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Regenerative Therapy of Osseous Defects Combined with Orthodontic Tooth Movement

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Abstract

Background: Combined orthodontic/regenerative therapy can resolve complex clinical problems and enhance bone formation. The purpose of this study was to evaluate the effectiveness of different times of initiating the active orthodontic tooth movement on the regenerative potential of the intrabony defects. **Methods:** Fifteen adult patients with at least three intrabony defects and malocclusion were included. A total of 45 defects were divided into three groups and treated in a split mouth design. The defects were treated with combined orthodontic regenerative therapy with immediate application of orthodontic tooth movement or delayed application of orthodontic tooth movement (test groups) or with regenerative therapy alone (control group). The following hard and soft tissue measurements were recorded prior to initial surgery and after six months and one year: probing depth (DP), clinical attachment level (CAL), bone density (BD) and bone fill (BF). **Results:** The most significant results were greater for the group treated with combined orthodontic/regenerative therapy with immediate orthodontic tooth movement. The measures for PD reduction and clinical attachment level gain were 4 ± 0.8 and 5.1 ± 1.4 mm respectively for immediate application of orthodontic tooth movement, and 3.7 ± 0.9 and 4.3 ± 0.6 mm with delayed application of orthodontic movement two months later. Moreover, immediate orthodontic tooth movement showed the most significant increase in bone density and bone fill, which reached 74.2 ± 14.2 and 3.7 ± 1.1 mm respectively at the end of the study period. **Conclusion:** This study evaluated the effect of orthodontic tooth movement on enhancement of periodontal regenerative outcomes. The results demonstrated that a significant improvement in clinical and radiographic parameters was observed. When comparing the different groups, a statistically significant difference was found with immediate application of orthodontic tooth movement.

Key words: Combined orthodontic regenerative therapy, bone grafts, alloplasts, membranes, bioabsorbable, periodontal regeneration, intrabony defects, follow-up studies

Introduction

Periodontitis is an inflammatory disease affecting the composition and integrity of periodontal structures, causing the destruction of connective tissue matrix and cells, the loss of fibrous attachment and the resorption of alveolar bone (American Academy of Periodontology, 1986; Grenstein and Lamster, 1997; Papapanou *et al*., 1997; Caffesse *et al*., 2002). The objective of periodontal therapy continues to be preservation of the dentition, maintaining health and comfort during the patient's lifetime. In addition, periodontal therapy includes not only the arrest of progressive periodontal disease, but also the restitution of those parts of the supporting apparatus that have been destroyed by disease (Allen, 1988; Cortellini and Bowers, 1995; Laurell *et al*., 1998).

Many events required for regeneration of periodontal tissues are similar to those required for formation of periodontal tissues. For example, in both situations, while not necessarily in this order, appropriate cells must be attracted to and attach at the site. An appropriate matrix must be secreted by cells in order to provide an environment conductive to cell proliferation and differentiation, resulting in cells having the capacity to function as periodontal ligament fibroblasts, cementoblasts or osteoblasts (Macneil and Cobb, 1999).

The boundaries of orthodontic tooth movement

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have broadened to include treatment of patients of all ages. Adult patients now represent a significant percentage of the population in almost every orthodontic practice. The treatment of those patients often raises some difficult issues (Basadra *et al.*, 1995). Many adult orthodontic patients have underlying periodontal defects that need to be resolved (Kokich, 2002).

Studies have shown that teeth with reduced but healthy periodontium can be orthodontically moved with no enhancement of periodontal destruction. In this case, orthodontic tooth movement acts as a stimulating factor of bone apposition when forces are maintained within physiological limits. However, enhanced periodontal destruction and connective tissue attachment loss were observed when teeth were moved into inflamed defects (Eliasson *et al.*, 1982; Reed *et al.*, 1985; Lindskog-Stokland *et al.*, 1993; Wennstrom *et al.*, 1993; Diedrich and Wehrbein, 1997; Vardimon *et al.*, 2001; Nemocovsky *et al.*, 2007).

In the present study, bioactive glass was used as the grafting material because a number of *in vivo* and *in vitro* studies have highlighted the potential for bioactive glass as an effective synthetic regenerative scaffold (Sculean *et al.*, 2002; Sculean *et al.*, 2005; Keles *et al.*, 2006). Moreover, bioabsorbable barrier membranes were selected to avoid several drawbacks that have been documented with non-absorbable barriers or with no barriers, including the risk of bacterial contamination on exposure of the membrane, and the need for a second reentry procedure, which may disrupt healing and create further bone and attachment loss (Eicholz *et al.*, 2000).

Materials and methods

Fifteen adult patients 25 to 48 years of age (10 female and 5 male) were included in this study. Each patient presented with a form of chronic periodontitis with malocclusion and evidence of at least three radiographic intrabony defects with associated probing depth of > 5.0 mm following initial non-surgical therapy. All the patients were non-smokers, systemically healthy and had no contraindications for periodontal therapy (Abramson, 1996). Pregnant females, as well as breast-feeding mothers and patients with history of periodontal surgery or antimicrobial therapy for the previous six months were excluded from this study. All patients were given information about the proposed treatment and were asked to sign a surgical consent form approved by the local ethics committee.

Initial periodontal therapy consisted of full mouth scaling and root planing utilizing both hand and ultrasonic instruments under local anesthesia. Four to six weeks following the initial phase of treatment, a reevaluation was performed to assess probing depth and clinical attachment level.

Measurements

All participants received an intraoral clinical status assessment, study casts and a complete radiographic evaluation (intraoral periapical, panoramic and cephalometric using digital radiology). All baseline clinical parameters were recorded the day of surgery. Measurements were made with a William's probe and recorded to the nearest millimeter at mid-facial, mid-lingual, mesial and distal line angles from the free gingival margin (FGM) to the base of the pocket to evaluate probing depth (PD) changes, and from the cementoenamel junction (CEJ) to the base of the defect (BD) to evaluate attachment level changes. Hard tissue measurements were obtained as follows: bone density (BD) was assessed using the DBS-Win software, which is a part of the recently introduced Vista scan system. The mean gray value in each region of interest was calculated (256 gray levels of color resolution) by assigning the gray value (0) to black, and the value 256 to white (Yokota *et al.*, 1994). To measure bone density, three successive parallel lines were plotted to cover the surface area of the defect. Then the gray levels at certain points on the lines were recorded. The mean values of those measurements represent the defect (*Figure 1*). To measure bone fill, we plotted a line from the crest of the alveolar ridge (as a reference point) to the base of defect (*Figure 2*).

Figure 1. Densiometric radiographic measurement.

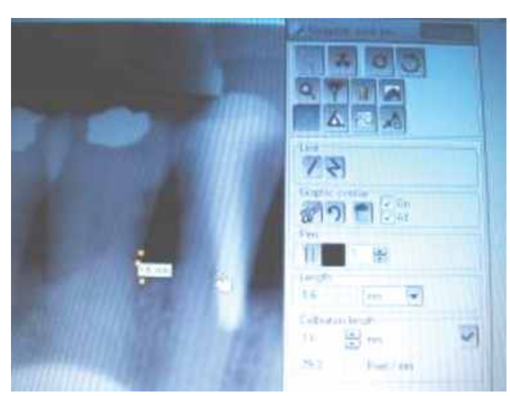


Figure 2. Linear radiographic measurement.

Figure 3. Periodontal probe showing 3 mm intrabony defect

Figure 4. Flap reflection and removal of granulation tissue from the defect.

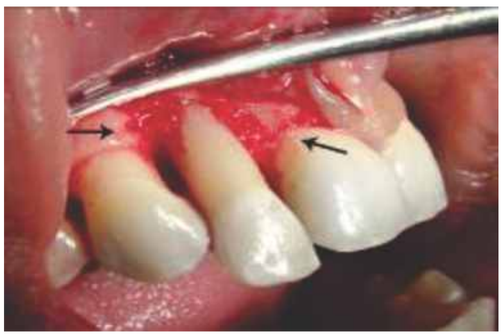


Figure 5. Bioglass was compressed into the intrabony defects.

Figure 6. Biocollagen membrane was placed over the defect and sutured with a sling suture.

Figure 7. The flap was sutured by using OOO silk suture to cover both bone graft and membrane.

Surgical procedures

Local anaesthesia (2% lidocaine containing 1:100,000 epinephrine) was utilized followed by intrasulcular incision. Full thickness flaps were elevated from both the buccal and the lingual aspects. All granulation tissues were removed from the defects. The 3- or 2-wall defects included in the study were those that were determined after flap reflection. The root surfaces were thoroughly debrided with hand and ultrasonic instruments (*Figure 3 and 4*). Root conditioning was applied using tetracycline solution for 3 minutes (Darhous *et al.*, 1995). The wound was rinsed several times with sterile saline solution. In all groups, the defects were filled with a bioactive glass (Bio-Glass: surface activated resorbable bioactive glass, manufactured in Egypt and distributed by Excellence Pharma Inc). The bone graft was mixed with sterile saline solution to obtain a sandy consistency. The resultant coagulum was transferred to the bone defects with a sterile amalgam carrier and compressed by manual pressure with a sterile condenser (*Figure 5*).

The collagen membrane (Biocollagen, Bioteck S.r.l Fermi, Arcugraro VI, Italy) was trimmed and adjusted to cover the defect and at least 2-3 mm of the surrounding bone. The coronal portion of the barrier was tightened and sutured on the root with resorbable sling suture (*Figure 6*). The flap was placed at the original presurgical levels and was sutured using vertical mattress sutures (*Figure 7*).

The patients were treated using the segmented arch technique to change the inclination of extruded, malaligned and migrated teeth. The forces used were

Before **After**

A **B**

Before **After**

C **D**

Figure 8. Clinical case presentation. A: Patients with periodontitis and crowding of upper and lower teeth with maxillary protrusion. B: After 12 months of treatment realignment of anterior teeth with correctable overjet. C: Patient with periodontitis, spacing between maxillary teeth and maxillary protrusion. D: After 12 months of treatment with correctable overjet and overbite and treatment of spacing.

light and continuous, about 10 to 15 g per tooth, depending on the amount of the periodontal support. The anchorage consisted of labial arch and two stainless-steel segments connecting posterior teeth. Titanium arch wires number 7 were used in the treatment protocol.

The orthodontic tooth movement was applied towards all the treated defects. The tooth movement in Group I was initiated immediately after finishing the periodontal surgery. In Group II, tooth movement was applied two months after periodontal treatment. Orthodontic tooth movement was not applied to Group III.

All patients included in the study were instructed to rinse twice daily for two minutes for two weeks after surgery with 0.12% chlorhexidine gluconate (Antiseptal, Kahira Co. for Pharm. And Chem., IND Cairo-ARE) and not to brush the treated area for the first two weeks. Systemic antibiotic therapy was prescribed: doxycycline hyclate, 100 mg every 12 hours for 10 days (Doxymycin, Nile Co. for Pharm and Chem. IND. Cairo-ARE) (Yukna *et al.*, 2001, 2002; Ogihara and Marks, 2002; and Cortellini and Tonetti, 2005). Recall appointments were carried out every week for the first month and then monthly for professional prophylaxis and oral hygiene reinforcement.

Statistical analysis

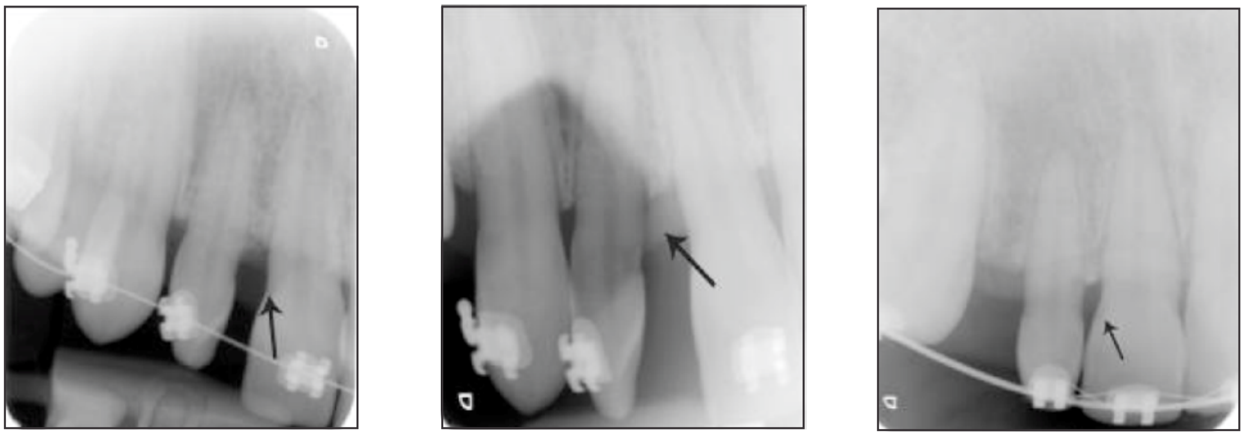
Data were presented as means and standard deviation (SD) values. Student's *t*-test was used to compare between means of the two groups. Paired *t*-tests were used to study the changes by time in each group. The significance level was set as $p \leq 0.05$. Standard analysis was performed with SPSS 16.0® (statistical package for scientific studies, SPSS Inc. Chicago, IL) for Windows.

Results

All 15 patients completed treatment and had no adverse reactions to therapy. Healing was uneventful in the 45 sites involved in this study.

Clinical parameters - probing depth

As shown in *Table 1* and *Figure 10*, the mean PD reduction in the three groups was recorded. With immediate application of orthodontic tooth movement (Group I), there was a reduction in PD measurements of 43.7% and 69.7% at 6 and 12 months, respectively. The mean percent change in PD between 6 and 12 months was 46%. With delayed orthodontic tooth movement (Group II), there was a decrease in PD by 40.8% and 62.4% at 6 and 12 months, respectively, compared to the baseline measurements. The mean



A B C

Figure 9. Radiographic case presentation. (A) Preoperative periapical radiograph showing 5 mm intrabony defect on the mesial surface of the upper left lateral incisior. (B) Six months postoperatively showing the same case with 3 mm defect fill record. (C) Twelve months postoperatively showing the same case with complete defect fill and adjustment of upper left lateral incisor.

Table 1. The means, standard deviations (SD), results of ANOVA and Duncan's tests for comparison of percentage decrease in PD among the three groups

Group	**Group I**		**Group II**		**Group III**		***p*-value**
Period	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	
	43.7	9.9	40.8	9.8	45.3	12.9	NS
Base line – 12 months	69.7	9.8	62.4	10.8	61.4	10.8	NS
6 months – 12 months	46	14.4	37.1	12.1	33.8	15.8	NS

Table 2. The means, standard deviations (SD), results of ANOVA and Duncan's tests for comparison of CAL among the three groups

Group	**Group I**		**Group II**		**Group III**		***p*-value**
Period	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	
Baseline – 6 months	42.7	13.2	43.3	23.9	47.9	13.2	NS
Baseline – 12 months	67.8	13.5	64.7	18.7	73.7	11.2	NS
6 – 12 months	44.8	14.5	37.8	17.7	51.1	18.3	NS

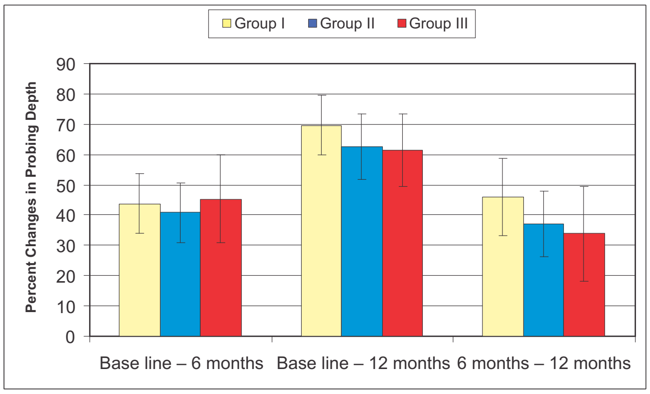


Figure 10. The mean percent changes in probing depth in Groups I, II and III during the study period.

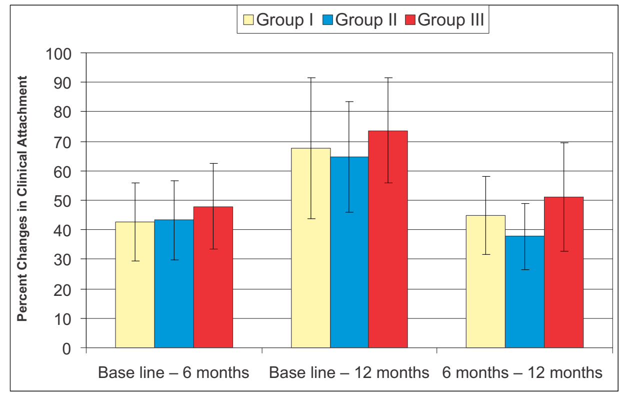


Figure 11. The mean percent changes in clinical attachment level in Groups I, II and III during the study period.

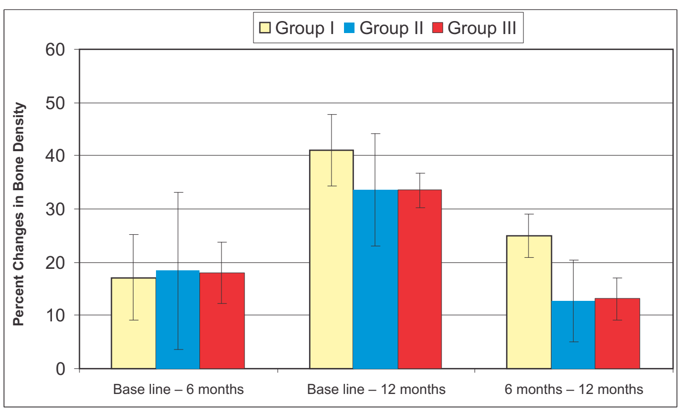


Figure 12. The mean percent change in bone density in Groups I, II and III.

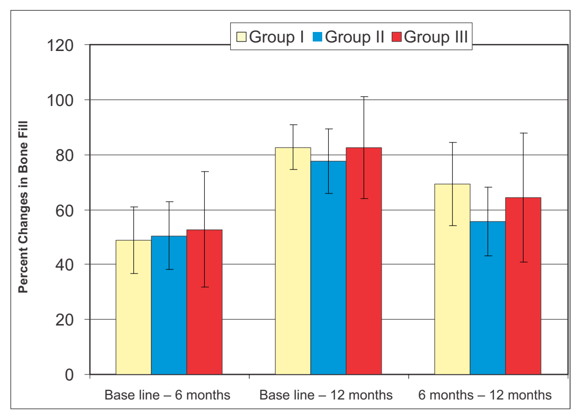


Figure 13. The mean percent change in bone fill in Groups I, II and III.

percent decrease in PD between 6 and 12 months was 37.1%. With no orthodontic tooth movement (Group III), there was a reduction in PD by 45.3% and 61.4% at 6 and 12 months. Statistical analysis regarding mean percent change in PD showed that there was no statistically significant difference among the three groups through all periods. However, the groups in which orthodontic tooth movement were combined with periodontal regenerative therapy (Groups I and II) showed greater reduction in PD than the group treated with periodontal regenerative therapy alone (Group III). In addition, immediate application of orthodontic tooth movement (Group I) showed the maximum reduction in mean PD measurements.

Table 2 and *Figure 11* show the mean percent change in clinical attachment level from baseline with immediate application tooth movement (Group I) was 42.7% and 67.8% at 6 and 12 months. With delayed application of orthodontic tooth movement (Group II), the mean percent change in CAL was 43.3% and 64.7% at 6 and 12 months, respectively. With no orthodontic tooth movement (Group III), the baseline

Table 3. The means, standard deviations (SD), results of ANOVA and Duncan's tests for comparison of percentage increase in bone density among the three groups.)

Group	Group I		Group II		Group III		*p*-value
Period	Mean	SD	Mean	SD	Mean	SD	
Baseline – 6 months	17.1	8.1	18.4	6.8	18	4.1	NS
Baseline – 12 months	41 [a]	14.8	33.6 [b]	10.5	33.5 [b]	7.6	HS
6 – 12 months	24.9 [a]	5.8	12.7 [b]	3.2	13.1 [b]	4	HS

[a]Greatest percent change; [b]lower percent change

Table 4. The means, standard deviations (SD), results of ANOVA and Duncan's tests for comparison of bone fill among the three groups

Group	Group I		Group II		Group III		*p*-value
Period	Mean	SD	Mean	SD	Mean	SD	
Baseline – 6 months	49	12.1	50.5	8	52.8	15.1	NS
Baseline – 12 months	82.7	12.4	77.6	11.7	82.4	12.5	NS
6 – 12 months	69.2	20.9	55.8	18.6	64.4	23.5	NS

Discussion

The present study was employed to evaluate osseous defects clinically and radiographically when treated with combined orthodontic/regenerative therapy at different times of initiation of orthodontic tooth movement. The concept of combining orthodontic tooth movement with regenerative periodontal therapy is based on the assumption that regenerative procedures could be enhanced by orthodontic tooth movement (Nemcovsky *et al.*, 1996; Diedrich, 1997; Stefania *et al.*, 2000; Vardimon *et al.*, 2001; Ogihara and Marks, 2002; Stefania *et al.*, 2002; Ogihara and Marks, 2006; Maeda *et al.*, 2007).

Previously, several authors have reported the use of combined orthodontic regenerative therapy in the treatment of osseous defects. Determination of the best time to initiate the orthodontic tooth movement has not been discussed. Therefore, to our knowledge, it appears that this is the first report to evaluate the effect of different times of initiation of orthodontic tooth movement. Immediate application of orthodontic tooth movement with regenerative surgery in the treatment of intraosseous defects was for the first time selected. In this study, selection of the period of two months (60 days) for initiation of orthodontic tooth movement in Group II was based upon several studies that evaluated periodontal regeneration from 60 to 90 days after regenerative therapy and noted advanced healing of the periodontal tissues (Caffesse *et al.*, 1993; Araujo *et al.*, 2001; Ogihara and Marks, 2006).

This study shows that orthodontic tooth movement, when applied with a certain duration and magnitude, could be used as an adjunct factor for periodontal regeneration. It was also noticed that the presence of an extrinsic mechanical stimulus causes bone repair. The osteoclastic – osteoblastic coupling mechanism required for the bone apposition/ resorption response corresponds with the results of this study. Osteoclastic recruitment is most likely to occur not only as a sign for increased resorption activity, but also it could act as a signal for bone deposition at a site in close proximity to the resorption activity (Vardimon *et al.*, 2001).

In the present study, bioactive glass was used as the grafting material because a number of *in vivo* and *in vitro* studies have highlighted its potential as an effective synthetic regenerative scaffold (Sculean *et al.*, 2002; Sculean *et al.*, 2005; Keles *et al.*, 2006). In addition, the collagen membrane was especially selected in this study owing to the following properties: it is chemotactic to fibroblasts, it provides a scaffold for periodontal ligament cell migration, it is a weak immunogen, and it can be easily manipulated and adapted (Yaffe *et al.*, 1984; Mattson *et al.*, 1999; Michele, 2002).

In this study, the groups in which orthodontic regenerative therapy was applied showed greater reduction in probing depth and more gain in clinical attachment level. These results were in agreement with Liou and Huang (1998), Cardaropoli *et al.* (2001), Nemcovsky *et al.* (2004) and Nemcovsky *et al.* (2007). However, others did not find this effect (Polson *et al.*, 1984; Wennstrom *et al.*, 1993). This may be attributed to failure of elimination of plaque-induced lesions prior to initiation of orthodontic therapy. Moreover, other factors responsible for this effect might be the lack of using periodontal regenerative surgeries and the improper oral hygiene measures during the course of orthodontic treatment.

The Vista scan system using the DBS-win software with a phosphor-image plate can produce images following exposure. This requires lower radiation dose levels and has the capability of computer image analysis. DBS-win software provides a special software program that enables accurate linear bone height measurements and bone density measurements around each tooth involved (Yalcinkaya *et al.*, 2006).

Regarding the amount of bone fill, it was significantly increased in all groups through the study period. Upon comparing the three groups, there was a greater increase in bone fill in Group I (in which immediate orthodontic tooth movement was applied) during the study period than in the other groups.

There was a significant increase in bone density in the three groups at the end of the study period. The groups in which the combined orthodontic regenerative therapy was used demonstrated more increase in bone density than the group in which periodontal regenerative surgery was used alone. In addition, Group I showed the highest increase in bone density at the end of the study period.

In conclusion, the combined orthodontic regenerative therapy resulted in favorable clinical and radiographic outcomes. It suggests that combined orthodontic/regenerative therapy might be a good option for achieving periodontal regeneration. Defects in which immediate orthodontic tooth movement was applied (Group I) demonstrated superior results than defects in which delayed orthodontic tooth movement was applied (Group II). Both groups showed more favorable results than Group III (defects treated with regenerative surgery alone).

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