes in alveolar bone thickness were measured in linear and angular directions and then analysed with Spearman correlative analysis. Then the samples were separated into two groups based on the type of tooth movement (tipping and torque), and then the data were analysed using Wilcoxon analysis to see differences in the bone thickness ($p < 0.05$). **Results:** There was a significant difference in the apical palate ($p < 0.05$) and a relationship between retraction and alveolar bone thickness in the mid-root area. In the angular direction, there was no significant difference and relationship; however, there was a significant difference in the labial crestal in the tipping group. In the torque group, the difference in bone thickness occurred in the crestal and apical palatal areas. **Conclusion:** The retraction and the type of tooth movement difference influence the alveolar bone thickness.

Keywords: alveolar bone thickness; retraction; tipping; torque

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INTRODUCTION

The reaction of periodontal tissue to orthodontic tooth movement is influenced by several factors: bone thickness, root height and morphology, bone dimensions, tooth angulation, and tooth position. Orthodontic treatment not only produces an esthetic facial and dental profile but also carries the risk of complications in the periodontal. The incisors may move labio-lingually/palatally due to compensatory or decompensated dental forces during orthodontic treatment. The thickness of the alveolar bone which supports the incisors is an important consideration in estimating the direction of tooth movement.^{1–3}

Several previous studies stated alveolar bone loss was more common in extraction cases.^{3–9} Sarikaya et al.² investigated changes in alveolar bone thickness in retracted anterior teeth. On the labial side, there was no significant change in bone thickness, while on the palatal side, there

was a reduction in bone thickness at the boundary between the CEJ to the middle of the tooth root.²

Yodthong et al.³ investigated the factors influencing alveolar bone thickness in the maxillary incisor retraction. After retraction, the thickness of the labial and apical bones showed a critical increment of remodelling. The massive contrast in the tipping group was in the crestal labial and apical palatal; the torque group obtained the same results. The outcomes confirmed the thickness of the alveolar in the incisors during retraction could be influenced by various tipping and torque movement of the teeth and the intrusion or extrusion of the teeth.³

Nayak et al.⁹ investigated the thickness of the alveolar bone during anterior tooth retraction with premolar extraction for the presence of dehiscence and fenestration. There was no significant remodelling in the maxillary incisor labial area, while significant changes in the palatal area occurred in the crestal and apical regions.⁹

Several methods are used to detect bone thickness. Using three-dimensional CT is more accurate in measuring levels of bone thickness. However, two-dimensional radiography is more practical and is most often used in daily practice with lower radiation levels despite some drawbacks such as superimposition or distortion.^{10,11} The objectives of this research were: 1. to assess changes of alveolar bone in linear and angular direction after maxillary incisors retraction; 2. to determine the correlation between alveolar bone thickness and the average of retraction on maxillary incisors; 3. to determine the differences in changes of bone thickness based on the type of tooth movement after the retraction of maxillary incisors.

MATERIAL AND METHODS

This cross-sectional review was supported by the ethical committee of Universitas Sumatera Utara number 10/KEP/USU/2022. Lateral cephalograms were obtained from the patient's records in the Orthodontics Department, Faculty of Dentistry, Universitas Sumatera Utara, Medan, Indonesia.

The 40 subjects (21 females and 19 males) were selected based on the inclusion criteria. Subjects aged ≥ 18 -40 years with skeletal Class I bimaxillary protrusion ($ANB = 2^\circ \pm 2$; mean age = 18.58 ± 4.2 years; treatment period = 28.81 ± 5.77 months; $ANB = 2.23 \pm 1.03^\circ$), medical records, and cephalograms before and after treatment were complete. Excluded patients included those with a crowding discrepancy over 3 mm, those under the influence of non-steroidal, anti-inflammatory and metabolic drugs before or during orthodontic treatment, and those with periodontal or gingival disease. After the extraction of two maxillary premolars, patients were treated with the edgewise technique using closed helical loops for anterior retraction. Cephalogram measurements

were performed on three labial and palatal areas. 'A single examiner re-examined cephalogram measurements at four weeks.

Image data of lateral cephalograms were taken at the pretreatment (T_0), and posttreatment (T_1) were imported into ImageJ Software 1.52a (2018) for analysis (Figure 1). The measurement variables used in this study were adjusted from a previous review.^{3,5} First, the amount of incisor retraction pre-and posttreatment was calculated by the distance tip of the central maxillary incisor (U1) to the N-perpendicular line (mm) of the Frankfurt horizontal plane (Figure 2). Second, the linear measurements were taken on the crestal (3 mm), mid-root (6 mm), and apical (9 mm) from CEJ to apex labial and palatal maxillary incisor. They were categorised as labial pretreatment (L1a, L2a, L3a), labial posttreatment (L1b, L2b, L3b), palatal pretreatment (P1a, P2a, P3a), and palatal posttreatment (P1b, P2b, P3b). For accuracy, the distance was measured using ImageJ software by triple magnification (Figure 3). Third, the angular measurements used the point between a. U1- the superficial labial line of maxillary central incisor and alveolar bone; b. U1- the palatal superficial line of maxillary central incisor and alveolar bone (Figure 4).

A paired hypothesis test formula separated the samples into two groups (tipping and torque), including the 20 samples in each group. Referring to the previous study,³ in the tipping group, the apex of the maxillary incisor moved anteriorly. In contrast, in the torque group, the apex of the maxillary incisor moved posteriorly in a superimposed pre-and posttreatment position.

The data will be analysed using the Shapiro Wilk test to see its normality. The Wilcoxon test used comparative analysis to examine differences in bone thickness pre-and post-treatment. Spearman's correlative analysis was used to investigate the relationship of the alveolar bone remodelling with other related variables. Statistical analysis was conducted using SPSS Version 26 (IBM, USA).

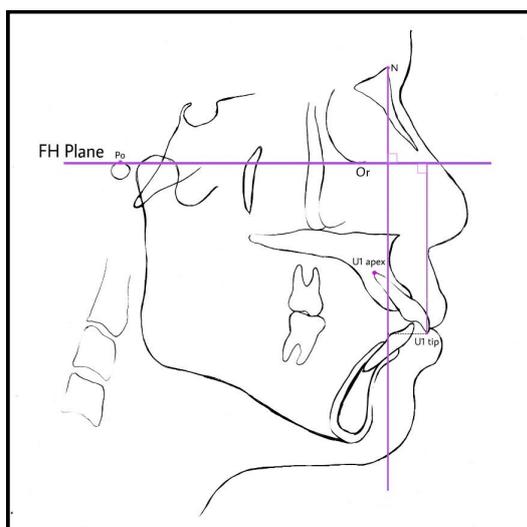


Figure 1. Landmarks of reference lines point to a measured amount of retraction.

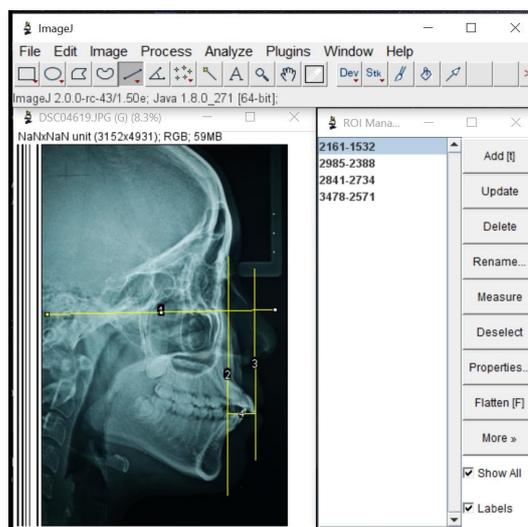


Figure 2. Lateral cephalogram analysed with ImageJ software.

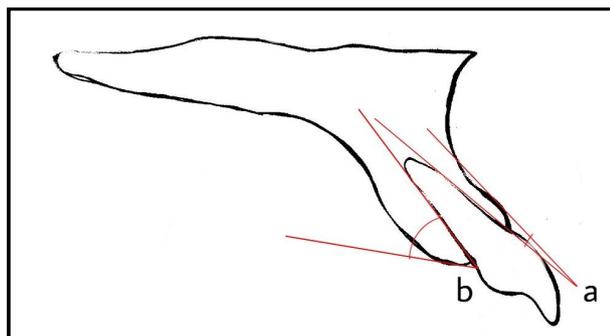


Figure 4. The angle between a) U1 (maxillary central incisor) – superficial labial line of maxillary central incisor and alveolar bone; b. U1 – palatal superficial line of maxillary central incisor and alveolar bone.

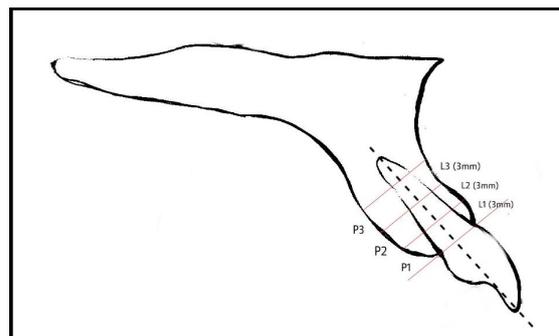


Figure 3. Measurement of alveolar bone thickness at 3 mm intervals from the cemento-enamel junction.

Table 1. Comparative analysis of labial and palatal alveolar bone in a linear direction (mm) pre-and post-treatment (paired t-test)

Variable	Pretreatment T ₀ (N=40) mean±SD		Posttreatment T ₁ (N=40) mean±SD		Mean change (δ)	p	
L1	L1a	1.352 ± 0.392	L1b	1.477 ± 0.459	δL1	0.125 ± 0.070	0.591
L2	L2a	1.283 ± 0.436	L2b	1.327 ± 0.555	δL2	0.044 ± 0.119	0.681
L3	L3a	1.506 ± 0.646	L3b	1.477 ± 0.885	δL3	-0.029 ± 0.239	0.681
P1	P1a	2.572 ± 0.864	P1b	2.492 ± 0.665	δP1	-0.008 ± 0.199	0.621
P2	P2a	3.446 ± 1.012	P2b	3.578 ± 0.934	δP2	0.123 ± 0.078	0.480
P3	P3a	4.434 ± 1.145	P3b	4.963 ± 1.391	δP3	0.529 ± 0.246	0.032*

*Wilcoxon; p<0.05; (-) in terms of reduced alveolar bone

Table 2. Comparative analysis of labial and palatal alveolar bone in angular direction (mm) pre-and post-treatment (paired t-test)

Variable	Pretreatment T ₀ (N=40) mean±SD		Posttreatment T ₁ (N=40) mean±SD		Mean change (δ)	p	
Lab (°)	θLa	9.304 ± 3.882	θLb	11.362 ± 6.118	δθL	2.058 ± 2.336	0.081
Pal (°)	θPa	28.939 ± 7.606	θPb	28.563 ± 3.901	δθP	4.806 ± 0.253	0.882

*Wilcoxon; p<0.05

Table 3. Correlation analysis of the changes in maxillary alveolar bone and average retraction

Variable	N	Average of retraction (mm)	
		r	p
L1	40	0.222	0.168
L2		0.394	0.012*
L3		0.284	0.075
Labial (°)		0.044	0.786
P1		0.167	0.303
P2		-0.050	0.761
P3		-0.153	0.345
Palatal (°)		-0.213	0.188

*Spearman; p<0.05

Table 4. Comparative analysis of the changes in maxillary alveolar bone in a linear direction (mm) pre-and post-treatment (paired t-test)

Variable	Tiping (N = 20) (δ) mean ±SD	p	Torque (N = 20) (δ) mean ±SD	p
L1	0.082 ± 0.521	0.023*	0.021 ± 0.535	0.717
L2	-0.469 ± 0.566	0.715	-0.042 ± 0.799	0.984
L3	-0.281 ± 0.996	0.235	1.500 ± 0.506	0.194
P1	-0.461 ± 1.031	0.600	-0.295 ± 0.950	0.021*
P2	0.103 ± 1.163	0.696	0.367 ± 1.157	0.208
P3	0.545 ± 1.510	0.123	0.512 ± 1.527	0.045*

*Wilcoxon; p<0.05; (-) in terms of reduced alveolar bone

RESULTS

The average retraction pre-and post-treatment was 4.806 ± 0.253 mm. Table 1 showed statistically significant differences in alveolar bone thickness in a linear direction at the P3 position pre-and post-treatment. The lowest mean labial alveolar bone thickness was found at L2a (1.283 ± 0.436 mm) and P1b palate (2.492 ± 0.665 mm), while the highest mean labial and palatal alveolar bone thickness were found at L3a (1.506 ± 0.646 mm) and P3b (4.956 ± 1.391 mm). The changes in the thickness of the labial and palatal alveolar bones in a linear direction were lowest at positions L3 (0.029 ± 0.246 mm) and P1 (0.008 ± 0.199 mm), while the greatest thickness changes were found at positions L1 (0.125 ± 0.070 mm) and P3 (0.529 mm). ± 0.246 mm). Table 2 shows the differences in the thickness of the labial and palatal alveolar bones in the angular direction. There was no significant difference in the retraction of maxillary incisors teeth pre-and post-treatment on the thickness of the labial and palatal alveolar bone in the angular direction. The average increase in the alveolar bone's thickness occurred in the labial area at 2.058 ± 2.336 , while the decrease in the alveolar bone's thickness occurred on the palate, which was 4.806 ± 0.253 .

Table 3 shows a correlation between the thickness of the alveolar bone in a linear direction at the L2 position. However, no correlation was found between the alveolar bone's thickness and the magnitude of retraction in an angular direction. Table 4 shows the results of statistical calculations in the tipping and torque group. There was a reduction in alveolar bone thickness, the lowest was at L3 (-0.281 ± 0.996 mm), and the highest was at L2 (-0.469 ± 0.566 mm). The highest increase in bone thickness was at the P3 level (0.545 ± 1.510 mm) and the lowest at L1 (0.082 ± 0.521 mm), while a significant difference in mean bone thickness was found at L1 (crestal) ($p < 0.05$) in the tipping group. As a result of changes in bone thickness in the torque group, there was a decrease in the average bone thickness with the lowest L2 (-0.042 ± 0.799 mm) and the highest result in the P1 area (-0.295 ± 0.950 mm), the lowest increase in bone thickness was at L1 (0.021 ± 0.535 mm), and the highest was at L3 (1.500 ± 0.506 mm) and a significant difference in P1 (crestal) and P3 (apical) bone thickness pre-and post-treatment ($p < 0.05$).

DISCUSSION

The occurrence of bone resorption on the stress side and bone apposition on the strain side is a process in tooth movement during orthodontic treatment. Tooth movement is directly proportional to bone remodelling, but in some studies, this has not been proven, especially in the retraction of anterior maxillary teeth. Many studies show the factors affecting the thickness of alveolar bone, especially those related to anterior tooth retraction.³⁻⁹ Previous studies have generally described the thickness of

the alveolar bone with varying results.^{2-6,11-17} However, none of the earlier studies used a sample of a skeletal Class I malocclusion and a comparison based on the type of tooth movement tipping and torque – if any. Previous studies used different techniques and mechanics from this research and generally used a skeletal Class II sample, which requires a larger number of retractions.^{2-6,11,14,18,19} In addition, the mechanics of retraction using closing loops in the edgewise technique is still common and is often used for incisor retraction cases. As we have seen, the type of retraction mechanics and the treatment technique can also affect the thickness of the alveolar bone. This study can also increase clinician awareness of the direction of anterior retraction to reduce the risk of fenestration or dehiscence in the alveolar bone.^{16,20,21}

Tables 1 and 2 show the difference and mean alveolar bone thickness of the maxillary labial and palatal incisors in linear and angular directions pre-and post-treatment. The maxillary incisor labial alveolar bone thickness increased in the crestal and mid-root areas after anterior retraction, while the apical labial bone thickness decreased. The maxillary mid-root and apical palatal alveolar bone thickness increased after anterior retraction, while the palatal crestal thickness decreased. The tables shows the results of statistical tests with a significant difference ($p < 0.05$) at the apical palatal level (9 mm from the CEJ), namely a decrease in bone thickness of 0.5 mm in the apical palatal area, while bone thickness in the angular direction in labial and palatal before and after treatment (θ , $P < 0.05$) were not significantly different. This study's results agree with Sarikaya et al.², who investigated linear changes in alveolar bone thickness in the maxillary incisors' crestal, mid-root, and apical regions. This study was conducted on 19 patient cases of premolar extraction in bimaxillary protrusion. After canine distalisation and continued incisor retraction for three months, the bone thickness significantly decreased in the mid-root area, and the bone thickness reduction was also greater in the apical palatal region (9 mm from the CEJ).²

The results of this study differ from Aakash et al.¹⁶, who investigated the effect of retraction on changes in alveolar bone thickness with sliding mechanics using a mini-implant in the case of bimaxillary protrusion. The number of retractions before and after treatment was measured in 15 samples, and the results showed a significant increase in alveolar bone thickness ($p > 0.05$) in the maxilla's crestal and apical labial areas. Alveolar bone thickness changes are significantly affected by retraction.¹⁶

The decrease in bone thickness in the palatal crestal area in this study did not occur in Nayak et al.⁹, which studied ten samples with bimaxillary protrusion cases. After three months of retraction using sliding mechanics, there was a decrease in bone thickness in the labial crestal area, which was due to the concentrated force on the alveolar crest.⁹

A study on changes in palatal bone thickness linearly and angularly with different results was conducted by Son et al.⁵. The study included 33 samples with sliding mechanics

using mini implants. Linear measurement of palatal alveolar bone thickness was performed at a distance of 2,4,8,10 mm from the CEJ boundary, showing a significant reduction in bone thickness in the entire palatal area of the central incisor ($p < 0.001$), except at a distance of 10 mm from the CEJ (apical). The labial side showed a significant difference from the palatal area in the angular direction, which showed a close relationship to the inclination of the tooth after retraction. Differences in alveolar bone thickness pre-and post-treatment were also significantly correlated with maxillary incisor retraction. Changes in bone thickness in the crestal region indicated excessive resorption in the cervical region of the teeth, but a significant ratio to the number of retractions in this study was not found.⁵

Different results in the study by Mao et al.¹⁴ showed a significant increase in the thickness of the labial alveolar bone ($p < 0.05$) in the mid-root area. Whereas in the palate, it occurred in the crestal area. The results of this study explain excessive incisor retraction can increase the thickness of the alveolar bone in the crestal and mid-root sections. Alveolar bone thickness can be maintained if the tooth movement is not too fast, and the force is not excessive. The labial area has a resorption rate which tends to be lower than the palatal area, so the tendency for bone prominence in the labial area can occur more easily.¹⁴

Table 4 shows a significant correlation between changes in bone thickness and the number of retractions in the mid-root area ($L2 r = 0.394$, $p = 0.012$). This result differs from the study by Yodthong et al.³ and Aakash et al.⁹, which showed a significant relationship in the crestal area. The difference in the results of this study may be due to the varying magnitude of the incisor retraction force. Differences in treatment mechanics, changes in inclination, and intrusion size are also the cause of the incompatibility of bone remodelling and retraction processes.^{3,16}

Changes in alveolar bone thickness in the apical region were associated with changes in the inclination and intrusion of the incisors. The inclination position of the anterior teeth plays a vital role in the function and stability of the treatment. Based on several previous studies, orthodontic treatment with extraction has the effect of root resorption, and bone loss is greater than the case without extraction.³

Significant changes in bone thickness were found in the labial crestal area of the tipping group after treatment (Table 4) ($L1 p = 0.023$; $p < 0.05$), while in the torque group, the alveolar bone thickness in the crestal area was not significantly different. Significant differences in bone thickness in the torque group occurred in the mid-root and apical palatal regions (Table 4) ($P1 = 0.021$ and $P3 = 0.045$; $p < 0.05$). These results may be due to differences in the type of movement, the direction of angulation, and the magnitude of the retraction force applied to the alveolar bone.³

Alveolar bone loss visible in this study was in the apical labial and palatal crest regions. This bone loss could be due to changes in the angulation of tooth movement. The

retraction force applied to the incisors concentrates more on the alveolar crest, increasing the cervical region's force. The significant decrease in bone thickness was due to the periodontal tissues' reaction centred in the anterior teeth' cervical area. Periodontal tissue reaction is also a factor causing variations in bone reaction to orthodontic forces. It depends on the width, height and morphology of the roots, angulation, and position of the teeth, dimensions of the teeth to the alveolar bone, bone anatomy, physiology and adaptability of the patient. The average decrease in bone thickness in the labial aspect in this study was statistically higher than in the palatal aspect. It could be due to a slower bone deposition process in the strain area compared to the stress area's resorption process. The results of this study are from research by Sarikaya et al.² and Ahn et al.²²

This study concluded a significant difference in the apical palate ($p < 0.05$) and a relationship between retraction and alveolar bone thickness in the mid-root area, while in the angular direction, there was no significant difference and relationship. There was a significant difference in bone thickness in the labial crestal on tipping. In the torque group, the difference in bone thickness occurred in the crestal and apical palatal areas. The retraction and the type of tooth movement influence the difference in the thickness of the alveolar bone. Increased awareness of the direction of anterior retraction in the tipping type of tooth movement can reduce the risk of fenestration and dehiscence of the root tip in a labial direction. In contrast, the type of torque movement must be aware of the direction of movement of 2/3 of the tooth root against the palatal cortical plate for treatment stability.

REFERENCES

1. Lin JC-Y, Yeh C-L, Liou EJ-W, Bowman SJ. Treatment of skeletal-origin gummy smiles with miniscrew anchorage. *J Clin Orthod.* 2008; 42(5): 285–96.
2. Sarikaya S, Haydar B, Çiğler S, Ariyürek M. Changes in alveolar bone thickness due to retraction of anterior teeth. *Am J Orthod Dentofacial Orthop.* 2002; 122(1): 15–26.
3. Yodthong N, Charoemratrote C, Leethanakul C. Factors related to alveolar bone thickness during upper incisor retraction. *Angle Orthod.* 2013; 83(3): 394–401.
4. Tian Y-L, Liu F, Sun H-J, Lv P, Cao Y-M, Yu M, Yue Y. Alveolar bone thickness around maxillary central incisors of different inclination assessed with cone-beam computed tomography. *Korean J Orthod.* 2015; 45(5): 245–52.
5. Son EJ, Kim SJ, Hong C, Chan V, Sim HY, Ji S, Hong SY, Baik U-B, Shin JW, Kim YH, Chae HS. A study on the morphologic change of palatal alveolar bone shape after intrusion and retraction of maxillary incisors. *Sci Rep.* 2020; 10(1): 14454.
6. Zhang F, Lee S-C, Lee J-B, Lee K-M. Geometric analysis of alveolar bone around the incisors after anterior retraction following premolar extraction. *Angle Orthod.* 2020; 90(2): 173–80.
7. Domingo-Clérigues M, Montiel-Company J-M, Almerich-Silla J-M, García-Sanz V, Paredes-Gallardo V, Bellot-Arcís C. Changes in the alveolar bone thickness of maxillary incisors after orthodontic treatment involving extractions - A systematic review and meta-analysis. *J Clin Exp Dent.* 2019; 11(1): e76–84.
8. Morais JF, Melsen B, de Freitas KMS, Castello Branco N, Garib DG, Cattaneo PM. Evaluation of maxillary buccal alveolar bone before

- and after orthodontic alignment without extractions: A cone beam computed tomographic study. *Angle Orthod.* 2018; 88(6): 748–56.
9. Nayak Krishna US, Shetty A, Girija MP, Nayak R. Changes in alveolar bone thickness due to retraction of anterior teeth during orthodontic treatment: a cephalometric and computed tomography comparative study. *Indian J Dent Res.* 2013; 24(6): 736–41.
 10. Helal NM, Basri OA, Baeshen HA. Significance of cephalometric radiograph in orthodontic treatment plan decision. *J Contemp Dent Pract.* 2019; 20(7): 789–93.
 11. Picanço PRB, Valarelli FP, Cançado RH, de Freitas KMS, Picanço GV. Comparison of the changes of alveolar bone thickness in maxillary incisor area in extraction and non-extraction cases: computerized tomography evaluation. *Dental Press J Orthod.* 2013; 18(5): 91–8.
 12. Wei D, Zhang L, Li W, Jia Y. Quantitative comparison of cephalogram and cone-beam computed tomography in the evaluation of alveolar bone thickness of maxillary incisors. *Turkish J Orthod.* 2020; 33(2): 85–91.
 13. Pudyani PS, Sutantyo D, Suparwitri S. Morphological changes of alveolar bone due to orthodontic movement of maxillary and mandibular incisors. *Dent J (Majalah Kedokt Gigi).* 2008; 41(1): 21.
 14. Mao H, Yang A, Pan Y, Li H, Lei L. Displacement in root apex and changes in incisor inclination affect alveolar bone remodeling in adult bimaxillary protrusion patients: a retrospective study. *Head Face Med.* 2020; 16(1): 29.
 15. Hong SY, Shin JW, Hong C, Chan V, Baik U-B, Kim YH, Chae HS. Alveolar bone remodeling during maxillary incisor intrusion and retraction. *Prog Orthod.* 2019; 20(1): 47.
 16. Aakash S, Purvesh S, Kumar GS, Romina K, Romil S, Bhumi M. Changes in alveolar bone thickness during upper incisor retraction. *Rev Latinoam Ortod y Odontopediatría.* 2017; : 19.
 17. Chen SSH, Greenlee GM, Kim JE, Smith CL, Huang GJ. Systematic review of self-ligating brackets. *Am J Orthod Dentofac Orthop.* 2010; 137(6): 726.e1-726.e18.
 18. Oliveira TMF, Claudino LV, Mattos CT, Sant'Anna EF. Maxillary dentoalveolar assessment following retraction of maxillary incisors: a preliminary study. *Dental Press J Orthod.* 2016; 21(5): 82–9.
 19. Thongudomporn U, Charoemratrote C, Jearapongpakorn S. Changes of anterior maxillary alveolar bone thickness following incisor proclination and extrusion. *Angle Orthod.* 2015; 85(4): 549–54.
 20. Masumoto T, Hayashi I, Kawamura A, Tanaka K, Kasai K. Relationships among facial type, buccolingual molar inclination, and cortical bone thickness of the mandible. *Eur J Orthod.* 2001; 23(1): 15–23.
 21. Al-Nimri KS, Hazza'a AM, Al-Omari RM. Maxillary incisor proclination effect on the position of point A in Class II division 2 malocclusion. *Angle Orthod.* 2009; 79(5): 880–4.
 22. Ahn HW, Moon SC, Baek SH. Morphometric evaluation of changes in the alveolar bone and roots of the maxillary anterior teeth before and after en masse retraction using cone-beam computed tomography. *Angle Orthod.* 2013; 83(2): 212–21.